

# Versatile Subwavelength Grating Microring Resonators for Label-Free and Multiplex-Compatible Detection of Respiratory Viruses

Wanxin LI<sup>1†</sup>, Rui LI<sup>1†</sup>, Jiewen LI<sup>1</sup>, Fatao CHEN<sup>1</sup>, Zheng CAO<sup>1</sup>,  
Yongkang DONG<sup>1</sup>, Yi ZOU<sup>2\*</sup>, and Xiaochuan XU<sup>1,3\*</sup>

<sup>1</sup>National Key Laboratory of Laser Spatial Information; Guangdong Provincial Key Laboratory of Integrated Photonic-Electronic Chip; Guangdong Provincial Key Laboratory of Aerospace Communication and Networking Technology, Harbin Institute of Technology, Shenzhen 518055, China

<sup>2</sup>School of Information Science and Technology, ShanghaiTech University, Shanghai 201210, China

<sup>3</sup>Particle Optics Technology Co., Ltd., Yantai 264006, China

<sup>†</sup>These authors contributed equally to this work and should be considered co-first authors

\*Corresponding authors: Yi ZOU and

E-mails: zouyi@shanghaitech.edu.cn and

Xiaochuan XU

xuxiaochuan@hit.edu.cn

**Abstract:** Respiratory viruses, such as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A (H1N1), and respiratory syncytial virus (RSV), remain major public health threats due to overlapping clinical symptoms and the limited speed, sensitivity, and multiplexing capacity of conventional diagnostic methods. Here, we present a label-free optical biosensing platform based on subwavelength grating microring resonators (SGMRRs) for the sensitive and specific detection of viral antigens. The sensor surface is functionalized with antibodies against three representative viral proteins, enabling quantitative detection via resonance wavelength shifts upon antigen binding. The platform achieves the refractive index limit of detection (LoD) of  $1.25 \times 10^{-4}$  RIU and enables the detection of the SARS-CoV-2 spike protein at 100 pg/mL, the H1N1 nucleoprotein at 10 pg/mL, and the RSV F-trimer protein at 10 pg/mL. The compact SGMRR design readily supports multiplexed integration through multi-ring or multi-channel architectures, highlighting its potential as a scalable and high-performance platform for rapid, quantitative, and point-of-care viral diagnostics.

**Keywords:** Silicon photonics; subwavelength grating microring; label-free biosensing; respiratory viruses

Citation: Wanxin LI, Rui LI, Jiewen LI, Fatao CHEN, Zheng CAO, Yongkang DONG, *et al.*, “Versatile Subwavelength Grating Microring Resonators for Label-Free and Multiplex-Compatible Detection of Respiratory Viruses,” *Photonic Sensors*, 2026, 16(3): 9560018.

## 1. Introduction

Respiratory viruses (RVs) remain a pressing global health concern, causing four million deaths

annually [1]. Early-stage infections often present with mild and nonspecific symptoms, yet they can rapidly progress to life-threatening conditions. The COVID-19 pandemic has further exposed critical

Received: 5 July 2025 / Revised: 14 November 2025

©The author(s) 2026. Published by Tsinghua University Press. This is an open access article under the Creative Commons Attribution 4.0 International License

(<http://creativecommons.org/licenses/by/4.0/>)

DOI: 10.26599/PhoS.2026.9560018

Article type: Research article



清华大学出版社  
Tsinghua University Press

SciOpen

vulnerabilities in global outbreak responses, particularly the challenge of differentiating viral etiologies based solely on overlapping clinical symptoms [2]. Pathogens, such as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus (H1N1), and respiratory syncytial virus (RSV), induce nearly indistinguishable manifestations – including cough, fever, and chest pain – complicating timely and accurate diagnosis [3–5]. Accurate identification of viral etiology is therefore essential for guiding clinical decision-making, optimizing antiviral therapy, and coordinating public health responses [5, 6]. Although gold-standard diagnostic methods, such as real-time reverse transcription polymerase chain reaction (RT-PCR) [7, 8] and enzyme-linked immunosorbent assay (ELISA) [9], offer excellent sensitivity, they suffer from limitations, including time-consuming procedures, complex instrumentation, and the need for skilled personnel. Lateral flow immunoassays (LFIAs), were widely adopted as antigen rapid diagnostic tests (Ag-RDTs), offering rapid and user-friendly operation, but relatively poor sensitivity and an elevated limit of detection (LoD) constrain their diagnostic applicability [10]. Consequently, there remains a critical need for diagnostic platforms that combine high sensitivity, rapid response, multiplexing capability, and operational simplicity to enable effective point-of-care testing (POCT) [11, 12].

Optical lab-on-a-chip (LOC) technologies emerged as promising solutions for POCT, offering rapid analysis, kinetic detection, user-friendly operation, and cost-effectiveness [13–16]. Among integrated photonic circuits (PICs) devices, microring resonators [17–21], Mach-Zehnder interferometers (MZI) [22–26], and photonic crystal cavities [27] stand out for their label-free operation, high sensitivity, complementary metal oxide semiconductor (CMOS) compatibility, and real-time monitoring capabilities [28]. Notably, microring resonators combine a compact footprint with

excellent optical performance, enabling scalable on-chip integration and the development of multiplexed sensor arrays, which are crucial for the simultaneous detection of multiple respiratory pathogens. However, the sensitivity of conventional evanescent-wave microring sensors decreases significantly with the increasing thickness of surface layers [29]. These layers, including oxide coatings, immobilized probe proteins, and target biomolecules, typically range from a few to several tens of nanometers, within which the evanescent field rapidly decays before effectively interacting with the analyte. Integration with subwavelength grating (SWG) structures allows microrings to overcome this limitation, achieving LoDs as low as the nanomolar to picomolar range [29–31].

In this work, we present a label-free optical biosensing platform based on subwavelength grating microring resonators (SGMRRs) for the sensitive and specific detection of respiratory viral antigens. The platform demonstrates a bulk refractive index LoD of  $1.25 \times 10^{-4}$  RIU. By combining high sensitivity with molecular specificity through antigen-antibody interactions, the system reliably detects viral proteins at concentrations as low as 100 pg/mL for SARS-CoV-2 and 10 pg/mL for H1N1 and RSV. The compact SGMRR design has potential for multiplexed detection by integrating individually functionalized microrings within shared or parallel fluidic channels, allowing simultaneous analysis of multiple viral antigens. These results underscore its scalability and utility for rapid, on-chip viral diagnostics, and public health monitoring.

## 2. Sensing mechanism and optical characterization of the SGMRR platform

Figure 1(a) schematically illustrates the SGMRR-based biosensing platform for detecting respiratory viral antigens. Target samples potentially containing SARS-CoV-2, H1N1, or RSV antigens – which complicate the diagnosis due to overlapping

symptoms – are introduced over sensor surfaces functionalized with specific antibodies. In this configuration, the sensing mechanism relies on the resonance condition of the microring resonator, expressed as

$$m\lambda_{\text{res}} = n_{\text{eff}}(\lambda_{\text{res}})L \quad (1)$$

where  $m$  is the resonance order,  $\lambda_{\text{res}}$  is the resonance wavelength,  $L$  is the optical path length of the ring, and  $n_{\text{eff}}$  is the wavelength-dependent effective

refractive index of the SWG waveguide. Antigen-antibody interactions perturb the refractive index near the waveguide surface, leading to a change in  $n_{\text{eff}}$  and a measurable resonance wavelength shift. The equivalent refractive indices of the SWG waveguide for electric fields polarized parallel ( $n_{\parallel}$ ) and perpendicular ( $n_{\perp}$ ) to the periodic interfaces, can be approximated using the Rytov formula [32]:

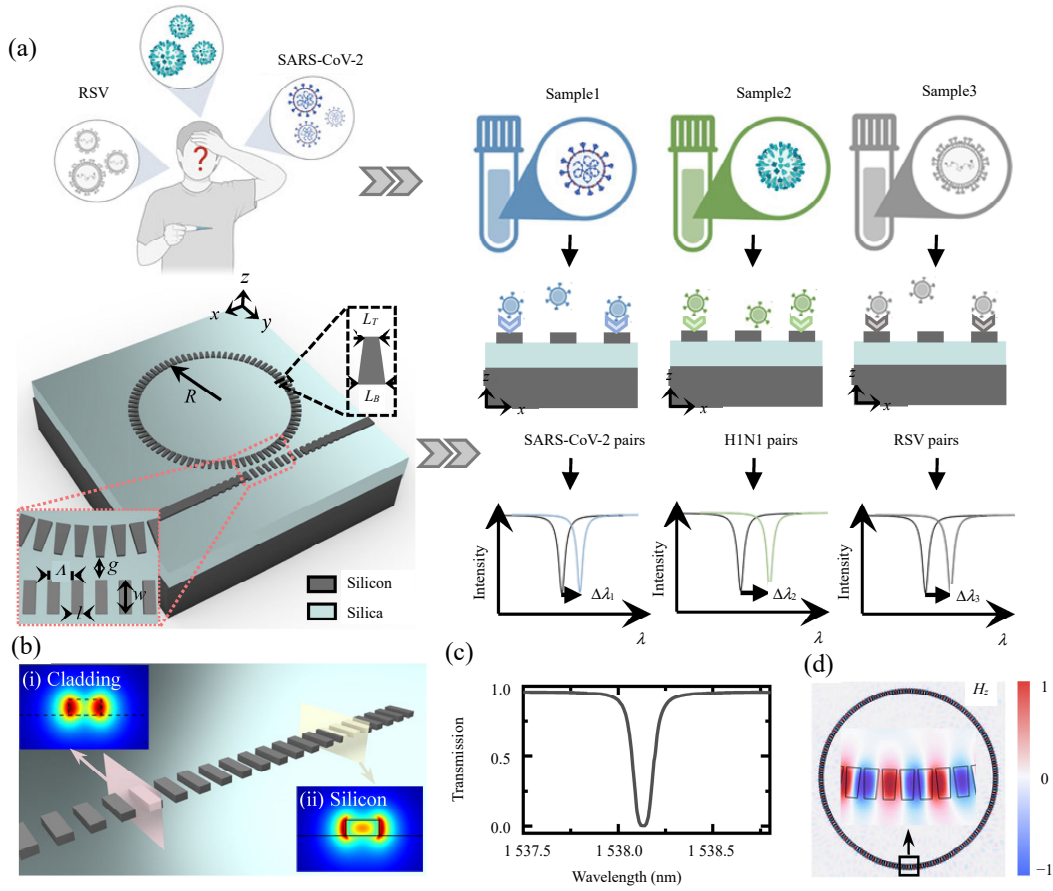


Fig. 1 Concept of SGMRR-based optical biosensing for respiratory virus detection: (a) schematic illustration of SGMRRs functionalized for label-free detection of viral antigens associated with SARS-CoV-2, H1N1, and RSV via antigen-antibody recognition. The SGMRR structure parameters:  $R=10\ \mu\text{m}$ ,  $A=300\ \text{nm}$ ,  $w=500\ \text{nm}$ ,  $g=0.5\ \mu\text{m}$ ,  $L_T=190\ \text{nm}$ ,  $L_B=240\ \text{nm}$ , and  $l=180\ \text{nm}$ , (b) simulated  $|E|$ -field distribution across the SWG waveguide cross section, showing the field in the silicon and cladding regions, (c) the transmission spectrum of the SGMRR, and (d) the magnetic field distribution ( $H_z$ ) of the SGMRR.

$$n_{\parallel}^2 \approx fn_{\text{silicon}}^2 + (1-f)n_{\text{cladding}}^2 \quad (2)$$

$$n_{\perp}^2 \approx fn_{\text{silicon}}^{-2} + (1-f)n_{\text{cladding}}^{-2} \quad (3)$$

where  $f$  is the silicon duty cycle,  $n_{\text{si}}$  and  $n_{\text{cladding}}$  are the refractive indexes of the silicon and cladding, respectively. Figure 1(b) shows the simulated electric-field distribution ( $|E|$ ) of the SWG waveguide. The optical mode is confined within the

high-index silicon pillars, while part of the field penetrates into the low-index gaps and cladding, thereby enlarging the effective sensing region and enhancing the mode-analyte interaction. The bulk sensitivity  $S_{\text{bulk}}$  is defined as the slope of the peak shift versus change in  $n_{\text{cladding}}$ . According to (1),  $S_{\text{bulk}}$  can be expressed as

$$S_{\text{bulk}} = \frac{\Delta\lambda}{\Delta n_{\text{cladding}}} = \frac{\lambda_{\text{res}}}{n_g} \frac{\partial n_{\text{eff}}}{\partial n_{\text{cladding}}} \quad (4)$$

where  $n_g = n_{\text{eff}} - \lambda \partial n_{\text{eff}} / \partial \lambda$  denotes the group index. The designed SGMRR adopts a typical all-pass configuration with a radius of 10  $\mu\text{m}$  and is side-coupled to a subwavelength-grating bus waveguide. The period of the SWG structure is 300 nm, which can effectively suppress diffraction ( $\lambda < \lambda_0 / 2n_{\text{eff}}$ ) [32]. Optimized trapezoidal silicon pillars are employed to reduce the bend loss [33], while key grating parameters – including the duty cycle, period, and geometry – can be tuned to enhance sensing performance. Figures 1(c) and 1(d) present the simulated transmission spectrum and resonant-mode magnetic-field distribution of the SGMRR, respectively. Benefiting from the enhanced field overlap and compact on-chip architecture, the proposed SGMRR platform is well-suited for highly sensitive and potentially multiplexed detection of respiratory viral antigens, with the specificity defined by the functionalized antibodies.

To implement the proposed SGMRR sensor and evaluate its optical response, devices are fabricated on a silicon-on-insulator (SOI) wafer consisting of a 220 nm-thick crystalline silicon layer atop a 2  $\mu\text{m}$  buried oxide ( $\text{SiO}_2$ ) layer. A diluted ZEP520A resist is spin-coated onto a piranha-cleaned chip and baked at 180  $^\circ\text{C}$  for 20 minutes prior to electron beam lithography (nB5, NanoBeam, UK), enabling high-resolution nanostructure patterning. The patterns are subsequently transferred into the silicon layer via inductively coupled plasma (ICP) etching. To protect the structures during bioassays and improve surface silanization, a 10 nm-thick silica layer is deposited using plasma-enhanced chemical vapor deposition (PECVD). Figure 2(a) presents scanning electron microscope (SEM) images confirming the successful fabrication of the grating structures, with insets (i) and (ii) highlighting the mode converter and coupling region, respectively. Following the fabrication, an automated optical

system integrated with a microfluidic system, as illustrated in Fig. 2(b), is employed for SGMRR sensor characterization. Light from a tunable laser (TSL-550, Santec, Japan) passes through a polarization controller and is vertically coupled into and out of the chip via grating couplers [34], with the position of the coupling fibers adjusted using an alignment stage. The output light is split into two paths: one directed to an optical power meter (MPM-210H, Santec, Japan) for real-time feedback control and coupling optimization, and the other to a photodetector connected to an automated data acquisition and analysis system. A temperature controller (AP-TEC-PRO, Apico, China) stabilizes the chip at 25  $^\circ\text{C}$  to minimize the thermal drift and ensure signal consistency. The microfluidic setup adopts a three-layer sandwich structure, consisting of a top cover, a middle layer with fluidic channels, and a bottom substrate for chip mounting. A syringe pump delivers solutions through the microchannels in a stable and controlled manner. The system incorporates parallel microfluidic paths designed to enable multiplexed or simultaneous detection. Within each channel, spatially distributed microrings can be individually functionalized with specific antibodies, thereby allowing concurrent detection of multiple targets, as illustrated in the inset. To evaluate bulk refractive index sensitivity, NaCl solutions ranging from 0% to 10% (in 2% increments) are sequentially introduced, and the resulting resonance shifts are recorded in real time, as shown in Fig. 2(c). A linear red shift is observed with the increasing concentration, yielding the bulk sensitivity of 350.49 nm/RIU from the linear fit shown in Fig. 2(d). The LoD is defined as  $3\sigma/S$ , where  $\sigma$  is the standard deviation of the resonance shift and  $S$  is the sensitivity. To ensure a conservative estimate, the highest observed standard deviation of 14.6 pm (within the range of 5.87 pm–14.6 pm) is used in the calculation, yielding the LoD of  $1.25 \times 10^{-4}$  RIU, as shown in the inset.

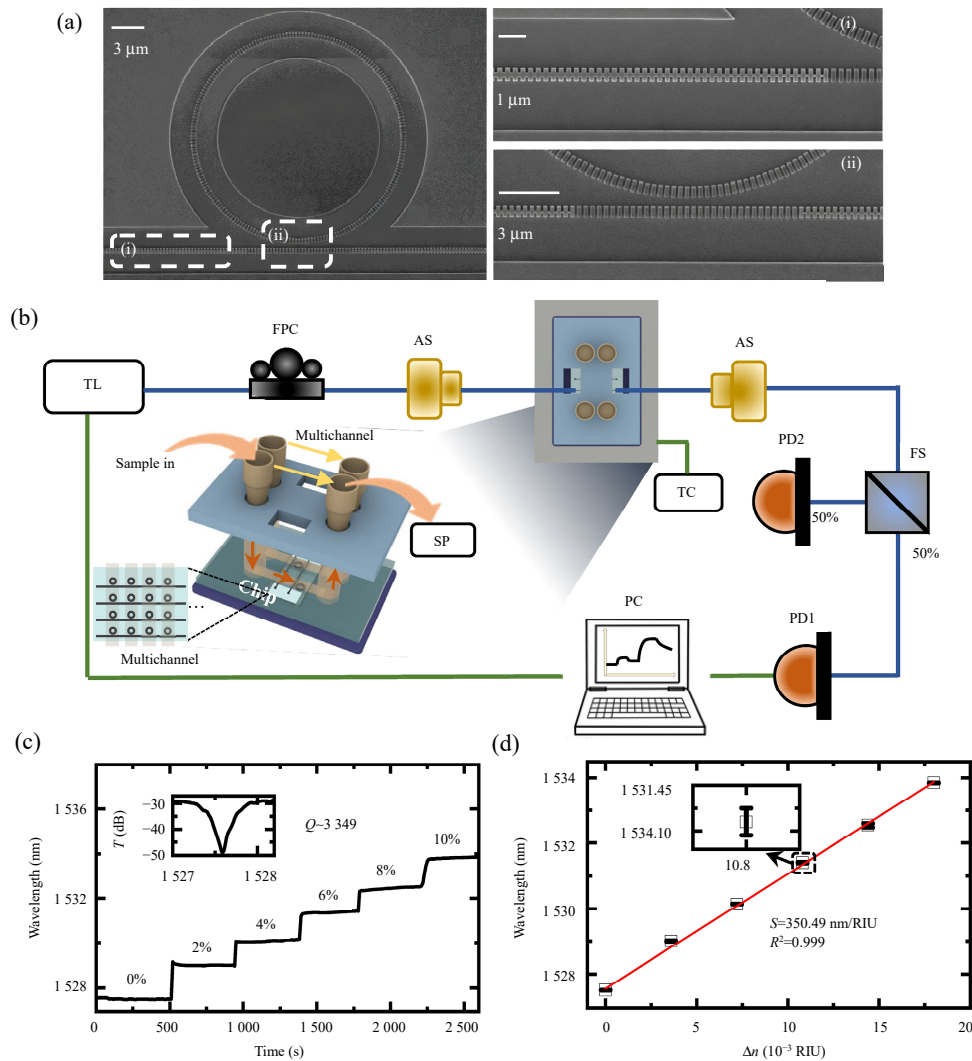


Fig. 2 Fabrication, experimental setup, and bulk refractive index sensing of the SGMRR sensor: (a) SEM images of the fabricated SGMRR [insets: (i) the mode converter and (ii) the coupling region], (b) the schematic of the optical measurement system integrated with a microfluidic system (TL: tunable laser; FPC: fiber polarization controller; AS: alignment stage; FS: fiber splitter; PD: photodetector; PC: personal computer; SP: syringe pump; TC: temperature controller), (c) resonance wavelength shifts in response to NaCl solutions with varying concentrations (inset: the transmission spectrum of the SGMRR), and (d) the linear fit of resonance wavelength shift versus the refractive index, yielding the bulk sensitivity of 350.49 nm/RIU (inset: the maximum observed standard deviation of 14.6 pm, used to conservatively estimate the LoD).

### 3. Biosensing

#### 3.1 Surface functionalization

Building on the demonstrated refractive index sensitivity, the SGMRR sensor is further functionalized for specific viral antigen detection following a standardized protocol, as illustrated in Fig. 3. A self-assembled monolayer of 3-aminopropyltriethoxysilane (APTES, Innochem, China) is first formed on the sensor surface to introduce amine groups ( $-\text{NH}_2$ ), followed by the thermal treatment at 120 °C for 1 hour to stabilize the silane layer. Glutaraldehyde (GA, Aladdin,

China) is subsequently applied to introduce aldehyde groups for covalent attachment of amine-terminated probe proteins. Specific antibodies are immobilized by injecting the antibody solutions at a flow rate of 20  $\mu\text{L}/\text{min}$  using a syringe pump. To suppress non-specific adsorption, the surface is subsequently blocked with the 1% bovine serum albumin (BSA, ABCone, China) in phosphate-buffered saline (PBS, Psaitong, China). Finally, viral antigens at concentrations of 10  $\text{pg}/\text{mL}$  and 100  $\text{pg}/\text{mL}$  are introduced to evaluate the sensor's detection performance.

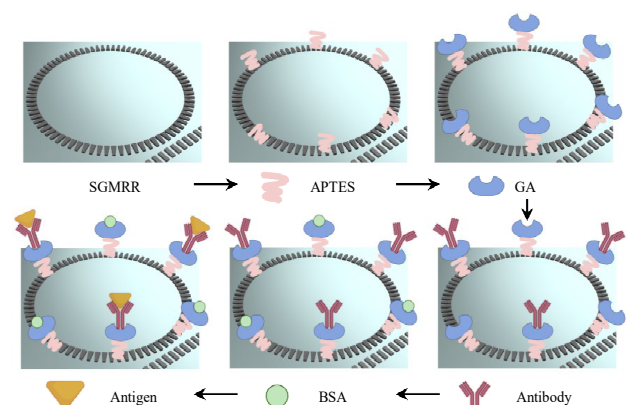


Fig. 3 Surface functionalization strategy for detection of respiratory virus antigens.

To demonstrate molecular specificity, three antigen-antibody pairs are used for detecting SARS-CoV-2, H1N1, and RSV. For SARS-CoV-2 detection, a spike (S) protein antibody (40150-D003, Sino Biological, China) and a recombinant spike S1-His protein (40591-V08H, Sino Biological,

China) are employed, leveraging the spike glycoprotein's structural accessibility and the critical role in the host cell entry, which make it highly immunogenic and readily detectable [35–37]. For H1N1 detection, a pan-influenza A nucleoprotein (NP) antibody (40205-R063, Sino Biological, China) and recombinant H1N1 NP (40205-V08B, Sino Biological, China) are selected, as the NP is highly conserved across influenza A subtypes and abundantly expressed during infection, making it an ideal biomarker for universal influenza diagnosis [38, 39]. For RSV detection, an anti-RSV fusion (F) antibody (DA091, Novoprotein, China) is paired with a prefusion-stabilized F-trimer protein (DRA230, Novoprotein, China), which retains native epitopes, such as the site Ø and site V, essential for immune recognition and typically masked in the postfusion state [40, 41].

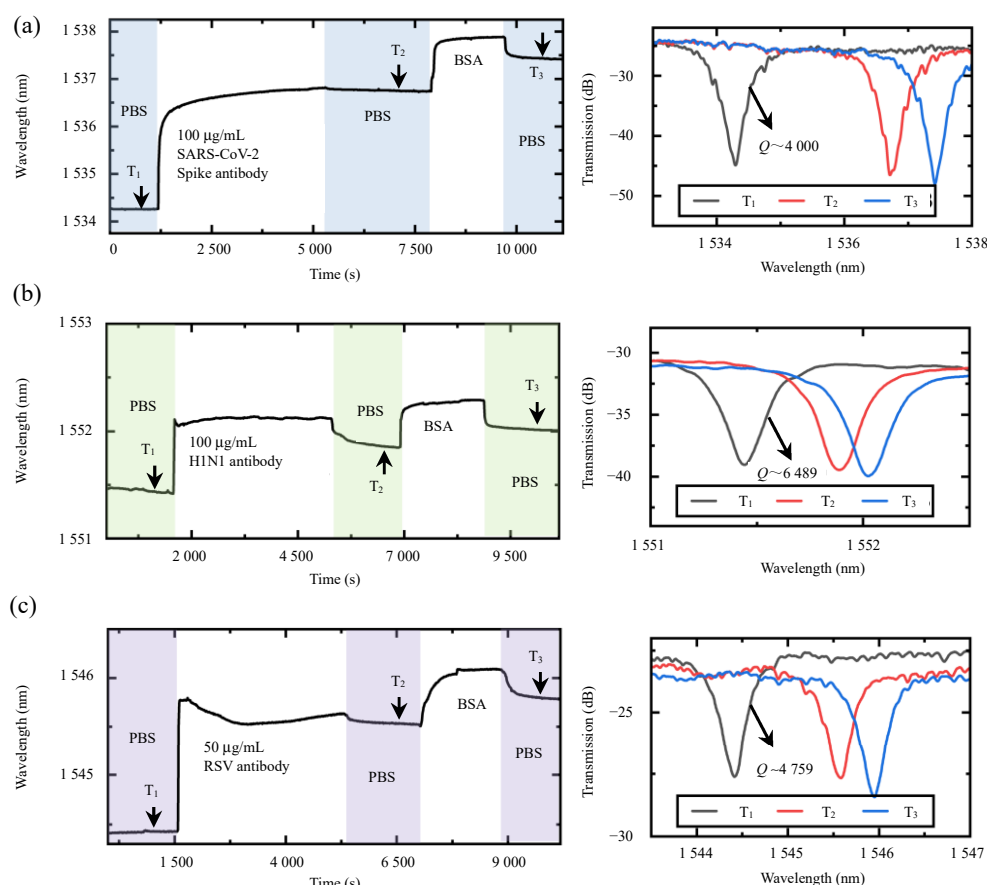


Fig. 4 Surface functionalization and antibody immobilization of SGMRRs: (a)–(c) time-resolved resonance wavelength shifts (left) and corresponding transmission spectra (right) at three equilibrium states: T<sub>1</sub> (baseline), T<sub>2</sub> (after antibody immobilization and PBS washing), and T<sub>3</sub> (after BSA blocking and PBS washing), for SARS-CoV-2 S, influenza A NP, and RSV F antibody systems, respectively.

After functionalization with the APTES and glutaraldehyde, the SGMRR sensor surfaces are consistently modified through antibody immobilization and the BSA blocking for three respiratory virus targets, with the PBS washing after each step to remove unbound biomolecules. As shown in Figs. 4(a)–4(c), each measurement includes time-resolved resonance shifts (left) and transmission spectra at three equilibrium states (right):  $T_1$  (baseline),  $T_2$  (after antibody immobilization and PBS washing), and  $T_3$  (after BSA blocking and PBS washing). All three antibodies induce distinct resonance shifts – an evident red shift upon immobilization followed by a slight blue shift after PBS washing – clearly confirming successful surface functionalization, despite variations in their detailed responses. The SARS-CoV-2 antibody produces a pronounced and stable red shift with only a slight blue shift after PBS washing, consistent with strong covalent attachment and limited desorption. Separately, RSV antibody injection exhibits a unique transient response – an initial rapid red shift followed by a gradual blue shift – before reaching equilibrium, likely caused by concentration gradients and dispersion effects during the solution exchange, where the injected solution initially increases the local refractive index before mixing with the residual PBS [42]. These variations are attributed to differences in the antibody size, coupling density, surface coverage, and interfacial interactions on the activated substrate, rather than differences in sensor performance. Subsequently, BSA blocking induces an additional red shift, and the following PBS washing results in a slight blue shift, indicating spectral stabilization at  $T_3$ . Cumulative resonance shifts measured at  $T_3$  are 3.17 nm, 0.57 nm, and 1.12 nm for SARS-CoV-2, influenza A, and RSV, respectively. Overall, the observed resonance behaviors confirm successful probe immobilization and establish a stable baseline for subsequent antigen detection.

### 3.2 Detection of various respiratory virus antigens

Figures 5(a)–5(c) illustrate the optical responses of SGMRRs functionalized with antibodies specific to the SARS-CoV-2 S protein, H1N1 NP, and RSV F protein, respectively. Each sensor is measured with two concentrations of viral antigens (10 pg/mL and 100 pg/mL) and results are presented in three formats: 1) time-resolved resonance shifts during antigen exposure and PBS washing, 2) transmission spectra at three equilibrium states ( $T_A$ : baseline before antigen exposure;  $T_B$ : after PBS washing following exposure to 10 pg/mL antigen;  $T_C$ : after PBS washing following exposure to 100 pg/mL antigen, and 3) averaged resonance shifts quantified during the final 10-minute equilibrium period. For SARS-CoV-2 detection shown in Fig. 5(a), no significant resonance shift is observed at 10 pg/mL, indicating that the refractive index perturbation is below the detection threshold. In contrast, exposure to 100 pg/mL antigen results in a pronounced red shift of 21.8 pm that stabilizes after PBS washing, confirming strong and specific binding. For the H1N1, a clear concentration-dependent response is observed, with average wavelength shifts of 2.36 pm at 10 pg/mL and 14.06 pm at 100 pg/mL, as shown in Fig. 5(b). A red shift followed by a slight reversal is observed during the 100 pg/mL injection, likely due to solution dispersion with residual PBS. In the case of the RSV [Fig. 5(c)], averaged wavelength shifts of 8 pm and 13.6 pm are obtained, with sharp transient perturbations during injection possibly caused by pump stroke fluctuations or microbubbles [42].

The comparative analysis across the three targets reveals that at 10 pg/mL, H1N1 and RSV antigens produce measurable responses, while the SARS-CoV-2 antigen remains below the detection threshold, likely due to differences in binding affinity, epitope accessibility, or conformational stability of the antigens. For instance, the prefusion-stabilized RSV F protein may expose

neutralizing epitopes more effectively, enhancing binding. In addition to biochemical factors, sensing performance is also affected by the initial optical characteristics of the SGMRRs. The measured  $Q$  factors prior to functionalization are 4 000, 6 829, and 4 759 for SGMRRs designated for SARS-CoV-2, influenza A, and RSV antibodies, respectively, with corresponding extinction ratios (ER) of 20 dB, 9 dB, and 8 dB. Differences in the  $Q$  factor and ER among SGMRRs primarily originate from fabrication-induced deviations that alter both the intrinsic loss and the coupling strength. According to the definition of the intrinsic LoD [ $i\text{LoD}=\lambda/(Q\times S)$ ],

where  $S$  is the sensitivity, and a higher  $Q$  enhances the theoretical sensitivity; however, this advantage is realized only when adequate coupling is maintained to ensure sufficient spectral contrast. Excessive coupling or optical loss compromises the ER and broadens the resonance, thereby diminishing the discernibility of wavelength shifts. Considering the additional scattering introduced by the subwavelength grating, the devices are therefore designed to operate in a slightly under-coupled regime, achieving a robust trade-off among sensitivity, spectral visibility, and fabrication tolerance.

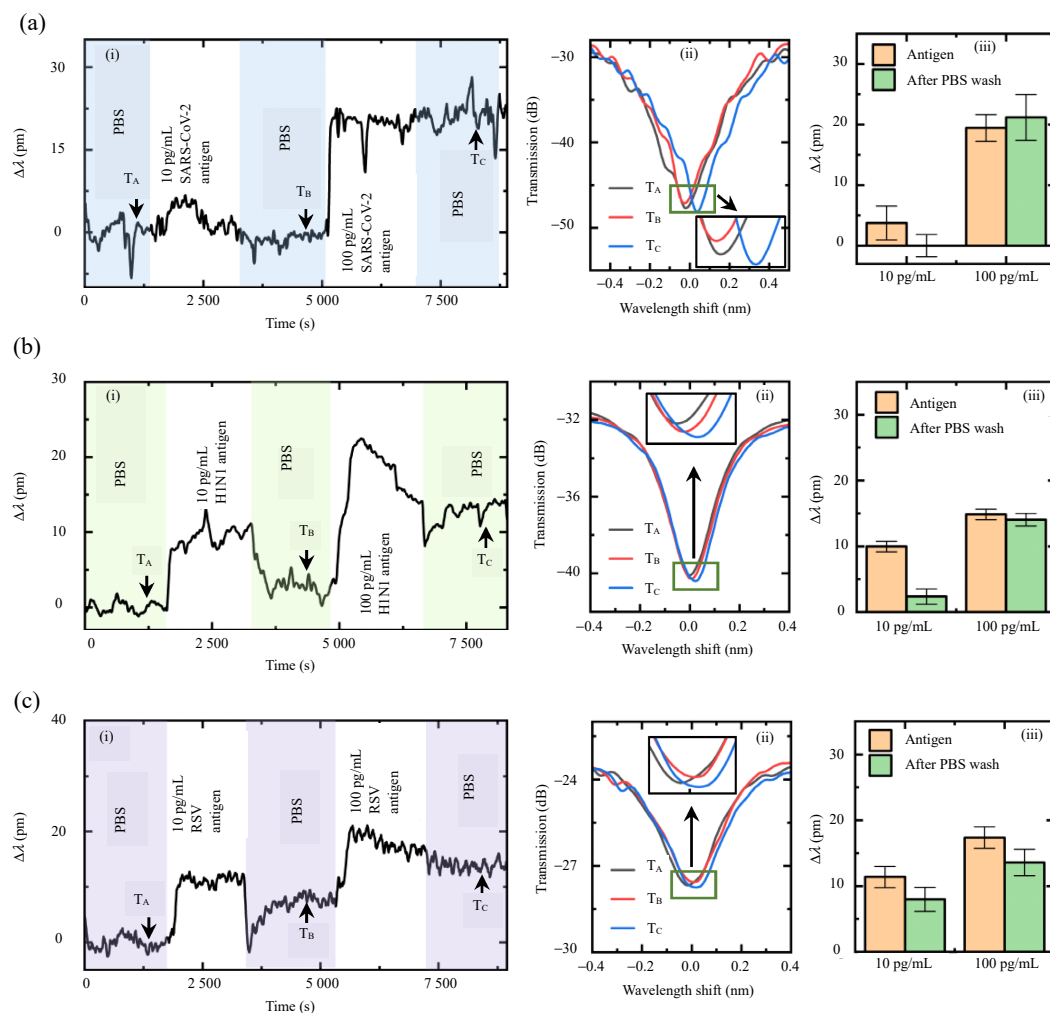


Fig. 5 Optical response of the SGMRR sensor to viral antigen binding: (a)–(c) optical response of SGMRRs functionalized with antibodies specific to the SARS-CoV-2 S protein, H1N1 NP, and RSV F protein, respectively. Each set includes: (i) time-resolved resonance shift during the antigen exposure and PBS washing; (ii) transmission spectra at three equilibrium states –  $T_A$  (baseline before antigen exposure),  $T_B$  (after PBS washing following 10 pg/mL antigen binding), and  $T_C$  (after PBS washing following 100 pg/mL antigen binding), with insets highlighting the corresponding spectral shifts; (iii) average resonance shifts during antigen binding and PBS washing in the final 10-minute equilibrium period.

#### 4. Discussion and conclusions

In this study, we present a label-free photonic sensing platform based on SGMRRs for multiplex-compatible detection of respiratory virus antigens. Leveraging the high sensitivity of SGMRRs, the platform reliably detects the SARS-CoV-2 spike protein at 100 pg/mL, the H1N1 nucleoprotein at 10 pg/mL, and the RSV F-trimer protein at 10 pg/mL.

To benchmark the sensing performance, Table 1 compares the proposed SGMRR platform with representative on-chip sensors reported for SARS-CoV-2, H1N1, and RSV detection. The listed devices include both interferometric and resonant architectures, enabling the direct comparison in the LoD, device footprint, and multiplexing compatibility. Interferometric sensors, such as MZIs, require millimeter-scale optical paths [24–26], which constrain the integration density and multiplexed operation. In contrast, resonant sensors, particularly microring resonators, feature compact footprints inherently suitable for multichannel detection. However, conventional strip-waveguide microrings rely on evanescent-field interaction, resulting in limited light-analyte coupling and moderate sensitivity [21].

The SGMRR preserves the compactness of microrings while introducing a subwavelength grating section that strengthens light-analyte interaction, thereby enhancing sensing efficiency and overall performance. The iLoD of  $1.3 \times 10^{-3}$  RIU in this work is marginally superior to that in [18], which is also based on an SWG structure, reflecting enhanced intrinsic light-matter interaction. However, the achievable bioassay LoD is still limited by detection-system factors, such as instrumental stability and noise. In addition, surface chemical properties can also influence the overall sensing performance. For instance, while the  $\sim 10$  nm SiO<sub>2</sub> passivation layer ensures surface-chemical robustness, it slightly reduces the overlap ( $\sim 3.5\%$ ) between the mode field and the surrounding analyte.

Further optimization of surface chemistry – such as improving antibody immobilization, refining blocking protocols, and minimizing nonspecific adsorption – could enhance the effective sensitivity. Additionally, recent studies have reported that the reflection-induced mode splitting in SGMRRs can facilitate the self-referenced configuration, leading to noise suppression [43].

The clinical relevance of the achieved sensing performance is evaluated. Based on the estimation reported in [44], the concentration of the SARS-CoV-2 spike protein in nasopharyngeal extraction buffers ranges from 50 pM to 7.8 nM (9 ng/mL–1.4  $\mu$ g/mL), indicating that our 100 pg/mL LoD lies well below the clinically relevant range, ensuring diagnostically meaningful sensitivity.

Although this work focuses on single-analyte detection, the SGMRR architecture inherently supports multiplexed sensing. Parallel assays can be realized through spatially distributed SGMRR arrays or independent microfluidic channels, each functionalized with a specific antibody for simultaneous detection of multiple viral antigens. The parallel channels configuration demonstrated here can be readily extended to multichannel arrays, offering a scalable platform for high-throughput, label-free respiratory-virus diagnostics. At this stage, the sensing capability of the SGMRR platform has been validated using recombinant viral proteins. Future studies will extend the application to complex biological matrices, such as serum and virus-containing nasopharyngeal specimens, to rigorously evaluate its diagnostic robustness and analytical performance in clinically relevant environments. Such validation will be crucial for translating this photonic platform into practical POCT applications. Overall, the convergence of the high sensitivity, rapid response, and multiplexing capability highlights the potential of the SGMRR architecture as a versatile foundation for scalable and high-throughput diagnostic systems.

Table 1 Sensing performance of different on-chip biosensors for detecting SARS-CoV-2, H1N1, and RSV biomarkers.

| Sensor                   | Material                                           | Target virus | Target analyte                                 | Footprint                      | LOD/performance                                      | Multiplex-compatible |
|--------------------------|----------------------------------------------------|--------------|------------------------------------------------|--------------------------------|------------------------------------------------------|----------------------|
| Asymmetric MZI [25]      | Si <sub>3</sub> N <sub>4</sub> on SiO <sub>2</sub> | SARS-CoV-2   | Anti-SARS-CoV-2 antibodies (S/RBD/NP antigens) | Sensing window ~12.5 mm        | 0.3 IU/mL pooled negative plasma                     | 8 channels           |
| Broadband MZI [24]       | Silicon nitride on SiO <sub>2</sub>                | SARS-CoV-2   | Anti-SARS-CoV-2 RBD IgG                        | Sensing windows ~2 mm and 1 mm | 80 ng/mL                                             | N.A.                 |
| MZI waveguide [26]       | Sol-gel silica                                     | H1N1         | Whole Influenza A virus                        | /                              | ~100 µg/mL influenza virus solution                  | N.A.                 |
| Microring resonator [21] | Silicon                                            | SARS-CoV-2   | Nucleocapsid protein                           | Round-trip length ~90 µm       | ~10 pg/mL (LOD <sub>RIU</sub> =10 <sup>-4</sup> RIU) | N.A.                 |
| SGMRR [18]               | SOI                                                | SARS-CoV-2   | Spike protein (antigen)                        | R=10 µm                        | 100 fg/mL (1.31 fM) (iLOD=2.1×10 <sup>-3</sup> RIU)  | 2 channels           |
|                          |                                                    | SARS-CoV-2   | Spike protein (antigen)                        |                                | 100 pg/mL (1.25×10 <sup>-4</sup> RIU)                |                      |
| This work (SGMRRs)       | SOI                                                | H1N1         | Influenza A H1N1 antigen                       | R=10 µm                        | 10 pg/mL (1.25×10 <sup>-4</sup> RIU)                 | 2 channels           |
|                          |                                                    | RSV          | RSV F protein                                  |                                | 10 pg/mL (1.25×10 <sup>-4</sup> RIU)                 |                      |

## Acknowledgment

This work is funded by the National Natural Science Foundation of China (NSFC) (Grant No. U22A2093); Science, Technology, and Innovation Commission of Shenzhen Municipality, China (Grant Nos. GXWD20231130113557001 and JCYJ20210324131614040); Basic and Applied Basic Research Foundation of Guangdong Province, China (Grant Nos. 2020B1515130006 and 2021B1515120056).

## Declarations

**Conflict of Interest** The authors declare that they have no competing interests.

**Permissions** All the included figures, tables, or text passages that have already been published elsewhere have obtained the permission from the copyright owner(s) for both the print and online format.

**Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

**Use of AI Statement** None.

## References

- [1] K. M. Wylie, “The virome of the human respiratory tract,” *Clinics in Chest Medicine*, 2017, 38(1): 11–19.
- [2] D. Tian, Y. Sun, J. Zhou, and Q. Ye, “The global epidemic of SARS-CoV-2 variants and their mutational immune escape,” *Journal of Medical Virology*, 2022, 94(3): 847–857.
- [3] S. A. Hashemi, S. Safamanesh, H. Ghasemzadeh-Moghaddam, M. Ghafouri, and A. Azimian, “High prevalence of SARS-CoV-2 and influenza A virus (H1N1) coinfection in dead patients in Northeastern Iran,” *Journal of Medical Virology*, 2021, 93(2): 1008–1012.
- [4] W. H. Kong, Y. Li, M. W. Peng, D. G. Kong, X. B. Yang, L. Wang, *et al.*, “SARS-CoV-2 detection in patients with influenza-like illness,” *Nature Microbiology*, 2020, 5(5): 675–678.
- [5] Z. Zhang, P. Ma, R. Ahmed, J. Wang, D. Akin, F. Soto, *et al.*, “Advanced point-of-care testing technologies for human acute respiratory virus detection,” *Advanced Materials*, 2022, 34(1): 2103646.
- [6] R. Mirzaei, P. Goodarzi, M. Asadi, A. Soltani, H. Aljanabi, A. S. Jeda, *et al.*, “Bacterial co-infections with SARS-CoV-2,” *IUBMB Life*, 2020, 72(10): 2097–2111.
- [7] A. Tahamtan and A. Ardebili, “Real-time RT-PCR in COVID-19 detection: issues affecting the results,” *Expert Review of Molecular Diagnostics*, 2020, 20(5): 453–454.
- [8] H. Y. Chung, M. J. Jian, C. K. Chang, J. C. Lin, K. M. Yeh, C. W. Chen, *et al.*, “Novel dual multiplex

- real-time RT-PCR assays for the rapid detection of SARS-CoV-2, influenza A/B, and respiratory syncytial virus using the BD MAX open system,” *Emerging Microbes & Infections*, 2021, 10(1): 161–166.
- [9] Y. Liu, Y. Tan, Q. Fu, M. Lin, J. He, S. He, *et al.*, “Reciprocating-flowing on-a-chip enables ultra-fast immunobinding for multiplexed rapid ELISA detection of SARS-CoV-2 antibody,” *Biosensors & Bioelectronics*, 2021, 176: 112920.
- [10] A. I. Cubas-Atienzar, K. Kontogianni, T. Edwards, D. Wooding, K. Buist, C. R. Thompson, *et al.*, “Limit of detection in different matrices of 19 commercially available rapid antigen tests for the detection of SARS-CoV-2,” *Scientific Reports*, 2021, 11(1): 18313.
- [11] M. J. Pioz, R. L. Espinosa, M. F. Laguna, B. Santamaria, A. M. M. Murillo, A. L. Hueros, *et al.*, “A review of optical point-of-care devices to estimate the technology transfer of these cutting-edge technologies,” *Biosensors*, 2022, 12(12): 1091.
- [12] A. Asghari, C. Wang, K. M. Yoo, A. Rostamian, X. Xu, J. D. Shin, *et al.*, “Fast, accurate, point-of-care COVID-19 pandemic diagnosis enabled through advanced lab-on-chip optical biosensors: opportunities and challenges,” *Applied Physics Reviews*, 2021, 8(3): 031313.
- [13] J. Wang, M. M. Sanchez, Y. Yin, R. Herzer, L. Ma, and O. G. Schmidt, “Silicon-based integrated label-free optofluidic biosensors: latest advances and roadmap,” *Advanced Materials Technologies*, 2020, 5(6): 1901138.
- [14] S. Rasheed, T. Kanwal, N. Ahmad, B. Fatima, M. Najam-ul-Haq, and D. Hussain, “Advances and challenges in portable optical biosensors for onsite detection and point-of-care diagnostics,” *TrAC Trends in Analytical Chemistry*, 2024: 117640.
- [15] M. A. Butt, B. I. Akca, and X. Mateos, “Integrated photonic biosensors: enabling next-generation lab-on-a-chip platforms,” *Nanomaterials*, 2025, 15(10): 731.
- [16] Z. Zhou, X. Ou, Y. Fang, E. Alkhazraji, R. Xu, Y. Wan, *et al.*, “Prospects and applications of on-chip lasers,” *eLight*, 2023, 3(1): 1–32.
- [17] W. Bogaerts, P. De Heyn, T. Van Vaerenbergh, K. De Vos, S. K. Selvaraja, T. Claes, *et al.*, “Silicon microring resonators,” *Laser & Photonics Reviews*, 2012, 6(1): 47–73.
- [18] S. Ning, H. C. Chang, K. C. Fan, P. Y. Hsiao, C. Feng, D. Shoemaker, *et al.*, “A point-of-care biosensor for rapid detection and differentiation of COVID-19 virus (SARS-CoV-2) and influenza virus using subwavelength grating micro-ring resonator,” *Applied Physics Reviews*, 2023, 10(2): 021410.
- [19] Z. Ma, Z. Zhang, X. Lv, H. Zhang, K. Lu, G. Su, *et al.*, “Dual sensitivity-enhanced microring resonance-based integrated microfluidic biosensor for A $\beta$ 42 detection,” *Talanta*, 2024, 275: 126111.
- [20] M. R. Bryan, J. N. Butt, J. Bucukovski, and B. L. Miller, “Biosensing with silicon nitride microring resonators integrated with an on-chip filter bank spectrometer,” *ACS Sensors*, 2023, 8(2): 739–747.
- [21] Y. Uchida, T. Arakawa, A. Higo, and Y. Ishizaka, “Silicon microring resonator biosensor for detection of nucleocapsid protein of SARS-CoV-2,” *Sensors*, 2024, 24(10): 3250.
- [22] Y. Xie, M. Zhang, and D. Dai, “Design rule of Mach-Zehnder interferometer sensors for ultra-high sensitivity,” *Sensors*, 2020, 20(9): 2640.
- [23] D. Kohler, G. Schindler, L. Hahn, J. Milvich, A. Hofmann, K. Lange, *et al.*, “Biophotonic sensors with integrated Si<sub>3</sub>N<sub>4</sub>-organic hybrid (SiNOH) lasers for point-of-care diagnostics,” *Light: Science & Applications*, 2021, 10: 64.
- [24] H. Sakamoto, Y. Minpou, T. Sawai, Y. Enami, and S. Suye, “A novel optical biosensing system using Mach-Zehnder-type optical waveguide for influenza virus detection,” *Applied Biochemistry and Biotechnology*, 2016, 178(4): 687–694.
- [25] G. Besselink, A. Schutz-Trilling, J. Veerbeek, M. Verbruggen, A. van der Meer, R. Schonenberg, *et al.*, “Asymmetric Mach-Zehnder interferometric biosensing for quantitative and sensitive multiplex detection of anti-SARS-CoV-2 antibodies in human plasma,” *Biosensors*, 2022, 12(8): 553.
- [26] M. Angelopoulou, E. Makarona, A. Salapatras, K. Misiakos, E. Synolaki, A. Ioannidis, *et al.*, “Directly immersible silicon photonic probes: application to rapid SARS-CoV-2 serological testing,” *Biosensors and Bioelectronics*, 2022, 215: 114570.
- [27] S. Chakravarty, X. Chen, N. Tang, W. C. Lai, Y. Zou, H. Yan, *et al.*, “Review of design principles of 2D photonic crystal microcavity biosensors in silicon and their applications,” *Frontiers of Optoelectronics*, 2016, 9(2): 206–224.
- [28] E. Luan, H. Shoman, D. M. Ratner, K. C. Cheung, and L. Chrostowski, “Silicon photonic biosensors using label-free detection,” *Sensors*, 2018, 18(10): 3519.
- [29] H. Yan, L. Huang, X. Xu, S. Chakravarty, N. Tang, H. Tian, *et al.*, “Unique surface sensing property and enhanced sensitivity in microring resonator biosensors based on subwavelength grating waveguides,” *Optics Express*, 2016, 24(26): 29724–29733.
- [30] S. Schmidt, J. Flueckiger, W. Wu, S. M. Grist, S. T. Fard, V. Donzella, *et al.*, “Improving the performance of silicon photonic rings, disks, and Bragg gratings for use in label-free biosensing,” in *SPIE, Biosensing and Nanomedicine VII*, San Diego, USA, 2014, vol. 9166, pp. 916600.
- [31] C. W. Chang, X. Xu, S. Chakravarty, H. C. Huang, L. W. Tu, Q. Y. Chen, *et al.*, “Pedestal subwavelength

- grating metamaterial waveguide ring resonator for ultra-sensitive label-free biosensing,” *Biosensors and Bioelectronics*, 2019, 141: 111396.
- [32] P. Cheben, R. Halir, J. H. Schmid, H. A. Atwater, and D. R. Smith, “Subwavelength integrated photonics,” *Nature*, 2018, 560(7720): 565–572.
- [33] Z. Wang, X. Xu, D. Fan, Y. Wang, and R. T. Chen, “High quality factor subwavelength grating waveguide micro-ring resonator based on trapezoidal silicon pillars,” *Optics Letters*, 2016, 41(14): 3375–3378.
- [34] X. Xu, H. Subbaraman, J. Covey, D. Kwong, A. Hosseini, and R. T. Chen, “Complementary metal-oxide-semiconductor compatible high efficiency subwavelength grating couplers for silicon integrated photonics,” *Applied Physics Letters*, 2012, 101(3): 031109.
- [35] Y. Guo, L. Huang, G. Zhang, Y. Yao, H. Zhou, S. Shen, *et al.*, “A SARS-CoV-2 neutralizing antibody with extensive spike binding coverage and modified for optimal therapeutic outcomes,” *Nature Communications*, 2021, 12(1): 2623.
- [36] G. Zhou and Q. Zhao, “Perspectives on therapeutic neutralizing antibodies against the novel coronavirus SARS-CoV-2,” *International Journal of Biological Sciences*, 2020, 16(10): 1718–1723.
- [37] R. Lu, X. Zhao, J. Li, P. Niu, B. Yang, H. Wu, *et al.*, “Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding,” *The Lancet*, 2020, 395(10224): 565–574.
- [38] A. J. Einfeld, G. Neumann, and Y. Kawaoka, “At the centre: influenza A virus ribonucleoproteins,” *Nature Reviews Microbiology*, 2015, 13(1): 28–41.
- [39] Y. Hu, H. Sneyd, R. Dekant, and J. Wang, “Influenza A virus nucleoprotein: a highly conserved multifunctional viral protein as a hot antiviral drug target,” *Current Topics in Medicinal Chemistry*, 2017, 17(20): 2271–2285.
- [40] J. S. McLellan, M. Chen, S. Leung, K. W. Graepel, X. Du, Y. Yang, *et al.*, “Structure of RSV fusion glycoprotein trimer bound to a prefusion-specific neutralizing antibody,” *Science*, 2013, 340(6136): 1113–1117.
- [41] M. B. Battles and J. S. McLellan, “Respiratory syncytial virus entry and how to block it,” *Nature Reviews Microbiology*, 2019, 17(4): 233–245.
- [42] M. Schasfoort, “*Handbook of Surface Plasmon Resonance*,” Cambridge, UK: Royal Society of Chemistry, 2017: 119–120.
- [43] W. Li, J. Li, L. Yu, Y. Feng, Y. Yao, Y. Sun, *et al.*, “Observation of Autler-Townes splitting in subwavelength grating metamaterial ring resonators,” *APL Photonics*, 2023, 8(1): 016102.
- [44] G. Eshaghi, D. Kaiser, H. R. Rasouli, R. Ennaciri, M. Frey, C. Neumann, *et al.*, “Highly sensitive and label-free detection of SARS-CoV-2 proteins via surface plasmon resonance using biofunctionalization with 1 nm thick carbon nanomembranes,” *Scientific Reports*, 2025, 15(1): 31248.