

An ultra-low detection-limit optofluidic biosensor based on all glass Fabry-Perot cavity

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Abstract: An all glass optofluidic biosensor with high quality-factor Fabry-Perot cavity (FPC) channel was reported. The all glass sandwich structure can completely eliminate the etching roughness of the channel surface, and can extend the operating wavelength to visible and ultraviolet regions compared with that of Si-based sensor. The quality-factor of the FPC channel is 875, and the system noise can be reduced to 1.2 nV by combining optical differential detection with phase lock-in detection. A detection limit of 15ng/mL for glucose solution, which corresponds to a refractive index unit of 2.0×10^{-9} , was experimentally demonstrated. The all glass FPC sensor features low cost and robust compared with surface-plasmon-resonance sensor and ring-resonator sensor.

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1. Introduction

Optofluidic biosensor based on refractive index (RI) detection has attracted tremendous interest, due to its high precision, real-time, and label-free analysis [1–3]. For RI detection, many optofluidic architectures have been proposed, including surface plasmon resonance (SPR) [4–7], ring-resonator [8–10], fiber grating [11, 12], and Fabry-Perot cavity (FPC) [13–20], etc.

Among these architectures, FPC sensor is suitable for both volume detection (living cell) [15, 18, 19] and surface detection [20]. Moreover, FPC biosensor has been experimentally demonstrated with a detection limit (DL) of 5.5×10^{-8} RIU (RI unit) [16], which approaches that of SPR (10^{-6} – 10^{-8} RIU) [2, 4, 5, 7] and is better than that of ring resonator ($\sim 10^{-7}$ RIU) [2, 9]. According to theoretical analyses [3–5, 21], DL is mainly decided by the quality-factor (Q-factor) of optical resonator, sensitivity, and system noise.

For FPC sensor, the Q-factor (<400) [13] is normally limited by etching roughness of the channel surface, and the system noise is still large, which is in the range of 4nV $\sim$ 50 μ V [16, 22]. In addition, the operating wavelength of the sensor is limited by the absorption window of the cavity materials (the wavelength needs to be longer than 0.9 μ m for Si-based FPC sensor). Moreover, the thermal-mismatch, which results from integrating different kinds of materials in the sensor, would increase signal drift and related noise.

In this paper, an all glass optofluidic biosensor with high Q-factor FPC channel was reported. The all glass sandwich structure can completely eliminate the etching roughness of the channel surface, and can extend the operating wavelength to visible and ultraviolet regions compared with that of Si-based sensor. The all glass structure can also reduce the thermal-mismatch in the sensor. The Q-factor of the FPC channel is 875, and the system noise can be reduced to 1.2 nV by combining optical differential detection (ODD) with phase lock-in detection (PLD). A detection limit of 15ng/mL for glucose solution (*Glu*), which corresponds to 2.0×10^{-9} RIU, was experimentally demonstrated. The all glass FPC sensor features low cost and robust compared with SPR sensor and ring-resonator sensor.

2. Methods

Schematic structure of the FPC biosensor is shown in Fig. 1(a). The device fabrication was carried out by following steps (Fig. 1(b)): (1) a hole with an area of 2.0mm $\times$ 8.0mm was fabricated on a glass-coverslip of 170 μ m thickness (which is the cavity length) by HF etching; (2) 3.5 pairs of SiO₂/Ta₂O₅ distributed Bragg reflector (DBR) were deposited on glass-slides, and then anti-reflection layers were deposited on the backside of the glass-slides; (3) finally, two glass-slides sandwiched with a glass-coverslip were bonded face-to-face by using UV adhesive. The DBR reflectivity is 54% at 1.55 μ m. The optical photograph of the fabricated FPC sensor was shown in Fig. 1(c).

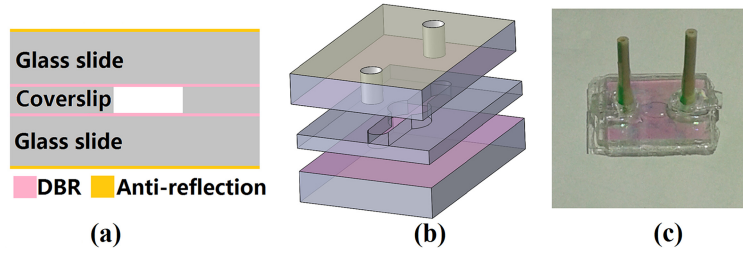


Fig. 1. (a) Schematic structure, (b) fabrication procedure, and (c) optical photograph of the FPC sensor.

The FPC channel is constructed with a hole on glass-coverslip (which functions as the sidewalls of FPC channel) and two DBR on glass-slide, which does not experience etching process. Thus, for FPC reflectors, the etching roughness, which is normally induced when the channel is etched on the substrate [13], can be eliminated in our case.

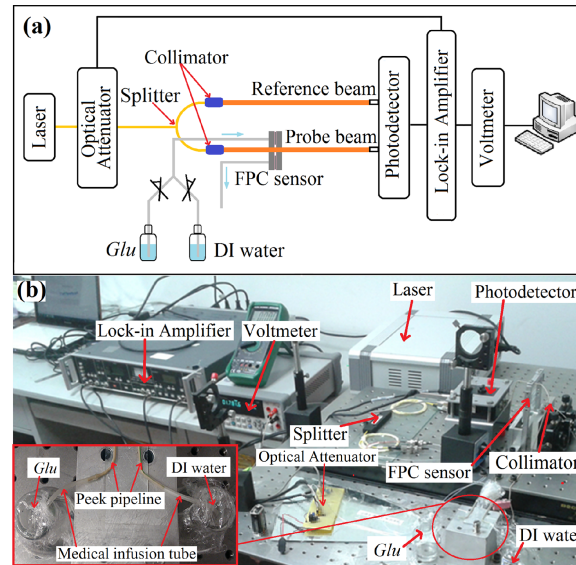


Fig. 2. (a) Schematic diagram and (b) optical photograph of the measurement system.

The measurement setup is shown in Fig. 2. A tunable laser (Opeak Corp.) with a single-mode fiber pigtail is used as the light source, which is connected in series to a variable optical attenuator (Cofiber MEMS VOA) and two fiber collimators via a 3dB fiber-optic beam splitter. The optical spot size, numerical aperture and work distance of the collimator is 0.9 mm, 0.275 and 10cm, respectively. Then, these two collimated beams, i.e., a reference-beam and a probe-beam (which vertically transmits through the FPC sensor), are received by a gain-switchable balanced photodetector (Thorlabs PDB450C). Finally, the output-signal of the photodetector is connected to a lock-in amplifier (EG&G 5209), which modulates the optical attenuator. An Agilent 34405A voltmeter is used to record the real time signal from the lock-in amplifier. The photodetector can convert the differential input light-power ΔP into an amplified voltage signal $V \times N$ (where $V/\Delta P = 1 \text{ V/W}$, and the amplification factor N can be manually tuned in the range of 10^3 - 10^7 according to the magnitude of ΔP). The time constant and the gain of the lock-in amplifier was 3s and 1, respectively, and the related noise bandwidth was 1/12 Hz.

The transmission spectra of the FPC sensor, which is filled with DI water or *Glu* (0.18 wt.%), are measured from the probe-beam (Fig. 3). The full width at half maximum (FWHM) of the resonant peak is 1.77nm, and the corresponding Q-factor ($\lambda/\Delta\lambda$) is 875, which is higher than that of previous reported Si-based FPC sensor [13, 17].

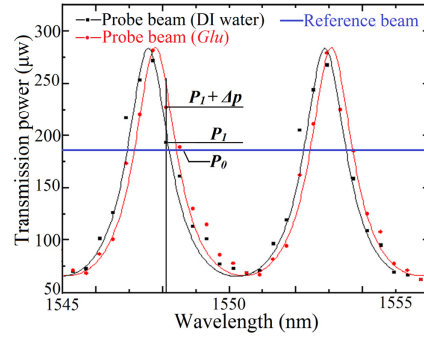


Fig. 3. Transmission spectra of FPC sensor when the channel was filled with DI water or glucose solution.

The ODD used in our FPC sensor is described as follows. As shown in Fig. 3, the red-shift of the spectrum is resulted from the *Glu*-induced increase of RI, so the differential optical power ΔP is a function of RI difference Δn at fixed wavelength. When the fluid in the FPC sensor is switched from DI water to *Glu*, the transmitted probe-beam power changes from P_I to $P_I + \Delta P$ (Fig. 3), and accordingly the differential input power of the photodetector is changed from $P_I - P_0$ to $P_I + \Delta P - P_0$ (where P_0 is the input reference-beam power, which is tuned to approach the probe-beam power P_I). The output-signal variation ΔV of the photodetector is proportional to input power variation ΔP .

With employing ODD, small signal ΔP (ranging from pW to μ W) can be extracted from the large output value $P_I + \Delta P$ ($\sim$ mW) for sufficient amplification, and system noise (such as fluctuation of optical power) can be effectively suppressed [16]. In addition, PLD was employed to further reduce the system noise [5, 6, 22]. The thermal mismatch in the sensor, resulted from integrating different kinds of materials, can be eliminated by using all glass structure.

3. Results and discussions

The measurement of RI-difference between DI water and *Glu* was performed at room temperature without temperature controlling. The laser wavelength was fixed at 1548.11nm. As shown in Table 1, a series of glucose samples was prepared by using successive dilution method, which does not need preparing trace amount of glucose (μ g $\sim$ ng) and can reduce inaccuracy, and the corresponding calculated Δn between the sample and DI water was also presented [12, 23]. The inaccuracy in each dilution process is less than 0.3%, and the maximum inaccuracy of 10 times dilution is less than 3% which is in the range of the error bars of experiment results. As shown in Fig. 2, the channel of the FPC sensor was filled with *Glu* sample and DI water in turn by using a 3-way valve.

Table 1. *Glu* samples with different concentrations and RI-difference Δn

	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
Concentration (wt. %)	0.18%	$0.18\% \times (1/5)$	$0.18\% \times (1/5)^2$	$0.18\% \times (1/5)^3$	$0.18\% \times (1/5)^4$
Δn (RIU)	2.6×10^{-4}	5.2×10^{-5}	1.04×10^{-5}	2.08×10^{-6}	4.17×10^{-7}
	Sample 6	Sample 7	Sample 8	Sample 9	Sample 10
Concentration (wt. %)	$0.18\% \times (1/5)^5$	$0.18\% \times (1/5)^6$	$0.18\% \times (1/5)^6 \times (1/2)$	$0.18\% \times (1/5)^6 \times (1/2)^2$	$0.18\% \times (1/5)^6 \times (1/2)^3$
Δn (RIU)	8.33×10^{-8}	1.67×10^{-8}	8.33×10^{-9}	4.16×10^{-9}	2.0×10^{-9}

The measurement result of sample 5 is shown in Fig. 4(a), and the time, when switching takes place between the *Glu* and DI water via the 3-way valve, was indicated by the arrows. The output voltage increased when switching from DI water to *Glu* and vice versa. Thus, as indicated in the figure, a Δn of 4.17×10^{-7} RIU corresponds to an output-signal ΔV of 0.31 μV . A drift (-0.6 nV/s) of the output-signal is observed, which decreases gradually with time and may result from the variation in ambient-temperature and related laser-power.

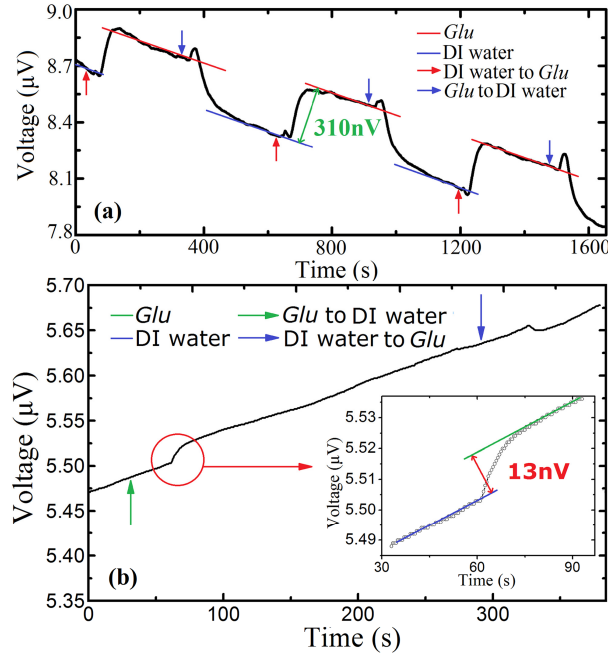


Fig. 4. (a) The measurement results of sample 5 and (b) sample 10.

Figure 4(b) shows the measurement result of sample 10. As shown in the Fig. 4(b), the output-signal ΔV is 13 nV, corresponding to a Δn of 2.0×10^{-9} RIU, which is the best DL experimentally demonstrated to our knowledge.

For the sample 1, 2, 3, 4, 6, 7, 8, and 9, the output-signal ΔV is 34.4 μV , 6.7 μV , 3.2 μV , 0.57 μV , 0.16 μV , 86 nV, 40 nV, and 21 nV, respectively. Based on measurement results, the relationship between the output-signal ΔV and the RI difference Δn can be obtained (as shown in Fig. 5).

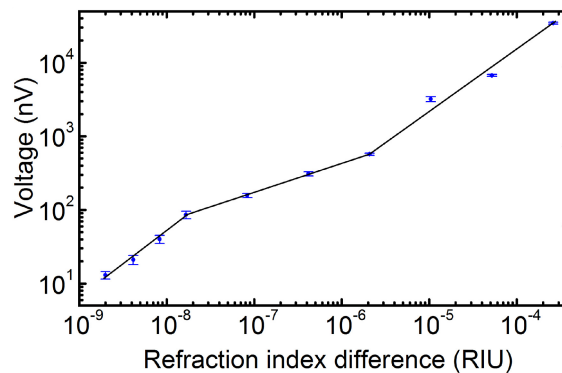


Fig. 5. Relationship between the output-signal and the refractive index difference.

The nonlinearity in Fig. 5 is observed for samples 5-7 with glucose concentrations in range of $2.88 \times 10^{-4} \sim 1.15 \times 10^{-5}$ (wt.%), during which the voltage signal is less sensitive to refractive index. This phenomenon may result from the absorption/desorption of the glucose molecules on the sidewall of fluid pipeline (such as the medical infusion tube as shown in the inset of Fig. 2(b), which is soft and used to connecting peek pipeline). The absorption tends to occur when DI water is flowing and glucose solution is stagnant, and desorption tends to occur when DI water is stagnant and glucose solution is flowing.

The absorption can affect glucose concentrations in the pipeline. The amount of absorbed glucose would be proportional to glucose concentration if the concentration is low (e.g., $< 1.15 \times 10^{-5}$ wt.%), and become saturated if the concentration is raised (e.g., $> 1.15 \times 10^{-5}$ wt.%). Thus, for samples 1-4 with relative high glucose concentration ($> 1.44 \times 10^{-3}$ wt.%), the effect of saturated absorption can be neglected. As for samples 5-7 with moderate concentration ($1.15 \times 10^{-5} \sim 2.88 \times 10^{-4}$ wt.%), the amount of absorbed glucose cannot be neglected, which does not change linearly with concentration due to the saturated absorption. Thus, the detected signal becomes less sensitive to concentration and related refractive index. For samples 8-10 with low concentration ($< 5.75 \times 10^{-6}$ wt.%), the amount of absorbed glucose can change linearly with concentration, so the detect sensitivity dose not be deteriorated by the absorption and becomes nearly equal to that of samples 1-4.

Such a low DL of 2.0×10^{-9} RIU can be attributed to the ultra-low system noise and the high Q-factor of the FPC sensor. In comparing with that of the Si/glass FPC sensor [16], the sensitivity $\Delta P/\Delta n$ ($1.323 \times 10^5 \mu\text{W}/\text{RIU}$) is two fold improvement, due to higher Q-factor and lower thermal-mismatch. The device parameters (including quality factors, finesse, etc.) of the optofluidic biosensors based on Fabry-Perot cavity are provided and listed in Table 2. The device sensitivity $\Delta P/\Delta n$ can be expressed as $\Delta P/\Delta n = (\Delta P/\Delta \lambda) \times (\Delta \lambda/\Delta n)$, where $\Delta P/\Delta \lambda$ is the slope of curve in transmission spectra (Fig. 3) and decided by the quality factor, and $\Delta \lambda/\Delta n$ can be obtained from $2nL = m\lambda$ (L is cavity length, and m is integer). Thus, $\Delta \lambda/\Delta n = 2L/m = \lambda_0/n_0$ (λ_0 is resonant wavelength with cavity reflective index of n_0) is actually independent on cavity length L , although the finesse is inversely proportional to the cavity length. It can be concluded that the sensitivity is mainly decided by quality factor rather than finesse of the cavity.

Table 2. Device parameters of some kinds of optofluidic biosensors based on Fabry-Perot cavity

	SOI [17]	Si/glass [16]	All Glass [this paper]	Si (DRIE) [13]
Q factor	861	620	875	400
Finesse	13	11	3	29
Cavity length (um)	35	25	170	24.5
Reflectivity (%)	75.3	75	54	90
DL (RIU)	1.1×10^{-5}	5.5×10^{-8}	2.0×10^{-9}	$\sim 1.7 \times 10^{-5}$

The noise of output voltage with or without employing ODD and PLD is shown in Fig. 6. The system noise was 50 nV without employing ODD or PLD. The noise was reduced to 10nV or 5 nV by employing PLD or ODD, respectively, and can be further reduced to about 1.2 nV by combining ODD with PLD. With combining ODD with PLD as well as reducing thermal mismatch of the FPC, the system noise is nearly tenfold improvement compared with that of the Si/glass FPC sensor [16].

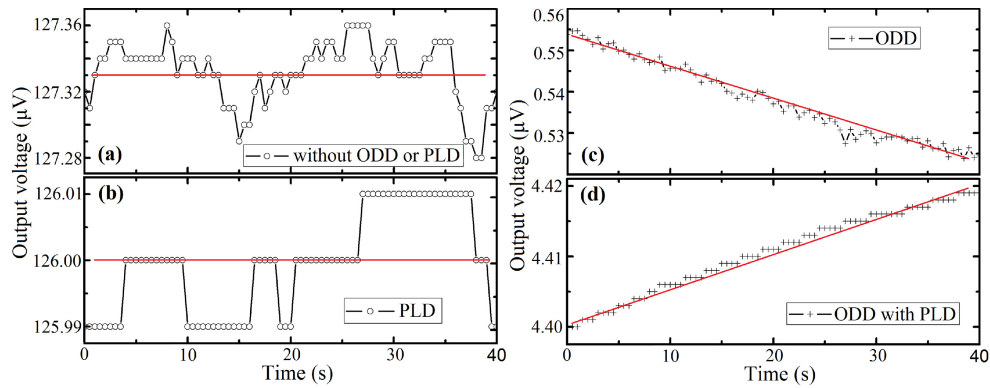


Fig. 6. Output voltage (a) without employing ODD or PLD, (b)with PLD, (c) with ODD, and (d) by combining ODD with PLD.

5. Conclusion

An all glass optofluidic biosensor with a glucose DL of 15ng/mL, which corresponds to 2.0×10^{-9} RIU, was experimentally demonstrated. Such a record DL was attributed to the high Q-factor and low system noise, by using all glass structure as well as combining ODD with PLD. The all glass structure can also extend the operating wavelength to visible and ultraviolet regions compared with that of Si-based sensor.

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