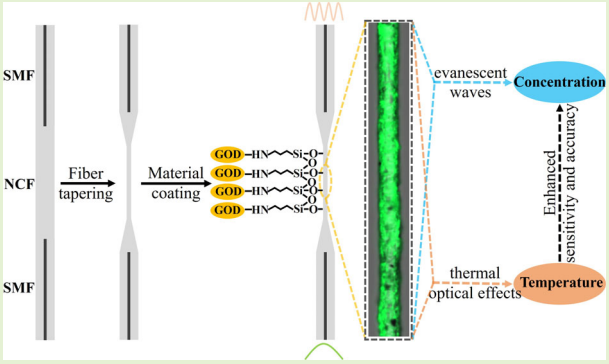
A glucose sensor for enhanced sensitivity and accuracy via in-situ temperature monitoring

Tingkuo Chen, Haiming Jiang, Kang Xie, and Hongyan Xia

Abstract—**This study aims to develop an advanced glucose sensor based on Single-mode fiber - No-core fiber - Single-mode fiber (SMF-NCF-SMF) microfibers modified with glucose oxidase (GOD) for accurate and simultaneous measurement of glucose concentration and temperature, which could significantly enhance diagnostic capabilities in medical and biological applications. The sensor utilizes the evanescent wave principle to detect glucose concentration and the thermal optical effect to measure temperature. Experimental results demonstrate a concentration sensitivity of 2.07 nm/(mg/mL) within the range of 0-3 mg/mL and a temperature sensitivity of -0.35 nm/°C within the range of 25-50°C. These findings highlight the distinct impacts of concentration and temperature on the interference wavelength. By establishing a demodulation matrix, the sensitivities for both concentration and temperature can be separately determined. In-situ temperature monitoring not only eliminates temperature interference but also ensures that GOD remains at its optimal temperature for maximum activity, thereby enhancing the sensitivity and accuracy of glucose concentration detection. Given its high sensitivity, accuracy, and simplicity, this sensor shows promising potential for widespread use in disease diagnosis and biological detection, paving the way for more advanced diagnostic technologies.**



Index Terms—**Glucose sensor, In-situ temperature monitoring, Glucose oxidase, No-core fiber, Microfiber**

I. Introduction

Diabetes is one of the most prevalent chronic diseases in modern society, and its incidence is rapidly increasing due to unhealthy lifestyles [1-4]. Sustained high blood sugar levels in diabetic patients can lead to irreversible damage across multiple organs, posing life-threatening risks. Complications of diabetes include cerebral arteriosclerosis, heart disease, kidney failure, cataracts, and foot ulcers [5-8]. Maintaining blood glucose within a normal range is pivotal for effectively managing diabetes and averting these potentially severe complications [9-12]. Various types of glucose sensors have been developed, encompassing colorimetric sensors, electrochemical sensors, and fluorescence sensors [13-17]. While these sensors satisfy the criteria for accurate blood glucose detection, they often necessitate intricate manipulation by trained professionals and expensive analytical equipment [18]. Consequently, there is a growing demand for user-friendly and cost-effective optical fiber sensing technologies that can be seamlessly incorporated into daily life [19]. By leveraging optical fiber sensing, the management of diabetes could be significantly enhanced, thus improving the overall quality of life for patients [20].

Glucose oxidase (GOD) exhibits high specificity, catalyzing reactions only with glucose, ensuring high selectivity in detection. Additionally, it can respond sensitively to minute changes in glucose concentration, providing high sensitivity in detection results. GOD can rapidly catalyze glucose reactions, enabling quick detection. This is particularly important for diabetic patients who need real-time blood glucose monitoring [21-23]. To create high-quality fiber-optic glucose sensors, research teams often turn to glucose oxidase (GOD), an enzyme material, as a surface modification component for optical fibers. Chen et al. constructed a surface plasmon resonance urine glucose sensor in 2022, also utilizing the SPR principle for detection [24]. They employed Polystyrene/GOD as the functional material, achieving a sensitivity of 3.10 pm/(mg/dL) within the 0-400 mg/dL range. In 2023, Xu et al. proposed a glucose sensor based on a large-diameter optical fiber [25]. This sensor utilizes glucose oxidase-graphene oxide-gold nanoparticles (GOD-GO-AuNPs) to coat the optical fiber and operates on the principle of localized surface plasmon resonance (LSPR). The sensor exhibits excellent stability and an exceptionally high sensitivity of 11.134 nm/(mg/mL). In 2024, Wen et al. proposed a self-powered non-invasive glucose sensor [26]. This biosensor employs glucose oxidase/titanium

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oxide/polydopamine/indium tin oxide (GOD/TiOx/PDA/ITO) coated on an optical fiber and utilizes SPR for sensing. The sensor exhibits a limit of detection (LOD) as low as 4.1 nM within the glucose concentration range of 10-100 μM. It can be seen that glucose sensors based on GOD indeed exhibit exceptional sensing capabilities. Also in 2024, Xu et al. unveiled an innovative non-invasive glucose sensor based on a glucose oxidase/platinum nanoparticles/polypyrrole/graphene oxide (GOD/PtNPs/PPy/GO) composite coated on an optical fiber, integrating surface plasmon resonance (SPR) technology for precise glucose detection [27]. This sensor showcases exceptional sensitivity with a low limit of detection (LOD) of 3.5 nM, spanning a wide glucose concentration range from 5 to 200 μM. The design harnesses the synergistic properties of platinum nanoparticles and graphene oxide for enhanced electrochemical activity and stability, while polypyrrole provides biocompatibility and robustness in various physiological environments. However, a less explored aspect in these studies is the influence of temperature on the performance of sensors based on GOD. The primary influences encompass two aspects: firstly, the activity of GOD is highly sensitive to temperature, and deviations from the optimal temperature can lead to insufficient catalytic reactions [28,29]. Secondly, due to the thermal expansion and thermo-optic effects of the optical fiber, the interference wavelength of the sensor is susceptible to temperature-related disturbances [30,31]. Therefore, it is crucial to take measures to ensure GOD operates at the optimal temperature and to explore temperature demodulation methods to enhance the performance of glucose concentration detection by the sensor. Current approaches involve the use of separate temperature sensors to monitor temperature variations [32,33]. However, differences in sensor placement can significantly reduce the effectiveness of modulation. In the context of glucose concentration measurement, in-situ monitoring of the glucose solution temperature is required [34]. Temperature detection plays a crucial role in improving the sensitivity and accuracy of the sensor in glucose concentration detection.

In this study, we propose a glucose sensing method characterized by a straightforward structural design, employing a GOD-modified Single-mode fiber - No-core fiber - Single-mode fiber (SMF-NCF-SMF) microfiber sensor. This innovative sensor not only enables the direct measurement of glucose concentration but also incorporates in-situ temperature monitoring, thereby enhancing the sensitivity and accuracy of the measurements. Specifically, the sensor detects glucose concentration through the evanescent wave on its surface and monitors temperature via the thermal optical effect of the SNS microfiber. To highlight the sensor's practicality, we conducted comprehensive tests to assess its stability and specificity. These findings collectively underscore the sensor's potential applications and its capacity to consistently deliver reliable performance across a range of conditions.

II. The Experiments and Sensing Principle

A. Materials

Single-mode fiber (SMF) and no-core fiber (NCF) were procured from YOFC (Wuhan, China). Glucose oxidase (GOD) was offered from Aladdin (Shanghai, China). 3-Aminopropyltriethoxysilane (APTES) was received from from Beyotime (Shanghai, China). Glucose, Fructose, Cholesterol, Anhydrous ethanol, Nacl and Kcl, were all provided from Macklin (Shanghai, China). H_2SO_4 and H_2O_2 were acquired from Guangzhou Chemical Reagent Factory (Guangzhou, China). Deionized water (DI) was prepared by Aquqpro pure water machine (Chongqing, China) in our laboratory.

B. Fabrication of GOD-modified SNS microfiber

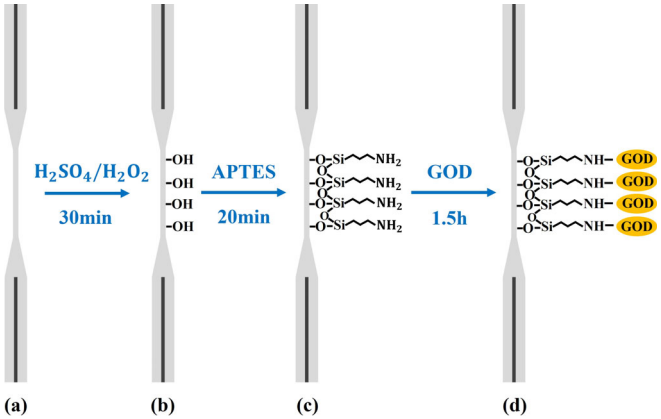

Fig. 1. Schematic illustration of the SNS microfiber surface modification: (a) SNS microfiber, (b) SNS microfiber surface with hydroxylation, (c) APTES-modified SNS microfiber, (d) GOD-modified SNS microfiber.

The manufacturing process of the GOD-coated SNS microfiber sensor involves the selection and preparation of optical fiber materials, structure construction, microfiber fabrication, and surface modification. The detailed process is as follows:

1. Optical Fiber Materials:
   • Two 30 cm segments of Single Mode Fiber (SMF)
   • A 15 mm segment of No-Core Fiber (NCF)
2. Optical Fiber Fusion:
   • Use an optical fiber fusion machine (FITEL S179A) to fuse the SMF and NCF segments, constructing the SMF-NCF-SMF (SNS) structure. This fusion process ensures minimal insertion loss and optimal alignment, which is crucial for maintaining signal integrity in the fiber connection.
3. Microfiber Fabrication:
   • Heat the SNS structure with a hydrogen-oxygen flame while extending it by 1.2 cm at a speed of 1750 μm/s.
   • The result is an SNS microfiber with a diameter of 7.2 μm. This diameter was chosen based on experimental results, as the optical fiber at this scale possesses optimal sensitivity and mechanical stability.
4. Cleaning Process:
   • Clean the SNS microfiber by immersing it in successive solutions of acetone, anhydrous ethanol, and deionized water. This multi-step cleaning process ensures the removal of organic contaminants and residual particles that might interfere with subsequent functionalization steps.
5. Surface Hydroxylation:
   • Treat the cleaned SNS microfiber with a hybrid solution of H_2SO_4 and H_2O_2 to render the surface hydroxyl (-OH) rich. The hydroxylation process increases the surface energy and reactivity of the fiber, facilitating the attachment of functional groups.
6. APTES Modification:

• Immerse the hydroxylated SNS microfiber in a 10% APTES solution to deposit APTES on the surface, generating amino (-NH_3) functionalities. The choice of APTES (3-aminopropyltriethoxysilane) is strategic as it forms stable silane bonds with the hydroxylated surface, providing a robust platform for further functionalization.

7. Enzyme Immobilization:

• Immerse the siliconized SNS microfiber in a 4 mg/ml glucose oxidase (GOD) solution to effectively bind GOD onto the APTES-coated surface. Immobilizing GOD on the sensor surface is crucial for its bio-recognition capability, allowing the sensor to detect glucose with high specificity and sensitivity.

C. Characterizations of the sensor

The morphology of the GOD-modified SNS microfiber sensor was observed by scanning electron microscopy (LYRA 3 XMU, Tescan, Czech) and laser confocal microscope (LSM800, Carl Zeiss, Germany).

D. Experimental system

The configuration of the GOD-modified SNS microfiber sensor system is depicted in Fig. 2. The proposed sensor is securely placed within a temperature-controlled vessel (JF-956s, JINFENG, China), designed to accommodate a glucose solution. An optical signal spanning the range of 1500-1600 nm is provided by the light source (SC-5, YSL, China). The transmission spectrum of the GOD-modified SNS microfiber sensor is acquired and analyzed using an optical spectrum analyzer (AQ6370D, Yokogawa, Japan). Given that the glucose concentration in the blood of healthy individuals falls within the range of 0.5 to 1.2 mg/ml, the glucose solution's concentrations were set at 0, 1.0, 2.0, and 3.0 mg/ml for investigation. To assess the sensor's sensitivity to temperature, the temperature-controlled vessel containing a glucose solution (2.0 mg/ml) was adjusted to various parameters: 25, 30, 35, 40, 45, and 50 °C.

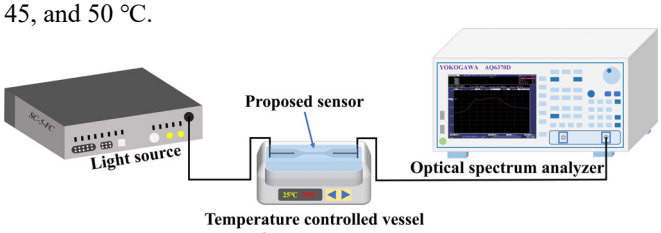

Fig. 2. Experimental setup for glucose concentration and temperature detection.

E. Operating principle

As incident light passes through the GOD-modified SNS microfiber sensor, multiple modes are excited within the structure. Some of the light emerges at the waist region of the sensor, engendering evanescent waves on the waist's surface. In comparison to the bare SNS microfiber, the GOD-modified SNS microfiber sensor showcases heightened sensitivity to shifts in the refractive index of its environment. This heightened sensitivity is attributable to the interaction between the evanescent waves and the high refractive index components (APTES and GOD). This interaction fosters a highly responsive detection of changes in the refractive index of the surroundings. When the GOD-modified SNS microfiber sensor is placed within a glucose solution, an enzymatic reaction occurs in the sensor's waist region. This reaction is initiated by the glucose oxidase (GOD) enzyme [35]:

$$\text{Glucose} + O_2 + H_2O_2 \xrightarrow{GOD} \text{Glucose Acid} + H_2O_2 \quad (1)$$

The kinetics of this reaction follows the Michaelis-Menten equation:

$$v = \frac{V_{max}[S]}{K + [S]} \quad (2)$$

where v is the reaction rate, V_{max} is the maximum reaction rate, [S] is the substrate concentration (glucose concentration), and K_m is the Michaelis constant, representing the affinity of the enzyme for the substrate.

In Equation (1), the glucose solution undergoes decomposition into gluconic acid and hydrogen peroxide through the catalytic activity of GOD. The resultant gluconic acid and hydrogen peroxide cause alterations in the refractive index (RI) of the surrounding medium of the GOD-modified SNS microfiber sensor. These changes lead to a redshift in the interference wavelength [36]. When temperature increases a blueshift of the interference wavelength in the GOD-modified SNS microfiber sensor occurs due to thermal expansion and thermal optical effects [37]. The specific process of temperature-assisted concentration detection is as follows:

1. Changes in glucose concentration lead to changes in the solution's refractive index, which the optical fiber sensor detects through shifts in the interference wavelength. The production of hydrogen peroxide and glucose acid during the enzymatic reaction alters the refractive index of the solution.

2. The kinetic parameters of the enzymatic reaction V_{max} and K_m determine the sensor's response time and sensitivity to glucose concentration changes. A higher V_{max} indicates a faster response to glucose concentration changes, while a lower K_m indicates higher sensitivity to low glucose concentrations.

3. Temperature variations affect the enzyme's activity and reaction rate, thereby influencing the refractive index changes. Therefore, temperature monitoring and compensation are crucial for ensuring the sensor's accuracy and sensitivity.

III. Results and Discussion

A. Morphology analysis of the proposed sensor

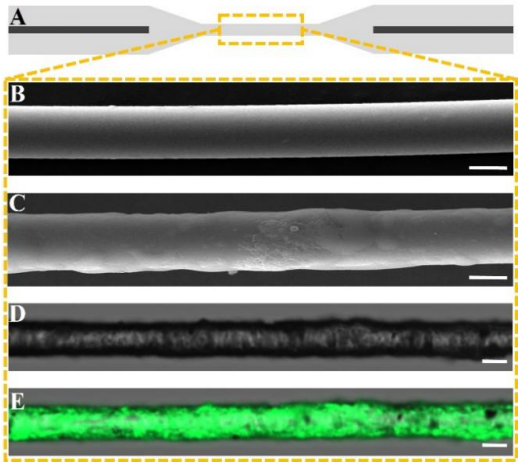

Fig. 3. (A) Schematic illustration of the SNS microfiber, (B) SEM images of bare SNS microfiber, (C) APTES-modified SNS microfiber; Microscope images of (D) APTES-modified, and (E) shows the fluorescence image of GOD-modified SNS microfiber. (scale bar = 5 μm).

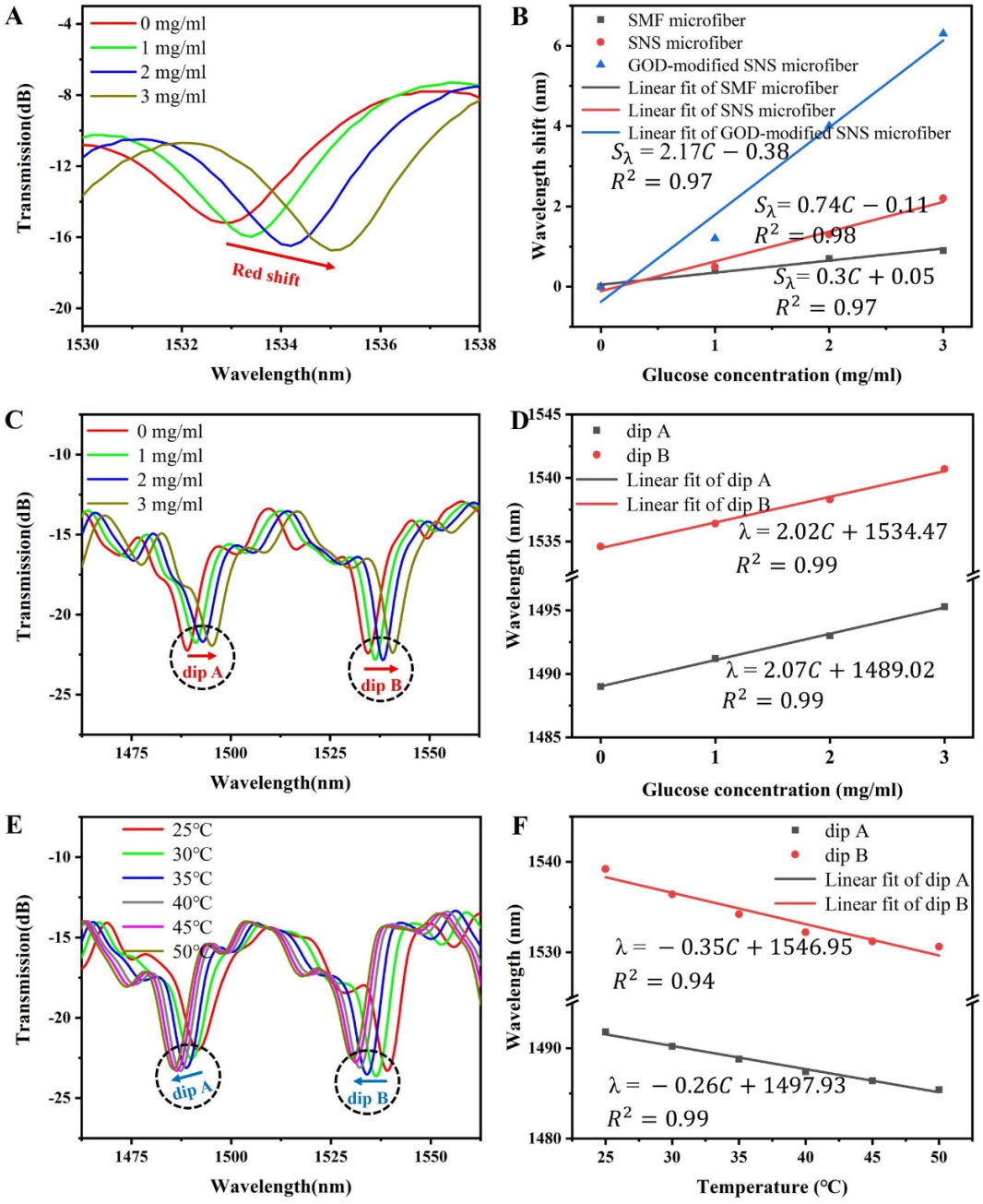

Fig. 4. (A) Transmission spectra of SNS microfiber with the glucose concentration, (B) Glucose sensitivity fitting diagram of SNS microfiber, (C) Transmission spectra of the GOD-modified SNS microfiber sensor with the glucose concentration, (D) Glucose sensitivity fitting diagram of the GOD-modified SNS microfiber sensor, (E) Transmission spectra of the GOD-modified SNS microfiber sensor from 25 to 50℃, (F) Temperature sensitivity fitting diagram of the GOD-modified SNS microfiber sensor.

After functionalization, the successful immobilization of APTES and GOD on the surface of the SNS microfiber was demonstrated through characterization of the waist region of the GOD-modified SNS microfiber sensor. This characterization was carried out using scanning electron microscopy (SEM) and laser confocal microscopy. In Fig. 3 (A), a schematic representation of the GOD-modified SNS microfiber is presented, clearly illustrating the structure of the SNS microfiber. Focusing on the characterization of the waist region, SEM images of the bare SNS microfiber and the APTES-modified SNS microfiber are shown in Fig. 3 (B) and (C), respectively. Compared to the smooth surface of the bare SNS microfiber, the surface of the APTES-modified SNS microfiber appears rougher, as depicted in the SEM images. Furthermore, the diameters of the bare SNS microfiber and the APTES-modified SNS microfiber were measured to be 7.2 μm and 7.4 μm, respectively, with an APTES coating thickness of 0.2 μm. These results collectively provide strong evidence for the uniform immobilization of APTES onto the surface of the SNS microfiber. To confirm the presence of GOD fixed onto the APTES-modified surface, laser confocal microscopy was utilized to observe the GOD-modified SNS microfiber. In Fig.

3 (D) and (E), fluorescence images of the APTES-modified SNS microfiber and the GOD-modified SNS microfiber are presented, respectively. Due to the intrinsic fluorescence of GOD, the GOD-modified SNS microfiber displays a robust fluorescent signal when excited by a 488 nm laser. This observation provides compelling support for the successful immobilization of GOD onto the APTES-coated surface. In summary, the results presented in this section collectively confirm the effective immobilization of APTES and GOD on the surface of the SNS microfiber. The utilization of SEM and laser confocal microscopy techniques has provided visual evidence of the modifications and coatings, enhancing the reliability of the findings.

B. Sensing performance of the proposed sensor

In Fig. 4(A), we present the transmission spectra of SNS microfibers within the glucose concentration range of 0-3 mg/ml. As the glucose concentration increases, the interference wavelength shifts by 2.2 nm towards longer wavelengths. This indicates that the uncoated SNS microfiber possesses substantial detection capabilities. To assess the detection performance of different microfibers, we conducted tests on SMF microfiber, SNS microfiber, and GOD-modified SNS microfiber sensor. As depicted in Fig. 4(B), the interference wavelengths of SMF microfiber, SNS microfiber, and GOD-modified SNS microfiber sensor red-shifted by 0.9 nm, 2.2 nm, and 6.3 nm, respectively. The red-shift in interference wavelength for SNS microfiber is twice that of SMF microfiber, demonstrating superior detection performance of SNS microfiber. In comparison, the GOD-modified SNS microfiber sensor exhibits an amplified red-shift several-fold. Thus, the introduction of APTES and GOD materials significantly enhances the detection performance of SNS microfiber for glucose concentration. Prior to assessing performance, we defined interference wavelengths near 1490 nm and 1540 nm as dip A and dip B, respectively. In Fig. 4(C), as glucose concentration increases from 0 mg/ml to 3 mg/ml, both dip A and dip B exhibit red-shifts of 6.2 nm and 6.3 nm, respectively. This trend aligns with the changes observed in SMF microfiber and SNS microfiber. Through linear fitting, we calculated average sensitivities of 2.02 nm/(mg/ml) for dip A and 2.07 nm/(mg/ml) for dip B for this sensor, as shown in Fig. 4(D). The slight differences in average sensitivities of dip A and dip B may be due to varying responses of optical signals in different wavelength bands to changes in glucose concentration.

The temperature performance of the GOD-modified SNS microfiber sensor was characterized. Fig. 4(E) presents the transmission spectrum of the sensor. As the temperature increases from 25 ℃ to 50 ℃, there is a noticeable blue shift in the interference wavelength. Specifically, blue shifts of 6.1 nm and 8.8 nm were observed at dip A and dip B, respectively. Through linear fitting, we calculated the average sensitivity of dip A to be -0.26 nm/℃ and dip B to be -0.35 nm/℃, as shown in Fig. 4(F). We postulate that the observed blue shift in the interference wavelength results from the combined effects of thermal expansion and thermal optical properties, leading to an increase in the refractive index of the SNS microfiber's cladding. The impact of APTES and GOD on the blue shift of the interference wavelength is also worth considering. Three GOD-modified SNS microfibers and three SNS microfibers were subjected to temperature tests within the range of 25 ℃ to 50 ℃, as shown in Fig. 5. The experimental results reveal that, at dip B, the interference wavelength exhibited a blue shift of 8.5 ± 0.4 nm for the GOD-modified SNS microfibers and 8.6±0.6 nm for the SNS microfibers. Mathematical statistics indicate that APTES and GOD have no significant impact on the temperature measurement of the sensor. Therefore, the SNS microfiber is the functional element for temperature detection.

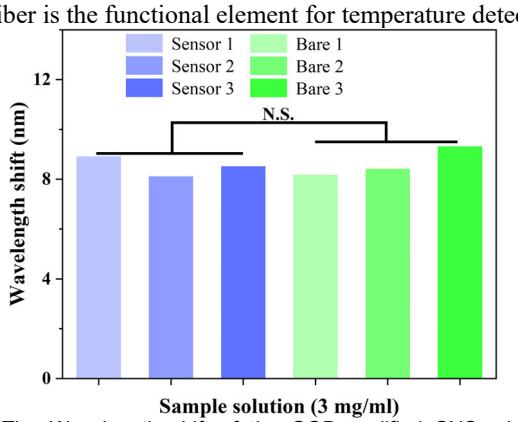

Fig. 5. The Wavelength shift of the GOD-modified SNS microfiber sensor and no-core microfiber from 25 to 50℃. (n=3, N. S.: Not significant)

TABLE I

Performance comparison of different fiber optic sensors for glucose concentration and temperature detection.

Sample	Sensing element	Sensitivity	Measurement range	LOD	Ref.
1	Microfiber with GOD	1.74 nm/(mg/ml)	0–3 mg/ml	\	[38]
2	Fiber SPR with PS/GOD	0.31 nm/(mg/ml)	0-4 mg/ml	\	[24]
3	Side-hole fiber SPR with GOD	34.20 nm/(mg/ml)	0-0.3 mg/ml	\	[28]
4	Fiber Bragg grating	9.94 pm/℃	20-80 ℃	\	[39]
5	Tapered few-mode fiber with silver plated capillary	35 pm/℃	29-56 ℃	\	[40]
6	fiber SPR with GOD/TiOx/PDA/ITO	\	10nM-100μM	4.1nM	[26]
7	fiber-optic SPR with PMBA	\	0.1-20mM	0.482mM	[41]
8	GOD-modified SNS microfiber	2.07 nm/(mg/ml) -0.35 nm/℃	0-3 mg/ml 25-50 ℃	0.177mM	This work

Table I displays various glucose concentration sensors and multifunctional temperature sensors with different structures, including fiber optic SPR, fiber bragg grating, tapered single-mode fiber, and microfiber. In terms of glucose concentration sensing, the GOD-modified SNS microfiber sensor exhibits a glucose concentration sensitivity of 2.07 nm/(mg/ml), surpassing the sensitivities of Sample 1 and Sample 2. Notably, compared to Sample 1 of the same type, this sensor demonstrates a 119% improvement in sensitivity. Although Sample 3 exhibits significantly enhanced glucose concentration sensitivity due to its unique structure, its application is not suitable for blood glucose detection because of the limited detection range. Regarding temperature sensing, the sensor exhibits a temperature sensitivity of -0.35 nm/℃, which is much higher than that of Sample 4 and Sample 5. We selected Sample 4 and Sample 5 as performance benchmarks for temperature sensing since it is meaningful to compare the proposed sensor with these two multifunctional sensors. In addition to temperature detection, Sample 4 and Sample 5 also possess refractive index and liquid level detection capabilities. The LOD of Sample 6 is much higher than that of Sample 7 and our proposed sensor, but its detection range is extremely narrow. For Sample 7 and our proposed sensor, which have similar detection ranges, our proposed sensor's LOD is much lower than that of Sample 7.

C. Stability and specificity analysis of the proposed sensor

To assess the stability of the GOD-modified SNS microfiber sensor, an experiment was conducted. The sensor was immersed in a 3 mg/ml glucose solution while maintaining the glucose solution's temperature at 25 ℃. The interference wavelength was recorded every minute over a 10-minute period. Observing Fig. 6, it becomes evident that at the experiment's commencement, the interference wavelength gradually decreases. However, from 8 to 10 minutes, the interference wavelength stabilizes. This stabilization is attributed to the thermal equilibrium process of the sensor system, the enzymatic reaction on the sensing surface, or external interferences when the sensor was initially placed in the glucose solution. Through statistical analysis, it was determined that the standard deviation and maximum value of the interference wavelength's displacement were 0.15 nm and 0.5 nm, respectively. Remarkably, the maximum translation of the interference wavelength accounted for just 8% (0.5 nm / 6.3 nm = 8%, The total displacement of interference wavelength of concentration is 6.3nm) of the total translation related to glucose concentration, and 6% (0.5 nm / 8.6 nm = 6%, The total displacement of interference wavelength of temperature is 8.6nm) concerning temperature. These findings underscore the sensor's stability and practical significance in real-world applications.

The GOD-modified SNS microfiber sensor is developed for the blood glucose monitoring of the human body, necessitating a specificity analysis due to the presence of complex components in the blood. Various interfering components (Fructose, Saccharose, Cholesterol, Urea, NaCl, KCl, CaCl) were tested at the same concentration range (0-3mg/ml) to assess the sensor's specificity. The sensor's wavelength shift in response to these interferences was measured under identical conditions. As depicted in Fig. 7, when exposed to a glucose solution, the sensor exhibited an interference wavelength shift of 6.6 ± 0.3 nm. This variation is statistically significant when compared to other components. This analysis confirms the sensor's strong specificity for glucose solutions.

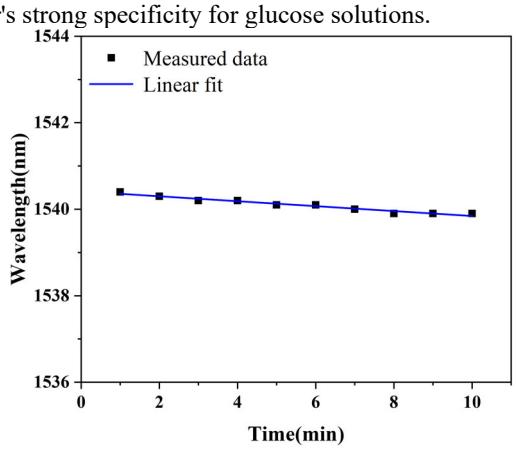

Fig. 6. Stability test of the GOD-modified SNS microfiber sensor.

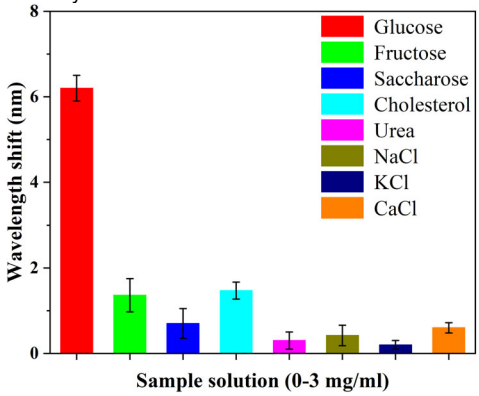

Fig. 7. Selectivity test of the GOD-modified SNS microfiber sensor from 0 to 3 mg/ml.

D. Demodulation matrix

Based on the experimental results, it is evident that the interference wavelength of the GOD-modified SNS microfiber sensor responds to both glucose concentration and temperature to varying degrees. Moreover, the interference wavelengths in both dip A and dip B bands of the sensor exhibit favorable linear relationships. The effective elimination of temperature interference through demodulation matrices further enhances the accuracy and sensitivity of concentration detection. The relationship between interference wavelength and glucose concentration and temperature can be derived as follows [42]:

$$\begin{pmatrix} \Delta\lambda_{dipA} \\ \Delta\lambda_{dipB} \end{pmatrix} = \begin{pmatrix} K_{A,C} & K_{A,T} \\ K_{B,C} & K_{B,T} \end{pmatrix} \begin{pmatrix} \Delta C \\ \Delta T \end{pmatrix} \tag{3}$$

Where $K_{A,C}$ and $K_{B,C}$ are the concentration demodulation coefficients of dip A and dip B respectively, and $K_{A,T}$ and $K_{B,T}$ are temperature demodulation coefficients of dip A and dip B respectively. ΔC and ΔT represent the change of concentration and temperature in a glucose solution respectively, and $\Delta\lambda_{dipA}$ and $\Delta\lambda_{dipB}$ represent the change of

interference wavelength shift of dip A and dip B respectively. It's calculated by formula (3):

$$\begin{pmatrix}\Delta C\\ \Delta T\end{pmatrix}=\frac{1}{\left|K_{B,T}K_{A,C}-K_{A,T}K_{B,C}\right|}\begin{pmatrix}K_{B,T} & -K_{A,T}\\ -K_{B,C} & K_{A,C}\end{pmatrix}\begin{pmatrix}\Delta\lambda_{dipA}\\ \Delta\lambda_{dipB}\end{pmatrix} \quad (4)$$

Substituting the actual values of $K_{A,C}$, $K_{B,C}$, $K_{A,T}$ and $K_{B,T}$ into the above equation, we obtain:

$$\begin{pmatrix}\Delta C\\ \Delta T\end{pmatrix}=\frac{1}{0.1688}\begin{pmatrix}-0.35 & 0.26\\ -2.07 & 2.02\end{pmatrix}\begin{pmatrix}\Delta\lambda_{dipA}\\ \Delta\lambda_{dipB}\end{pmatrix} \quad (5)$$

IV. Conclusions

In this study, we propose an SNS microfiber sensor modified with optimal GOD activity to enhance concentration detection performance via in-situ temperature monitoring to eliminate its interference. Experimental results indicate that the sensor exhibits a concentration sensitivity of 2.07 nm/(mg/ml) within the range of 0 to 3 mg/ml and a temperature sensitivity of -0.35 nm/℃ in the temperature range of 25 to 50 ℃. Furthermore, the sensor demonstrates remarkable stability and selectivity, making it an ideal choice for continuous blood glucose monitoring in diabetic patients. This sensing scheme provides a novel approach for in-situ temperature detection in the analysis of biological components and home healthcare measurements. However, while the sensor exhibits excellent performance under laboratory conditions, challenges remain in achieving consistency and cost control during large-scale production. In addition to glucose concentration and temperature, future efforts could integrate the detection of other biomarkers into the same sensor, developing a multi-parameter monitoring platform that provides more comprehensive data support for medical diagnostics.

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References

[1] L. Guariguata, D. Whiting, C. Weil, N. Unwin, "The International Diabetes Federation diabetes atlas methodology for estimating global and national prevalence of diabetes in adults," Diabetes Res. Clin. Pract. vol. 94, no. 3, pp. 322-332, Dec. 2011.
[2] E. K. Spanakis, S. H. Golden, "Race/Ethnic Difference in Diabetes and Diabetic Complications," Curr. Diabetes Rep. vol. 13, no. 6, pp. 814-823, Dec. 2013.
[3] P. Zhang, X. Zhang, J. Brown, D. Vistisen, R. Sicree, J. Shaw, G. Nichols, "Global healthcare expenditure on diabetes for 2010 and 2030," Diabetes Res. Clin. Pract. vol. 87, no. 3, pp. 293-301, Mar. 2010.
[4] W. R. Rowley, C. Bezold, Y. Arikan, E. Byrne, S. Krohe, "Diabetes 2030: Insights from Yesterday, Today, and Future Trends," Popul. Health Manag. vol. 20, no. 1, pp. 6-12, Feb. 2017.
[5] E. W. Gregg, N. Sattar, M. K. Ali, "The changing face of diabetes complications," Lancet Diabetes Endo. vol. 4, no. 6, pp. 537-547, Jun. 2016.
[6] A. J. Bandodkar, S. Imani, R. Nuñez-Flores, R. Kumar, C. Y. Wang, A. M. V. Mohan, J. Wang, P. P. Mercier, "Re-usable electrochemical glucose sensors integrated into a smartphone platform," Biosens. Bioelectron. vol. 101, pp. 181-187, Mar. 2018.
[7] M. M. Rahman, A. J. S. Ahammad, J. H. Jin, S. J. Ahn, J. J. Lee, "A comprehensive review of glucose biosensors based on nanostructured metal-oxides," Sensors, vol. 10, no. 5, pp. 4855-4886, May 2010.
[8] C. Chen, Q. Xie, D. Yang, H. Xiao, Y. Fu, Y. Tan S. Yao, "Recent advances in electrochemical glucose biosensors: a review," RSC Adv. Vol. 3, no. 14, pp. 4473-4491, 2013.
[9] E. Sainsbury, N. V. Kizirian, S. R. Partridge, T. Gill, S. Colagiuri, A. A. Gibson, "Effect of dietary carbohydrate restriction on glycemic control in adults with diabetes: a systematic review and meta-analysis," Diabetes Res. Clin. Pract. vol. 139, pp. 239–252, May 2018.
[10] Y. Bai, F. Feng, L. Zhao, C. Wang, H. Wang, M. Tian, J. Qin, Y. Duan, X. He, "Aptamer/thrombin/aptamer-AuNPs sandwich enhanced surface plasmon resonance sensor for the detection of subnanomolar thrombin," Biosens. Bioelectron. vol. 47, pp. 265-270, Sep. 2013.
[11] D. Olczuk, R. Priefer, "A history of continuous glucose monitors (CGMs) in self-monitoring of diabetes mellitus," Diabetes Metab. Synd. Vol. 12, no. 2, pp 181-187, Apr. 2018.
[12] K. A. Driscoll, K. D. Corbin, D. M. Maahs, R. Pratley, F. K. Bishop, A. Kahkoska A, A. Kahkoska, K. K. Hood, E. Mayer-Davis, "Biopsychosocial aspects of weight management in type 1 diabetes: a review and next steps," Curr. Diab. Rep. vol. 17, no. 8, pp. 58, Aug. 2017.
[13] S. J. Cho, H. B. Noh, M. S. Won, C. H. Cho, K. B. Kim, Y. B. Shim, "A selective glucose sensor based on direct oxidation on a bimetal catalyst with a molecular imprinted polymer," Biosens. Bioelectron. vol. 99, pp. 471-478, Jan. 2018.
[14] W. R. Zhu, N. Hao, X. D. Yang, K. Wang, "Cascade-catalyzed enzyme-free colorimetric detection of glucose based on manganese dioxide-oxygen doped carbon nitride composites," Chinese J. anal. Chem. vol. 48, no. 6, pp. 727-732, Jun. 2020.
[15] X. Mao, Y. Lu, X. Zhang, Y. Huang, "β-Cyclodextrin functionalization of metal-organic framework MOF-235 with excellent chemiluminescence activity for sensitive glucose biosensing," Talanta, vol. 188, pp. 161-167, Oct. 2018.
[16] C. M. Zhang, Z. W. Zhang, Q. Yang, W. Chen, "Graphene-based Electrochemical Glucose Sensors: Fabrication and Sensing Properties," Electroanal. vol. 30, no. 11, pp. 2504-2524, Nov. 2018.
[17] S. Naaz, S. Poddar, S. P. Bayen, M. K. Mondal, D. Roy, S. K. Mondal, P. Chowdhury, S. K. Saha, "Tenfold enhancement of fluorescence quantum yield of water soluble silver nanoclusters for nanomolar level glucose sensing and precise determination of blood glucose level," Sensor. Actuat. B-Chem. vol. 255, pp. 332-340, Feb. 2018.
[18] H. Zhang, X. Li, Z. Qian, S. Wang, F. Q. Yang, "Glucose oxidase-mediated sodium alginate gelation: equipment-free detection of glucose in fruit samples," Enzym. Microb. Technol. vol. 148, pp. 109805, Aug. 2021.
[19] C. Tiangco, D. Fon, N. Sardesai, Y. Kostov, F. Sevilla III, G. Rao, L. Tolosa, "Fiber optic biosensor for transdermal glucose based on the glucose binding protein," Sensor. Actuat. B-Chem. vol. 242, pp. 569-576, Apr. 2017.
[20] J. L. C. Perez, J. Gutiérrez-Gutiérrez, C. P. Mayoral, E. L. Pérez-Campos, M. D. S. P. Canseco, L. T. Carrillo, L. P.-C. Mayoral, M. V. Treviño, E. L. Apreza, R. R. Laguna, "Fiber Optic Sensors: A Review for Glucose Measurement," Biosensors, vol. 11, no. 3, pp. 61, Mar. 2021.
[21] S. Yu, L. Ding, H. Lin, W. Wu, J. Huang, "A novel optical fiber glucose biosensor based on carbon quantum dots-glucose oxidase/cellulose acetate complex sensitive film," Biosens. Bioelectron. vol. 146, pp. 111760, Dec. 2019.
[22] K. C. Chen, Y. L. Li, C. W. Wu, C. C. Chiang, "Glucose Sensor Using U-Shaped Optical Fiber Probe with Gold Nanoparticles and Glucose Oxidase," Sensors, vol. 18, no. 4, pp. 1217, Apr. 2018.
[23] C. C. Hsu, W. Y. Chung, C. Y. Chang, C. C. Wu, C. L. Lee, "Enzymatic Glucose Fiber Sensor for Glucose Concentration Measurement with a Heterodyne Interferometry," Sensors, vol. 23, no. 6, pp. 2990, Mar. 2023.
[24] J. Zhang, X. Mai, X. Hong, Y. Chen, X. Li, "Optical fiber SPR biosensor with a solid-phase enzymatic reaction device for glucose detection," Sensor. Actuat. B-Chem. vol. 366, pp. 131984, Sep. 2022.
[25] B. Xu, X. Xiang, L. Ding, Z. Luo, J. Zhao, J. Huang, H. Li, X. Jiang, "A Novel Large-Diameter Optical Fiber Glucose Biosensor Based on Glucose Oxidase– Graphene Oxide–Gold Nanoparticles," IEEE Sens. J. vol. 23, pp. 6832-6839, Apr. 2023.
[26] X. Wen, X. Yang, Z. Ge, H. Ma, R. Wang, F. Tian, P. Teng, S. Gao, K. Li, B. Zhang, S. Sivanathan, "Self-powered optical fiber biosensor integrated with enzymes for non-invasive glucose sensing," Biosens. Bioelectron. vol. 253, pp. 116191, Jun. 2024.
[27] Y. Xu, X. Zhang, X. S. Zhu, Y. W. Shi, "Silver-coated hollow fiber surface plasmon resonance sensor for glucose detection with enhanced limit of detection," Nanoscale, vol. 16, pp. 7085-7092, Mar. 2024.

[28] S. Wu, Q. Tan, E. Forsberg, S. Hu, S. He, "In-situ dual-channel surface plasmon resonance fiber sensor for temperature-compensated detection of glucose concentration," Opt. Express, vol. 28, no. 14, pp. 21046-21061, Jul. 2020.
[29] H. M. Kalisz, J. Hendle, R. D. Schmid, "Structural and biochemical properties of glycosylated and deglycosylated glucose oxidase from Penicillium amagasakiense," Appl. Microbiol. Biotechnol. Vol. 47, no. 5, pp. 502-507, May 1997.
[30] Z. Wang, D. L. Chen, X. C. Yang, S. X. Liang, X. H. Sun, "Temperature sensor of single-mode-no-core-single-mode fiber structure coated with PDMS," Opt. Fiber Technol. vol. 68, pp. 102793, Jan. 2022.
[31] Q. Wang, H. Zhang, D. N. Wang, "Cascaded multiple Fabry-Perot interferometers fabricated in no-core fiber with a waveguide for high-temperature sensing," Opt. Lett. vol. 44, no. 21, pp. 5145-5148, Nov. 2019.
[32] V. G. Pahurkar, Y. S. Tamgadge, A. B. Gambhire, G. G. Muley, "Glucose oxidase immobilized PANI cladding modified fiber optic intrinsic biosensor for detection of glucose," Sensor. Actuat. B-Chem. vol. 210, pp. 362-368, Apr. 2015.
[33] S. Yu, L. Ding, H. Lin, W. Wu, J. Huang, "A novel optical fiber glucose biosensor based on carbon quantum dots-glucose oxidase/cellulose acetate complex sensitive film," Biosens. Bioelectron. vol. 146, pp. 111760, Dec. 2019.
[34] B. Li, X. Yan, X. Zhang, F. Wang, S. LI, T. Suzuki, Y. Ohishi, T.Cheng, "No-core optical fiber sensor based on surface plasmon resonance for glucose solution concentration and temperature measurement," Opt. Express, vol. 29, no. 9, pp. 12930-12940, Apr. 2021.
[35] Y. Yuan, X. Yang, D. Gong, F. Liu, W. Hu, W. Cai, J. Huang, M. Yang, "Investigation for terminal reflection optical fiber SPR glucose sensor and glucose sensitive membrane with immobilized GODs," Opt. Express, vol. 25, no. 4, pp. 3884-3898, Feb. 2017.
[36] L. Chen, Y. K. Leng, B. Liu, J. Liu, S. P. Wan, T. Wu, J. H. Yuan, L. Y. Shao, G. Q. Gu, Y. Q. Fu, H. Y. Xu, Y. H. Xiong, X. D. He, Q. Wu, "Ultrahigh-sensitivity label-free optical fiber biosensor based on a tapered singlemode- no core-singlemode coupler for Staphylococcus aureus detection," Sensor. Actuat. B-Chem. vol. 320, pp. 128283, Oct. 2020.
[37] K. Tian, G. Farrell, X. Wang, Y. Xin, Y. Du, W. Yang, H. Liang, E. Lewis, P. Wang, "High sensitivity temperature sensor based on singlemode-no-core-singlemode fibre structure and alcohol," Sensor. Actuat. A-Phys. vol. 284, pp. 28-34, Dec. 2018.
[38] Y. Li, H. Ma, L. Gan, Q. Liu, Z. Yan, D. Liu, Q. Sun, "Immobilized optical fiber microprobe for selective and high sensitiveglucose detection," Sensor. Actuat. B-Chem. vol. 255, pp. 3004-3010, Feb. 2018.
[39] Q. Chen, D. N. Wang, F. Gao, "Simultaneous refractive index and temperature sensing based on a fiber surface waveguide and fiber Bragg gratings," Opt. Lett. vol. 46, no. 6, pp. 1209-1212, Mar. 2021.
[40] Y. Li, Z. Song, J. Pan, H. Lu, J. Hu, "In-line reflected fiber sensor for simultaneous measurement of temperature and liquid level based on tapered few-mode fiber," Opt. Express, vol. 30, no. 5, pp. 7870-7882, Feb. 2022.
[41] G. Gumilar, S. Chowdhury, G. Shukri, A. Patah, N. Nugraha, J. Henzie, I. Anshori, Y. V. Kanetid, B. Yuliarto, "The revelation of glucose adsorption mechanisms on hierarchical metal-organic frameworks using a surface plasmon resonance sensor," J. Mater. Chem. B, vol. 11, no. 20, pp. 4428-4444, Mar. 2023.
[42] X. Chen, X. Li, D. Yi, X. Hong, Y. Chen, "Plasmonic tapered-fiber interference sensor for simultaneously detecting refractive index and temperature," Opt. Lett. vol. 46, no. 24, pp. 6071-6074, Dec. 2021.

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