Reflection-based thin-core modal interferometry optical fiber functionalized with PAA-PBA/PVA for glucose detection under physiological pH

Wang, Yan Ru; Tou, Zhi Qiang; Ravikumar, Raghunandhan; Lim, Yi Yin; Ding, Zhe Wen; Zhao, Chun Liu; So, Ping Lam; Chan, Chi Chiu

2019

Wang, Y. R., Tou, Z. Q., Ravikumar, R., Lim, Y. Y., Ding, Z. W., Zhao, C. L., . . . , Chan, C. C. (2019). Reflection-based thin-core modal interferometry optical fiber functionalized with PAA-PBA/PVA for glucose detection under physiological pH. *Journal of Lightwave Technology*, 37(11), 2773-2777. doi:10.1109/JLT.2018.2879318

<https://hdl.handle.net/10356/137184>

<https://doi.org/10.1109/JLT.2018.2879318>

© 2018 IEEE. Personal use of this material is permitted. Permission from IEEE must be obtained for all other uses, in any current or future media, including reprinting/republishing this material for advertising or promotional purposes, creating new collective works, for resale or redistribution to servers or lists, or reuse of any copyrighted component of this work in other works. The published version is available at: <https://doi.org/10.1109/JLT.2018.2879318>.

Downloaded on 26 Apr 2023 16:32:47 SGT

Reflection based thin core modal interferometry optical fiber functionalized with PAA-PBA/PVA for glucose detection under physiological pH

Yan Ru Wang², Zhi Qiang Tou², Raghunandhan Ravikumar², Yi Yin Lim², Zhe Wen Ding³, Chun Liu Zhao³, Ping Lam So⁴, Chi Chiu Chan^{1,*}

Abstract—A PAA-PBA/PVA functionalized thin core fiber (TCF) optical sensor is proposed for glucose detection. The unique Michelson type fiber interferometer sensor was fabricated by splicing a short segment of thin-core fiber (TCF) with single-mode fiber (SMF) where the tip of TCF was melted into a rounded shape. Phenylboronic acid-derivatized poly (acrylic acid), PAA-PBA, was synthesized by grafting PBA onto the PAA chain using N-hydroxysuccinimide (NHS) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) as coupling reagent. Multilayer films of PAA-PBA and poly(vinyl alcohol) (PVA) were subsequently functionalized onto the fiber-optic Michelson interferometer (MI) structure through layer-by-layer assembly. Experiments showed that the PAA-PBA/PVA functionalized fiber-optic probe exhibits glucose-sensitive behavior under physiological pH. The proposed sensor which offers benefits like simple fabrication, compact size and glucose selectivity has potential applications in a bio-device such as insulin release system.

Index Terms—Biological sensing and sensors, Fiber optics, Multilayer design, Polymers.

I. INTRODUCTION

GLUCOSE plays an important role in physiology as an essential substance in human life. Blood glucose monitoring under physiological conditions provides guidance for disease diagnosis and medical treatment (e.g. diabetes) [1]. The development of glucose sensors has gradually attracted the attention of researchers over the past few decades. Conventional glucose sensors are electrochemical-based and commonly rely on enzymes such as glucose oxidase (GOD) or glucose dehydrogenase (GDH) due to their high selectivity to glucose molecules [2]. However, these sensors are very difficult to manufacture because the enzymes are very sensitive to the changes of external environment and easily degenerated. Thus, the research for alternative glucose-sensitive materials has gained tremendous interest recently. Phenylboronic acid

(PBA) which is known for forming boronate ester bonds with 1, 2- or 1, 3-diols, was originally used for carbohydrates detection in spectroscopic techniques [3-5]. The binding affinity and selectivity of PBA derivatives to diol compounds can be suitably tailored owing to the versatile chemical structure of PBA [6]. In the past few years, many types of sugar-sensitive sensors based on PBA derivatives have been reported [7-12]. The most commonly used detection techniques are based on electrochemical or fluorescent methods, which undoubtedly limits their use in the complex environments.

Fiber-optic sensors are superior to conventional electrical ones in some aspects such as miniaturization, immunity to electromagnetic interference, and remote sensing capabilities.[13] Some fiber-optic based sensors utilizing various techniques including evanescent wave sensing via tapering [14], surface Plasmon resonance (SPR) [15, 16], gratings [17, 18] and interferometry [19] have been reported for glucose detection. By coating with various glucose-sensitive materials, including enzymes and PBA derivatives composite materials, the fiber optic sensors can be made sensitive to glucose. However, certain limitations within these sensors including the fragility of the tapered fibers that limit feasibility for real world applications. Specialty fibers like polymer optical fiber (POF) [20, 21] or special technologies like SPR, femtosecond laser micromachining [22] increases the cost of the fiber sensors.

In this Letter, we report a glucose sensor based on PAA-PBA/PVA functionalized fiber-optic Michelson interferometer (MI). The MI was fabricated by splicing a short segment of thin-core fiber (TCF) with single-mode fiber (SMF) and the tip of TCF was melted into a rounded shape by arc fusion splicing. The PAA-PBA and poly (vinyl alcohol) (PVA) multilayer films were then assembled on the sensor surface using layer-by-layer (LbL) technique through boronate ester bonds formation between PBA and PVA [23-25]. The binding reaction of glucose and PBA groups in the polymer films results in the film swelling or decomposition and the refractive index near the sensor probe will be changed, thus subsequently the reflectance spectrum of the sensor will be modulated. The glucose response of the PAA-PBA/PVA functionalized sensor was experimentally evaluated under physiological pH (pH=7.4).

¹Sino-German College of Intelligent Manufacturing, Shenzhen Technology University, Shenzhen 518118, China.

²School of Chemical and Biomedical Engineering, Nanyang Technological University, 637457, Singapore.

³Institute of Optoelectronic Technology, China Jiliang University, Hangzhou 310018, China.

⁴School of Electrical and Electronic Engineering College of Engineering, Nanyang Technological University, 637457, Singapore.

*Corresponding author: ccchan@sztu.edu.cn.

II. EXPERIMENTAL

A. Materials

PAA (35wt.%), PBA (98%), PVA (99+% hydrolyzed), D-(+)-Glucose (99.5+% (GC)), NHS and EDC were supplied by Sigma-Aldrich. Hydrochloric acid (HCl, 37%), sulfuric acid (H₂SO₄, 95%~97%), sodium hydroxide (NaOH), and sodium chloride (NaCl) were procured from Merck while hydrogen peroxide (H₂O₂, 30%) was from VWR. Single mode optical fiber of core diameter 8μm and cladding diameter 125μm was bought from Yangtze Optical Fiber and Cable Company Ltd. Thin core fiber, with core diameter of 4μm and cladding diameter of 125μm, was purchased from NKT.

Deionized water with a resistivity of 18.2MΩcm from the Milli-Q system was used throughout the experiment.

B. Apparatus

The precision fiber cleaver (CT-30) and electric arc fusion splicer (FSM-100P+) for fiber cleaving and splicing were supplied by Fujikura. The amplified spontaneous emission (ASE, OS8143-23) light source which was used to provide a broadband light in the wavelength range from 1520 nm to 1610 nm was procured from Chengdu Huaying laser. The optical spectrum analyzer (OSA, AQ6370) which was used to acquire the reflectance spectral data were both procured from Yokogawa. The digital pH meter (Orion 320) was purchased from Thermo Scientific. Magnetic stirrer (PC-420D) and dip coater (KSV NIMA Dip Coater Multi Vessel Small) were purchased from Corning and KSV NIMA respectively. Fourier-transform Infrared spectrometer (FTIR, ALPHA T) and vacuum freeze drier (LP8-3S-16X-P) were supplied by LabX.

C. Fabrication of the fiber-optic Michelson interferometer (MI)

The sensor was fabricated by splicing one end of a short segment of thin core fiber (TCF) with a single mode (SMF) lead in/out fiber and the TCF end was melted into a rounded tip (see Fig. 1). In order to obtain a rounded tip, the fusion splicer was set to the splicing parameters as follows: the discharge intensity was set to 7 bit above the standard power, the duration time of discharge was set to 10 s, and the fiber-feeding rate was 0.03 μm/ms.

Fig. 1. Schematic diagram of the proposed fiber-optic MI sensor (left) and (right) the micrograph of the prepared sensor under 10X magnification.

D. Synthesis of PBA-derivatized PAA (PAA-PBA) and PVA solution

1% PAA-PBA solution was prepared as follows. 11mg of NHS and 116.5mg of EDC were separately dissolved in 0.5ml of 2-(N-morpholino) ethanesulfonic acid (MES, 0.1M) buffer. 154mg of PAA was dissolved in 7.8ml of MES buffer. 227mg of PBA was dissolved in 4.6ml of phosphate buffered saline

(PBS, 0.1M, pH7.4). Firstly, the previously dissolved PAA, NHS, and EDC solutions were mixed thoroughly with vortex mixer and the pH of the mixture was adjusted to pH 5.0 with 0.1M HCl. Next, the PBA solution was added and the pH of the mixture was adjusted to 6.0 with NaOH to ensure that no white residues appeared in the mixture. The mixture was then left to stir and react overnight at room temperature. The product was subsequently dialyzed for 5 days to remove all impurities of low molecular weight and then freeze dried to remove the water inside. The resulting product was a white solid that was subsequently dissolved in PBS for subsequent use.

To prepare the 1% PVA solution, 333mg of PVA was dissolved in 5ml of deionized water and the mixture was placed on a magnetic stirrer (125 °C, 300rpm) until it was homogenous and turned transparent. The mixture was then left to cool to the room temperature.

Fig. 2. Schematic of the reaction between PAA-PBA/PVA.

Fig. 3. Schematic diagram of the sensor functionalized with PAA-PBA/PVA.

E. Layer by layer (LbL) assembly on the optic fiber

The layer-by-layer method (LbL) was utilized to assemble multilayer polymer films on the fiber surface. Firstly, the fiber was treated with piranha solution (mixture of HCl and H₂O₂ in 7:3 volume ratio) at 120°C for 15mins and subsequently rinsed with deionized water and dried with nitrogen stream. The treated fiber was subsequently dipped into the PVA solution by using a dip coater with a pulling speed of 1 mm/s. It is important to ensure that the TCF segment of the fiber was completely immersed and did not touch the walls of the tube to produce a homogenous layer of film. The PVA-coated fiber was then left to dry in air for 2mins and then dipped into the PAA-PBA solution. The PAA-PBA/PVA coated fiber was then left to dry in air for 2mins. This completes the deposition of the first bilayer of the polymer film. This deposition cycle was repeated to obtain multilayer polymer films functionalized fiber probe. Lastly, the (PAA-PBA/PVA)_n-functionalized fiber was dried in air before heating in an oven at 125 °C for 30 minutes. During the heating process, the PAA-PBA/PVA reacted with each other through the boronate ester formation between the PBA and PVA. It is noteworthy that PVA also combined with the PAA during the heating which made the entire membrane

more compact. Then the fiber was immersed in PBS to remove excess polymers that had not been cross-linked. Fig.2 shows the schematic of the reaction between PAA-PBA/PVA and the schematic of the surface functionalized sensor is shown in Fig.3.

F. Experimental setup

The set-up comprises of amplified spontaneous emission (ASE) broadband light source, optical circulator, sensor probe and optical spectrum analyzer (OSA) that were connected as shown in Fig.4. The light emitted from ASE light source was directed to the sensor probe through the optical fiber circulator. The reflected signal from the sensor was then guided to the OSA for measurement.

Fig.4. Schematic of the experimental setup.

G. Principles of the fiber sensor

A short segment of TCF was spliced to a lead in/out SMF fiber that formed the sensing probe. A modal interferometer was formed by the interference between cladding modes in the TCF that were excited due to core diameter mis-matched between the SMF and TCF, and the core propagating mode. In details, the fundamental core mode from the SMF diffracts and excites some cladding modes in the TCF as it propagates into the latter. The rounded TCF tip serves to reflect and excite higher order cladding modes [26]. The reflected modes are recoupled into the core of the SMF. Since the core and cladding modes transverse in different back paths, they have different propagation constants and hence effective indices. As a result, an interference reflection spectrum arising from the interference between the core and cladding modes is obtained, similar to that of a Michelson type interferometer.

III. RESULTS AND DISCUSSION

A. Characterization of PAA-PBA

Fig.5 shows the FTIR spectra of PAA and PAA-PBA. The FTIR spectrum shows a peak at 1717 cm^{-1} which is the characteristic absorption peak of C=O stretch in PAA and is also observed in PAA-PBA. This indicates that there are some unreacted COOH groups in PAA-PBA. The absorption peak at 704 cm^{-1} and 1343 cm^{-1} are characteristics of the aromatic C-H out-of plane bending bands and typical B-O stretching. It is noteworthy that the characteristic amide C=O stretch centered at 1658 cm^{-1} and amide N-H band at 1554 cm^{-1} are detected in PAA-PBA, but not in PAA. These indicate that a new amide bond was formed due to the successful cross-linking between amino groups of PBA and carboxylic acid groups of PAA and provides further proof that the phenyl-boronic acid is

successfully grafted onto the PAA chain.

Fig.5. FTIR spectra of PAA and PAA-PBA.

B. Characterization of PAA-PBA Glucose response of the functionalized fiber probe

A series of reflectance spectra during the assembly process were recorded (see Fig.6). A short wavelength shift is observed with the increase in the number of assembly layers. The reflectance dip of the fiber coated with 2 layers of PAA-PBA/PVA has a blue shifts of 6.7 nm as seen in the Fig.6 as the result of surface refractive index of the fiber-optic probe increases. When the assembly process proceeds to the third layer, the reflectance spectrum is no longer a regular change due to the high surface refractive index of the probe, and then the coating was stopped. Thus, a three-layer polymer film (PAA-PBA/PVA)₃ was functioned on the fiber surface.

Fig.6 (a). The reflectance spectra during 3 layers assembly process.

Fig.6 (b). The reflectance spectra during 5 layers assembly process.

The reason of such a big change in the reflection spectrum when the third layer was added is: Taken the surface refractive index and the cladding refractive index of the fiber as a whole as the outer cladding refractive index. It is well known that the polymer PAA-PBA/PVA membrane has a high refractive index. When PAA-PBA/PVA membrane assembled on the optic fiber, the refractive index of the outer cladding is increased, then the refractive index difference between the core mode and the cladding mode of the fiber decreased. Thus, as the assembled layer increases, the reflectance peak shifts to shorter wavelength. But when the refractive index of the outer cladding is increased to such an extent that the refractive index difference between the core mode and the cladding mode of the fiber reaches a critical point, the reflection spectrum at this time no longer follows the previous trend (as the layer increases, the reflectance peak shifts toward the shorter wavelength), but a sudden change occurs (as the 3 layers in the Fig.6). In the actual experiment, we have tried to coat more layers based on this change, but due to the destruction of the refractive index matching conditions, the reflection spectrum of the sensor probe becomes disordered and extremely unstable (the two curves in FIG. 6 (b) for the 4 layers are spectra recorded at different times, indicating the instability). Continue adding layers to five, the refractive index of the outer cladding continues to increase and the reflectance spectrum to become almost a straight line as can be seen from figure 6 (b). Therefore, we can conclude that the refractive index difference between the core mode and the cladding mode of the fiber reaching a critical point when adding the third layers. Therefore, we choose to stop the coating at this critical point for better sensitivity.

The glucose response of the (PAA-PBA/PVA)3 functionalized sensor was evaluated by immersing the sensor probe in sample solutions of varying glucose concentrations (0-10mM) at room temperature (25 °C). The sample solutions were prepared by dissolving different concentrations of glucose in PBS (pH=7.4). During the measurement, the sensor immersed in a concentration of glucose solution, the reflection spectra were recorded until the spectrum was stable before transferred it into the next concentration, the reaction time in each concentration during the experiment was about 1 minute. The reflectance spectra at

varies glucose concentrations are shown in Fig.7. The reflectance dip shifts to longer wavelengths as the glucose concentration increases.

In the multilayer films, PBA moieties of PAA-PBA formed boronate ester bonds with 1,3-diol units of PVA. The negative tetrahedral form of PBA has a greater association constant compared to the neutral trigonal form and is more likely to react with 1,2- or 1,3-diol to form boronate ester. When the PAA-PBA/PVA functionalized sensor probe is immersed into the glucose solution (pH=7.4), the glucose molecules bind with PBA groups in two ways [23]: bind with the free PBA groups and convert them to negatively charges; compete with PVA for binding to PAA-PBA in the multilayer films (as shown in Fig. 8). The latter is the main part in this binding reaction. As a result, with the increase in concentration of glucose, more boronate esters are formed between PBA and low weight glucose, leading to the film swelling or decomposition and the surface refractive index of the sensor probe decreases and thus the reflectance spectrum shifts to longer wavelengths.

Fig.7. The reflectance spectra at varying glucose concentrations.

Fig.8. Schematic illustration of the glucose-sensitive of the PAA-PBA/PVA film.

To present a more intuitive relationship between wavelength and glucose concentration, logarithmic transformation of glucose concentration was carried out and is presented in Fig.9. It is observed that the dip wavelength varies linearly with the logarithm of glucose concentration (unit in mM) in the range of 10 μ M-10mM ($R^2=0.9877$) and is expressed as:

$$y = 0.50[x] + 1542.2$$

where y represents the dip position of the reflectance spectrum, i.e., the dip wavelength (unit in nm); x represents the logarithm

of glucose concentration (the unit of glucose concentration in M).

Fig.9. The plot of dip position vs glucose concentration.

Noted that the boronate ester bonding between PBA and PVA may not be the only crosslinking mechanism, as other forces, such as hydrogen bonding between PVA and PAA also contributes to the film build-up. These bonds are usually irreversible, thereby providing high stability for the multilayer films so that the PVA in the films does not fall off the film during the glucose-induced decomposition. Furthermore, the sensor presents glucose-sensitive behaviour at physiological pH may originate from the presence of the amide group in the PBA.

In order to investigate the temperature cross sensitivity, the sensor was placed into a heating condition from 25°C to 90°C. The results show that the peak wavelength of the sensor does not display obvious changes (approximately 1 nm) with temperature. Hence, the sensor can be used for temperature-insensitive RI measurement. Regarding the pH cross-sensitivity, we have mentioned earlier that this especially chemically synthesized PBA derivative binds to glucose at pH near 7.4, which is suitable for the detection of the glucose concentration under physiological conditions. This characteristic already shows that PBA derivatives-based glucose sensor does not exist the pH cross sensitivity problem. Therefore, when the sensor is used to detect the glucose concentration under physiological conditions, the cross sensitivity problem caused by temperature and pH can be ignored.

IV. CONCLUSION

A thin core fiber optics glucose-sensitive sensor based on PAA-PBA/PVA multilayer films has been demonstrated. LbL assembly of the PAA-PBA and PVA films on the optical fiber MI surface were used to fabricate the sensor probe. The glucose response of the (PAA-PBA/PVA)₃ functioned fiber was evaluated in the glucose concentration range of 0μm-10mM and results shows that the proposed sensor has excellent sensitivity to glucose under physiological pH. The proposed

sensor offers much simpler fabrication and high selectivity and has potential applications in insulin delivery system.

REFERENCES

- [1] E. F. Pfeiffer, "The glucose sensor: the missing link in diabetes therapy," *Hormone and metabolic research. Supplement series*, vol. 24, pp.154-164, 1990.
- [2] E.H. Yoo and S. Y. Lee, "Glucose biosensors: an overview of use in clinical practice," *Sensors*, vol. 10, no. 5, pp. 4558-4576, 2010.
- [3] H. Eggert, J. Frederiksen, C. Morin, and J.C. Norrild, "A new glucose-selective fluorescent bisboronic acid. first report of strong α-Furanose complexation in aqueous solution at physiological pH," *The Journal of Organic Chemistry*, vol. 64, no. 11, pp. 3846-3852, 1999.
- [4] T. James, "Saccharide-selective boronic acid based photoinduced electron transfer (PET) fluorescent sensors," *Creative Chemical Sensor Systems*, pp. 107-152, 2007.
- [5] S.Gamsey, J. T.Suri, R. A.Wessling, and B. Singaram, "Continuous glucose detection using boronic acid-substituted viologens in fluorescent hydrogels: linker effects and extension to fiber optics," *Langmuir*, vol. 22, no.21, pp. 9067-9074, 2006.
- [6] M.Seno, K.Yoshida, K.Sato, and J. I. Anzai, "pH-and sugar-sensitive multilayer films composed of phenylboronic acid (PBA)-modified poly (allylamine hydrochloride) (PBA-PAH) and poly (vinyl alcohol) (PVA): A significant effect of PBA content on the film stability," *Materials Science and Engineering: C*, vol. 62, pp. 474-479, 2016.
- [7] T.Seki, M.Namiki, Y.Egawa, R. Miki, K.Juni, and T.Seki, "Sugar-responsive pseudopolyrotaxane composed of phenylboronic acid-modified polyethylene glycol and γ-cyclodextrin," *Materials*, vol. 8, no. 3, pp.1341-1349, 2015.
- [8] Takahashi, Shigehiro, and Jun-ichi Anzai, "Phenylboronic acid monolayer-modified electrodes sensitive to sugars," *Langmuir*, vol. 21, no.11, pp. 5102-5107, 2005.
- [9] Y.Egawa, T.Seki, S.Takahashi, and J. I. Anzai, "Electrochemical and optical sugar sensors based on phenylboronic acid and its derivatives," *Materials Science and Engineering: C*, vol. 31, no.7, pp.1257-1264, 2011.
- [10] Ruijiang Ma, and Linqi Shi, "Phenylboronic acid-based glucose-responsive polymeric nanoparticles: synthesis and applications in drug delivery," *Polymer Chemistry*, vol. 5, no. 5, pp. 1503-1518, 2014.
- [11] Xi Zhang, Ying Guan, and Yongjun Zhang, "Dynamically bonded layer-by-layer films for self-regulated insulin release," *Journal of Materials Chemistry*, vol. 22, no. 32, pp. 16299-16305, 2012.
- [12] R.Watahiki, K.Sato, K.Suwa, S.Niina, Y.Egawa, T. Seki, and J. I. Anzai, "Multilayer films composed of phenylboronic acid-modified dendrimers sensitive to glucose under physiological conditions," *Journal of Materials Chemistry B*, vol. 2, no. 35, pp. 5809-5817, 2014.
- [13] F. Chiavaioli, C. Gouveia, P. Jorge, and F. Baldini, "Towards a uniform metrological assessment of grating-based optical fiber sensors: From refractometers to biosensors," *Biosensors*, vol. 7, no.2, pp. 23, 2017.
- [14] H. W. Qiu, S. C. Xu, S. Z. Jiang, Z. Li , P. X. Chen, S. S. Gao, C. Zhang and D. J. Feng, "A novel graphene-based tapered optical fiber sensor for glucose detection," *Applied Surface Science*, vol. 329, pp. 390-395, 2015.
- [15] S. K. Srivastava and D. G. Banshi, "Localized surface plasmon resonance-based fiber optic U-shaped biosensor for the detection of blood glucose," *Plasmonics*, vol. 7, pp. 261-268, 2012.
- [16] S. Singh and B. D. Gupta, "Fabrication and characterization of a surface plasmon resonance based fiber optic sensor using gel entrapment technique for the detection of low glucose concentration," *Sensors and Actuators B: Chemical*, vol. 177, pp. 589-595, 2013.
- [17] A. Deep, U. Tiwari, P. Kumar, V. Mishra, S. C. Jain, N. Singh, P. Kapur, and L. M. Bharadwaj, "Immobilization of enzyme on long period grating fibers for sensitive glucose detection," *Biosensors and Bioelectronics*, vol. 33, pp. 190-195, 2012.
- [18] B.Jiang, K.Zhou, C.Wang, Q.Sun, G. Yin, Z.Tai and L.Zhang, "Label-free glucose biosensor based on enzymatic graphene oxide-functionalized tilted fiber grating," *Sensors and Actuators B: Chemical*, vol. 254, pp.1033-1039, 2018.
- [19] S. Tierney, S. Volden and B. T. Stokke, "Glucose sensors based on a responsive gel incorporated as a Fabry-Perot cavity on a fiber-optic readout platform," *Biosensors and Bioelectronics*, vol. 24, no. 7, pp. 2034-2039, 2009.
- [20] H. U. Hassan, J. Janting, S. Aasmul, and O. Bang, "Polymer Optical Fiber

- Compound Parabolic Concentrator Fiber Tip-Based Glucose Sensor: In Vitro Testing," *IEEE Sensors Journal*, vol. 16, pp. 8483-8488, 2016.
- [21] R. Ballerstadt, C. Evans, A. Gowda and R. McNichols, "Fiber-coupled fluorescence affinity sensor for 3-day in vivo glucose sensing," *Journal of diabetes science and technology*, vol. 1, pp. 384-393, 2007.
- [22] H. U. Hassan, A. Lacraz, K.Kalli and O. Bang, "Femtosecond laser micromachining of compound parabolic concentrator fiber tipped glucose sensors," *Journal of Biomedical Optics*, vol. 22, no. 3, pp. 037003-037003, 2007.
- [23] Z. Ding, Y. Guan, Y. Zhang, and X. X. Zhu, "Layer-by-layer multilayer films linked with reversible boronate ester bonds with glucose-sensitivity under physiological conditions," *Soft Matter*, vol. 5, no. 11, pp. 2302-2309, 2009.
- [24] H. Q. Yao, F. W. Chang, and N. F. Hu, "PH-switchable bioelectrocatalysis based on layer-by-layer films assembled through specific boronic acid-diol recognition," *Electrochimica Acta*, vol. 55, no. 28, pp. 9185-9192, 2010.
- [25] B. Wang, K. Yoshida, K. Sato and J. I. Anzai, "Phenylboronic Acid-Functionalized Layer-by-Layer Assemblies for Biomedical Applications," *Polymers*, vol. 9, no. 6, pp. 202, 2017.
- [26] W. C. Wong, C. C. Chan, L. H. Chen, Z. Q. Tou and K. C. Leong, "Highly sensitive miniature photonic crystal fiber refractive index sensor based on mode field excitation," *Optics letters*, vol. 36, no. 9, pp. 1731-173, 2011.