Application performance of silicon-based different biosensors

Yiqian Lang *
Department of Chemistry, University College London, London, United Kingdom
* Corresponding Author Email: yiqian.lang.23@ucl.ac.uk

Abstract. Biosensor is the equipment for biomolecules detection and it has been widely applied in a diverse of different fields such as disease diagnosis and harmful substance detection. Introducing different types of functional materials into biosensor can give it unique characteristics such as high sensitivity and high selectivity. Silicon, carbon nanotubes, gold, graphene and platinum are all trending materials for designing biosensors. Silicon is a non-toxic material that is commonly used as an element for biosensors. Different types of silicon-based functional materials have also been developed, where these silicon-based biosensors can provide more sensitive, specific and easy sensing. This research describes the detection performance of several silicon-based biosensors and discuss their advantages and disadvantages from the experimental results. In addition, this research will give a description of their applications and future development prospects. As the study of silicon-based biosensor get more deeper, it has great potential used in clinical or medical analysis.

Keywords: Biosensors; silicon materials; application.

1. Introduction

Biosensor is the instrument that is sensitive to the biological substance and transfer its concentration into electrical or optical signal. It is composite of biological recognition element, transducer and reader device which amplify the signal and process the data. The data obtained can be converts to specific quantitative or semi-quantitative analytical information. The advent of biosensors makes the detection and analyze of substance easier. The development of technology of biosensors is certainly crucial in the measurement science. Biosensors possess high selectivity, high sensitivity, fast analysis speed and cost-effective. There are huge number of biological molecules, the difference of structures and properties between them might be small which is difficult to detect. The method for efficient detection of these various molecules is required. Thus, types of biosensors are invented according to the experimental requirements and the characteristics of molecules, including electrochemical biosensors, optical biosensors, fluorescent biosensors and piezoelectric biosensors. Multiple types of biosensors allow it utilized in many areas such as medical diagnosis and detection of harmful substances in food.

As the research of biosensors gradually deepen, it has a wide range of application prospects and has a place in the advance of biotechnology. While application of biosensors is based on the application of materials, such as gold, graphene, carbon nanotubes and platinum. The good properties of the materials can give the biosensors specific properties and functions. Silicon is a common element in nature with high thermal stabilities and excellent electrical conductivity. Silicon and its various nanostructure are well-known used as semiconductor in electronics, optics and photovoltaics. However, the biosensors with silicon-based nanostructure is not as popular as it is semiconductor. In recent years, the research of silicon-based nanostructured biosensors has grown. Mostly investigating the application and properties influenced by the arrangement of silicon-based nanostructure. The current arrangement of silicon-based nanostructured biosensors mainly involves porous silicon, silicon nanowire, silicon nanophotonic structures. Porous silicon used in non-enzymatic glucose biosensors is effectively in human blood sample detecting. The structure of porous provides higher surface area and improve the performance of typical biosensors [1]. Silicon nanowire has good optical properties due to its 1-dimensional structure. The properties make silicon nanowire can be used in detecting complex sample and gives the results sensitively, label-free and in real time. Therefore, silicon nanowire biosensors have been applied as a new quantitating detection in clinical application. For example, quantitating tumor marker ctDNA utilized by the silicon nanowire biosensors can increase the ultralow detection limit and shown in a great specificity, repeatability and reproducibility [2]. However, the inhomogeneity of silicon nanowire device and the inference of complex composition of biological sample will limit the selectivity of silicon nanowire biosensors [3]. This causes the application of silicon biosensors in the medical practice is tough. Silicon nanophotonic biosensors is used as an analytical tool for the OP pesticides monitoring, environmental applications and clinical use due to its high sensitivity, speediness, high specificity and real time detection [4]. Therefore, silicon-based nanoparticles used in biosensors has high sensitivity, optical, cost-efficient, high specificity and give the result in real time. It has greater performance, especially in sensitivity, and it has great value of application in clinic, diagnosis and environmental monitoring in the future. To this end, this research will mainly discuss the application of silicon-based biosensors.

2. Different types of silicon-based biosensors

Yaghoubi et al. developed a new silicon-based biosensor and used it to label-free detection of bacteria [5]. They utilized the reflectometric interference on the Fourier transform spectroscopy (RIFTS) to detect the bacterium: *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*), *Klebsiella aerogenes* and *Bacillus subtilis* in real time and label-free. Concanavalin A (ConA) and wheat germ agglutinin (WGA) possess the strongest binding affinity respective with *E. coli* and *S. aureus* which improved the efficiency of detection. Further experiments with *Klebsiella aerogenes* and *Bacillus subtilis* confirmed the speculation that WGA and ConA contains greater interaction affinity for Gram-positive and Gram-negative bacteria separately. Due to the particular carbohydrate-binding properties, acceptable specificity and low price of lectin, its combination with PSi to form biosensors that provides an efficient, stable and low-cost assays rather than typical antibodies or nucleic acids-based detection techniques. However, due to the relatively small size of lectins molecules compared to antibodies and the polyvalence (multiple binding sites) of lectins. The binding sites on the surface of these molecules are more concentrated, hence lectins have weaker affinity than antibodies.

Maniya et al. fabricated mesoporous PSi optical biosensor for detection of heat shock protein 70 (HSP70) [6]. HSP70 is a large biomolecule that can easily block the pores of PSi. PSi monolayer samples are made by electrochemical etching and thermal oxidation additionally enhanced the stability. The porosity and thickness values of PSi platform produced were 68%±3% and 2400±30 nm, respectively. The average pore diameter of PSi was discovered to be approximately 40±20 nm. In the testing of HSP70, the PSi optical biosensor indicated the limit of detection is 1290±160 ng/mL in the range of 3000–500000 ng/mL. The large biomolecule HSP70 and anti-HSP70 was verified the non-blocking of pores by reflectance spectroscopy and RIFTS. Also, the PSi biosensor has no binding immunoglobulin G (IgG) on the sensor surface which proved the specificity of PSi biosensor. The HSP70 biomarker can be detected with high specificity using this biosensor. Currently reported biosensor for HSP70 detection has the major drawbacks of costly electrodes or complicated manufacture and analyzing program. PSi provides a reduced price, simple and label-free HSP70 identification due to its benefits. The HSP70 biomarker can be detected with high specificity using this biosensor.

Silicon-based photonic crystal microcavity biosensors was created by Yang et al. for the recognizing the plasma protein of pancreatic cancer patients [7]. The biosensor was composite of complementary metal oxide silicon (CMOS) with great multiplexed compatibility and applied slow light effect of defect-engineered photonic crystal waveguide (PCW). The biosensor was based on the principle of PCW resonator, the modifications of refractive index caused by the combination between the sensors and target biomolecules displayed the changes of the resonance wavelength and frequency. The experimental results revealed the eventual detectable limit for all platforms were considerably conducted by analyte absorbance, equipment limited spectral noise and temperature noise. This biosensor could label-free monitor sixty-four distinguish biomarkers in the identical chip at the same time. The study analyzed three proteins in plasma samples from patients and compared them with classic enzyme-linked immunosorbent assays (ELISA). The device was particularly sensitive in determining extremely minute amounts of biomarkers representing the beginning stages of pancreatic cancer. In the experimental assay, the level of the pancreatic cancer biomarker detected in the patient's plasma samples was 8.8 femto-molar (0.3346 pg/mL) concentration, which is 50 times lower than the value detected by ELISA. In addition, the greatest sensitivity and specificity of this biosensor has been approved in the determination and drug screening of single lung cancer bookmakers. The components of silicon-based photonic crystal microcavity biosensors were used commercially available criterion CMOS foundry that ensure massive production at low cost.

Rodríguez-Montelongo et al. applied PSi DNA biosensors for diagnosis of risky human papilloma virus 16 and 18 (HPV 16 and HPV18) which probably cause precancerous and cancerous lesions occur [8]. They made a use of standard amino-silane and glutaraldehyde chemistry (PSiMc/HPV-ssDNA) to allow ssDNA oligonucleotides of HPV 16 and 18 forming bioconjugation with the PSi pores. The modification makes the average pore diameter of PSiMc decreased from 20.5±6 nm to 8.5±4.4 nm without blocking the pores. After the biosensor attach with the complementary DNA, the changes of effective refractive index of device detected identify the virus. Moreover, they placed the hybrid apparatus in the mixture of DNA molecules with the complementary and non-complementary bases for determine the behavior of HPV/PSi biosensor. This biosensor could recognize the complementary strands of DNA selectively that verified by fluorescence microscopy and spectroscopy. Therefore, it can be used for distinguish the complementary and non-complementary DNA. They also found the fluorescent signal of hybrid DNA is around five times greater than not hybridized DNA. According to the detection the negative sample, the biosensor showed excellent selectivity and capable to identify the viral category. This biosensor takes the benefit of analysis, quantification and typing simultaneously.

Qiu et al. set up the silicon-based field-effect biosensor to measure the variation of cardiac extracellular calcium ion that induced by drug [9]. Calcium ion generally take part in adjust all biological functions of the body. Calcium ions is regards as the vital signals via ion transporters in cardiac excitation-contraction coupling. Light-addressable potentiometric sensor (LAPS) biosensor is only applied in monitoring metabolic pH in solution environment. They combined the LAPS platform with all-solid-state silicone-rubber ion-sensitive membrane (ISM) for calcium ion detection outside the cardiac cell. This confers the biosensor ion sensitive, field-effect-based and programme manipulable properties. The experimental results show that the pH of solution had only a minimal effect on the test performance of biosensors. The use of L-type calcium channels blocker verapamil weakens the antagonism of ion channel, resulting in a decrease in extracellular calcium ion concentration. Calcium channel agonist BayK8644 showed the opposite effect. However, both of them could bar the cell activity at intensive drug content. As a result, BayK8644 is more suited for calcium ion transportation. The biosensor could assist more precise drug selection from the extra detailed data about calcium ion.

Kim et al. constructed a top-down technique silicon-based electrolyte-gated transistors (Si-EGTs) to label-free analyze peanut allergens (PAs): Arachis hypogaea 1 (Ara h1) and Ara h3 extreme sensitively [10]. The introduction of EGT can enhance the binding probability of biomolecules, resulting in an amplification of the absolute sensing current. Micro- and nano-semiconductor machining tools were used to assemble the biosensor. The surface of Si-EGTs was modified by antigen-binding fragment (Fab) which is specifically directed against PAs for selective detection of PAs. Si-EGT has demonstrated superior inherent electrical features with a low threshold voltage (0.7 V), sub-threshold swing (<70 mV/dec) and gate leakage (<10 pA). From the subthreshold regime to the linear regime, the response of the voltage-related sensitivity (S_V) was consistent. The current-related sensitivity (S_I) exhibited elevated values in subthreshold region and S_I value reduced along with drain current reduction. According S_I characteristics, Si-EGT achieves the lowest limit of detection (LOD) figures that have been published in the literature to date for the measurement of the several sensor techniques are as low as 25 pg/mL. As shown in Fig. 1, non-specific binding tests further validated the outstanding specificity. As a consequence, Si-EGT can be used for ultra-sensitive and energy-efficient PAs recognition and assay in food sample.

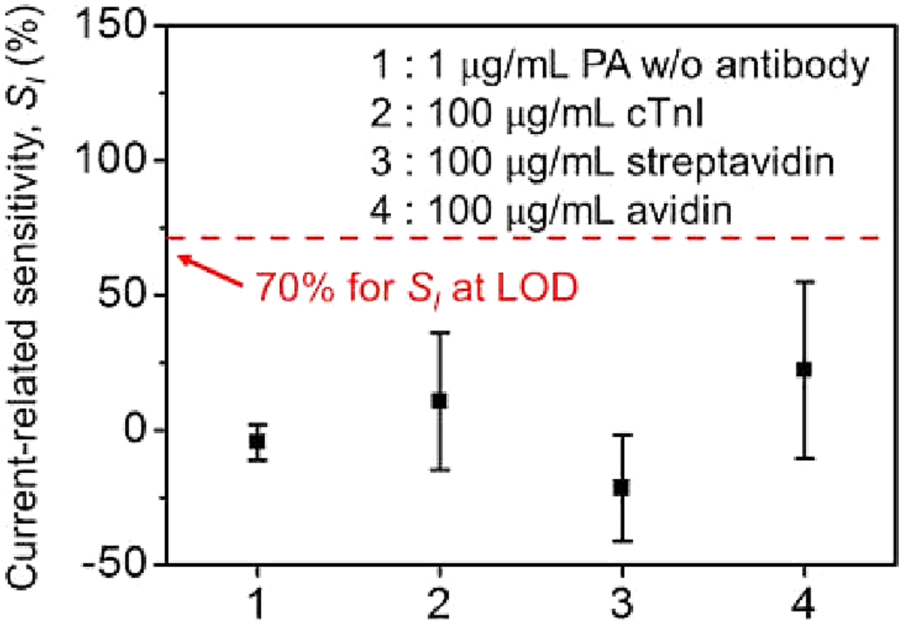

Fig 1. Selectivity analysis of the developed biosensing method [10].

3. Conclusion

This research discusses the application performance of different types of silicon-based biosensors. The silicon-based biosensor can be conjugated with lectins of ConA and WGA for bacterium detection, showing remarkable binding affinity with *E. coli* and *S. aureus* respectively. Label-free sensing of HSP70 by the PSi optical biosensor has limit of detection 1290±160 ng/mL. It has superior specificity towards the HSP70 biomarkers. Silicon-based photonic crystal microcavity biosensor can simultaneously identify sixty-four different biomarkers in the same chip. The biosensor determines minimal quantities of biomarkers which acting as precursors of pancreatic cancer sensitively and accurately compared to ELISA. PSi DNA biosensors for diagnosis of risky HPV 16 and HPV18 can monitor, quantifies and differentiate viral types at the same type. The pH of environment has negligible effect on the measurement of cardiac extracellular calcium ion that lead by drug. Si-EGTs can label-free, sensitive and specific analyze PAs and illustrate wonderful internal electrical performances.

References

[1] Ahmed J, Rashed M A, Faisal M, et al. Novel SWCNTs-mesoporous silicon nanocomposite as efficient non-enzymatic glucose biosensor. Applied Surface Science, 2021, 552: 149477.

[2] Li D, Chen H, Fan K, et al. A supersensitive silicon nanowire array biosensor for quantitating tumor marker ctDNA. Biosensors and Bioelectronics, 2021, 181: 113147.

[3] Lu Z, Liu T, Zhou X, et al. Rapid and quantitative detection of tear MMP-9 for dry eye patients using a novel silicon nanowire-based biosensor. Biosensors and Bioelectronics, 2022, 214: 114498.

[4] Ramirez-Priego P, Estévez M C, Díaz-Luisravelo H J, et al. Real-time monitoring of fenitrothion in water samples using a silicon nanophotonic biosensor. Analytica chimica acta, 2021, 1152: 338276.

[5] Yaghoubi M, Rahimi F, Negahdari B, et al. A lectin-coupled porous silicon-based biosensor: label-free optical detection of bacteria in a real-time mode. Scientific Reports, 2020, 10(1): 16017.

[6] Maniya N H, Srivastava D N. Fabrication of porous silicon-based label-free optical biosensor for heat shock protein 70 detection. Materials Science in Semiconductor Processing, 2020, 115: 105126.

[7] Yang C J, Yan H, Tang N, et al. Ultra sensitivity silicon-based photonic crystal microcavity biosensors for plasma protein detection in patients with pancreatic cancer. Micromachines, 2020, 11(3): 282.

[8] Rodríguez-Montelongo S A, Moreno-Gutiérrez D S, Terán-Figueroa Y, et al. Porous Silicon-Based DNA Biosensor for Human Papillomavirus Detection: Towards the Design of Fast and Portable Test. Silicon, 2023, 15(5): 2371-2383.

[9] Qiu Y, Ma C, Jiang N, et al. A Silicon-Based Field-Effect Biosensor for Drug-Induced Cardiac Extracellular Calcium Ion Change Detection. Biosensors, 2023, 14(1): 16.

[10] Kim D, Jin B, Kim S A, et al. An ultrasensitive silicon-based electrolyte-gated transistor for the detection of peanut allergens. Biosensors, 2022, 12(1): 24.