Progress in Medical Application of Silicon Nanowire Field Effect Tube Biosensor

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Abstract: In recent years, the silicon nanowire field effect transistor (SiNW FET) biosensor with a single crystal silicon core and one-dimensional nanostructure has become a hot research object, and is widely used in biomedical detection, suitable for the detection of biomarkers. In this paper, the applications of SiNW FET biosensors in the medical field in recent years are critically reviewed. Firstly, the basic structure, working mechanism, and the two preparation methods of "top-down" and "bottom-up" of SiNW FET biosensors are briefly introduced, especially the specific sensing mechanism of SiNW FET biosensors. Then, the three application directions of SiNW FET biosensors currently used in the biomedical field are summarized, including the detection of proteins, DNA/RNA, and viruses, and the limitations of the current research are pointed out. Finally, the possible research directions in the future are proposed, such as surface modification, flexible substrate integration, and nanotechnology. The challenges of SiNW FET biosensor development in the future are discussed extensively.

1 INTRODUCTION

In recent years, the silicon nanowire field effect transistor (SiNW-FET) biosensors have become widely popular research objects due to their advantages, such as extensive customizable parameters, high carrier mobility, ideal subthreshold slope, and nanoscale sensitivity. Yong et al. (2021) found that the lowest detectable concentration of HBsAg using SiNW-FET was 100 fg/mL, demonstrating its characteristic of ultra-high sensitivity. Due to its nanoscale size, the SiNW-FET biosensor is highly suitable for detecting most biomarkers, such as proteins, DNA/RNA, cells, and viruses. This makes the SiNW-FET biosensor have great application value and advantages in the medical field, providing accurate detection for the treatment of many diseases and thereby increasing the possibility of curing diseases.

In 2001, Field-effect transistors that utilize silicon nanowires were first reported to be applied in the detection of biological and chemical molecules (Li et al., 2022; Vu et al., 2023), surface-modified silica samples and SiNW-FET channels using silane-PEG, enabling precise quantification of cTnI and other protein biomarkers at an ultra-low level. In the field of medicine, the detection of various biomarkers by sensors has been successfully applied and has broad prospects for medical applications.

This paper first introduces the basic structure, preparation method, and working mechanism of the SiNW-FET biosensor. Subsequently, the medical application progress of these biosensors in the detection of proteins, DNA/RNA, and viruses was summarized. Based on the existing research methods and achievements at present, some possible solutions were provided for other medical application fields in the future.

2 THE BASIC STRUCTURE AND WORKING MECHANISM OF SINW FET BIOSENSOR

2.1 Structure of SiNW-FET Biosensor

Figure 1 shows functionalized silicon nanowires with source and drain electrodes at both ends. Specific antibodies are coated on the silicon nanowires, which

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can bind specifically to the target antigen and cause changes in electrical signals, manifested as changes in source-drain current. After specific binding with the antigen, the surface charge density changes, which in turn affects the conductivity of SiNW. Measuring the current can help detect the presence of the target antigen.

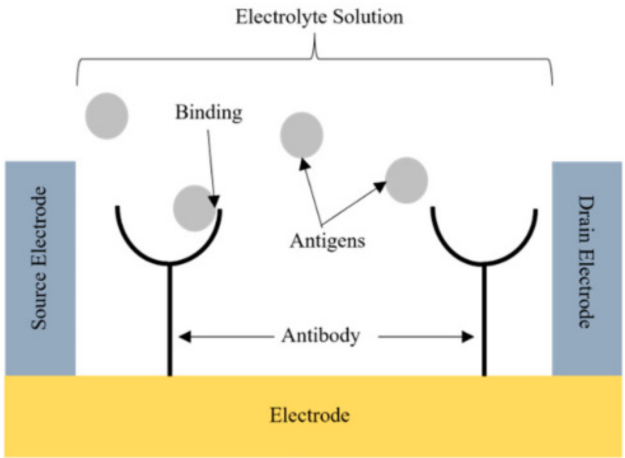

Figure 1: Structure of SiNW FET biosensor (Hadded et al., 2025)

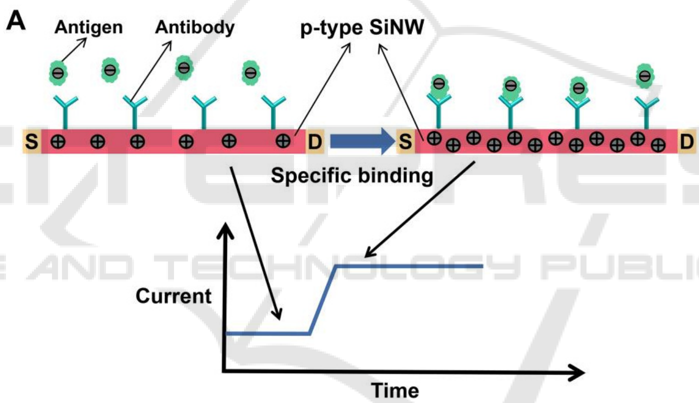

Figure 2: Detection principle of SiNW-FET biosensor (Li et al., 2022)

As shown in Figure 1, SiNW FET is a gate voltage semiconductor control device. Currently, the two main preparation methods for SiNW FET chips are "top-down" and "bottom-up". The "top-down" method has a mature preparation process, using advanced technologies such as nanomanufacturing and photolithography, which can prepare SiNWs with diameters of tens of nanometers from silicon wafers in specific environments, allowing for very large-scale integration. However, the top silicon layer's patterning and etching can result in geometric changes, which affect electrical parameters and require controlled conditions to reduce variations. The "bottom-up" approach can synthesize SiNWs with diameters ranging from a few nanometers to several hundred nanometers, and their quasi one-dimensional properties enable them to exhibit outstanding performance in fields such as electronics, optoelectronics, energy, and biomedical applications. However, there are technical challenges in achieving large-scale reproducible production (Tintelott et al., 2021; Arjman et al., 2022). In addition, silicon nanowires contain specific receptors that can bind to target biomarkers. Different types of SiNW FET biosensors can bind to different target molecules, and specific receptors coated on silicon nanowires can be customized for the target molecules that need to be recognized. In terms of biological detection, customizable SiNW FET biosensors can be surface-modified according to specific biomarker molecules, making them widely applicable to various detection needs.

2.2 The Working Mechanism of SiNW-FET

Figure 2 illustrates this, when charged biomarker molecules bind specifically to specific receptor (probe) molecules on silicon nanowires, the conductivity of SiNW changes. Among them, changes in current between the source and drain electrodes can be recorded by the semiconductor analyzer. If biomarker molecules are negatively charged, their binding with specific receptor (probe) molecules will increase conductivity and current. On the contrary, if biomarker molecules are positively charged, their binding with specific receptor (probe) molecules will reduce conductivity and current (Li et al., 2022).

From the perspective of changes in charge density, the sensing mechanism of SiNW FET is actually to recognize different biomarker molecules by binding to them, resulting in changes in the electric field on the surface of SiNW (Zhang, & Ning, 2012). The SiNW-FET biosensor has successfully measured the concentration of miRNAs at the fly molar level through surface modification, also known as surface modification, which is an important method for preparing SiNW FET biosensors with specific recognition functions (Vu et al., 2022).

3 APPLICATION SCENARIOS AND CASE ANALYSIS IN THE MEDICAL FIELD

3.1 Protein Detection

Protein is a kind of nutrient and plays an important role in human life activities. Protein is a component of many substances, such as most hormones in the human body, the protein coat of viruses, and ribosomes in bacteria. Therefore, the precise detection of proteins is a crucial aspect in medical applications.

The detection of Cys-C in the human body is of great significance for the prevention of acute kidney injury (AKI). Blood is one of the bodily fluids that contains the cysteine protease inhibitor Cys-C. It is considered to be an early indicator of AKI that is linked to glomerular filtration rate (GFR) (Hu et al., 2023). Hu et al. (2023) concluded that it is evident that the SiNW-FET biosensor they prepared has advantages in detecting the biomarker Cys-C for early renal failure. The detection limit is 0.25 ag/mL when the Cys-C concentration range is 1 ag/mL and 1 ng/mL, enabling linear detection to be performed. Liu et al. (2023) fabricated a single-molecule device based on SINW-FET by performing point modifications and constrained reactions on the side walls of SiNW. The experimental results show that the biosensor constructed using high-performance SiNW-FET molecular nanocircuits has high temporal resolution and sensitivity. Complex polymorphic current signals can be observed in the low DQ47 concentration range (5-500 nm) at a temporal resolution of 17μs. Their SiNW-FET single-molecule platform is mentioned as being suitable for various label-free biological detections with a single-molecule resolution.

Glycated hemoglobin A1c (HbA1c) is an indicator for measuring the long-term blood glucose control of complications related to chronic diabetes. The SiNW-FET sensor can rapidly determine the level of HbA1c in human blood and is suitable for immediate diagnosis (Vu et al., 2022). Anand et al. (2021) pointed out that compared with the determination methods carried out in professional laboratories, the SiNW-FET sensor has the advantages of low cost, rapidity, and convenience. It uses A short synthetic engineered DNA or RNA oligonucleotide called an aptamer. Self-assembling into a unique recognition motif is capable of capturing target molecules with high affinity and specificity.

A large number of relevant studies have shown that SiNW-FET biosensors have great potential and can gradually be more widely applied in the detection and targeted therapy of substances composed of proteins in organisms in the future.

3.2 Detection of DNA/RNA

The presence of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) in the cells of all living organisms is crucial for protein encoding and storage of genetic information (Lu et al., 2024). Circulating tumor DNA (ctDNA) is a method that shows promise for detecting cancer, targeted therapy, and prognosis. Li et al. (2023) modified DNA probes on SiNW arrays through silanization, and the experimental results showed that Human serum samples were successfully identified by the SiNW-FET biosensor that was prepared, demonstrating promising clinical application potential in the future.

At present, biosensors used for detecting DNA mainly use peptide nucleic acid (PNA) as probes, which specifically bind to ctDNA to capture target DNA. The biosensor's surface is bonded to the PNA probe using covalent bonding modification technology, and a stable complex is formed by base complementary pairing principle and DNA-specific binding (Lu, H. et al., 2024). When a normal ctDNA (ncDNA) solution is dropped onto the electrode, there is almost no potential change. This new technique uses complementary pairing of DNA probe bases to achieve excellent selectivity and ultra-high sensitivity, and can detect abnormal ctDNA methylation levels by chemically modifying SiNW FET biosensors (Wang et al., 2022). Yusoh et al. (2021) used p-type silicon on insulator (SOI) wafers to fabricate SiNW biosensors, and Based on the results, a 10-wire SiNW device that was etched with 25% by weight TMAH and 10% by volume IPA was the most sensitive, reaching 82.8 AM-1, with a minimum LOD of 1.93 fM. They successfully detected dengue fever DNA and pointed out that the sensitivity of SiNW FET DNA biosensors was affected by three factors: wire quantity, wire size, and surface roughness.

The diagnosis of various diseases is greatly affected by microRNA (miRNA) sensing, especially cancer. To date, SiNW FET biosensors have been able to accurately assess the concentration of miRNAs at the femtomolar level through a simple surface modification method. By using mSAM of silane PEG-NH on the SiNW surface, Vu et al. (2022) enhanced the performance of SiNW FET DNA biosensors for miRNA detection, resulting in more significant signal changes of DNA/RNA complexes under high ionic strength conditions and improved detection accuracy.

The SiNW FET biosensor for detecting DNA/RNA has great application value and potential, which may provide new ideas and methods for the diagnosis and treatment of major diseases and cancers.

3.3 Virus Detection

The virus is a microbial pathogen whose genetic material contains only one type of nucleic acid. It must parasitize within living cells and is very common in the human living environment. For detecting whether the human body is infected with a virus, the currently widely used method is antigen kits, such as the COVID-19 rapid test kit (Li et al., 2021).

The SiNW-FET biosensor, which has the advantages of real-time monitoring and being label-free, can be mass-produced in the semiconductor industry and is therefore suitable for the convenient detection of COVID-19. Wang et al. used anti-IL-6 antibodies or anti-IL-6 aptamer probes as specific biometric elements on SiNW-FETs and concluded that using aptamer-functionalized SiNW-FETs to identify IL-6 levels in patients with severe COVID-19 has the potential to be significant. However, further research is necessary to confirm if aptamer-functionalized SiNW-FET can fulfill the clinical requirements for determining the severity of COVID-19 patients (Li et al., 2021).

Dengue fever is a viral infection transmitted by arthropods that is prevalent worldwide and belongs to the genus Flavivirus of the Flavivirus family. Zhang et al. (2010) reported that this SiNW-FET biosensor is powered by electricity and integrates biomolecules with technology that is compatible with metal-oxide-semiconductor (CMOS), facilitating the detection of charge changes when the target analyte is bound to a fixed probe. The experimental results show that, to demonstrate the concept, the SiNW sensor was combined with RT-PCR technology, using nucleic acid hybridization and electrical detection, has been developed for label-free, specific, rapid, and highly sensitive detection of dengue virus in research.

The SiNW-FET biosensor is used for virus detection and can provide a rapid and convenient detection method for influenza and viral infectious diseases, as well as a specific treatment plan for a possible disease, which has great potential.

4 CONCLUSION

This article summarizes the application of SiNW FET biosensors in the medical field in recent years. Firstly, the preparation methods and working mechanisms of SiNW FET biosensors are introduced, mainly involving surface modification, "top to bottom" and "bottom to top" technologies, nano manufacturing, etc. The customizable specificity, label-free nature, and high detection efficiency of SiNW FET biosensors have excellent development prospects in the future. The examples given in this article reflect the wide application of SiNW FET biosensors in targeted detection and treatment of more tumor cells, detection of new viruses, and determination of animal health status.

At present, SiNW FET biosensors have great potential and application value in the medical field, but there are still limitations, such as some limitations in medical care point diagnosis and in addressing the inherent stiffness and brittleness of wearable silicon applications. However, it is expected that in the future, surface modification, flexible substrate integration, and nanotechnology will continue to develop to overcome these limitations.

In summary, SiNW FET biosensors are convenient, fast, highly sensitive, and specific for detecting proteins in medical applications. DNA/RNA、 Viruses provide an efficient and novel solution, demonstrating their enormous potential for clinical applications. Future research directions may include surface modification, nanotechnology, etc., to overcome wearable applications, as well as the use of SiNW FET biosensors to detect biomarkers of various other diseases and assist in treatment. They have broad research value and good development prospects.

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