Topical Review

Recent advances in field effect transistor biosensor technology for cancer detection: a mini review

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Abstract
Cancer is an incurable disease, and the treatment process is extremely painful. Early detection may ease the treatment process and prevent cancer from spreading beyond the primary disease area. However, conventional screening tests have long detection times and lack the required sensitivity for early detection. Consequently, traditional cancer biosensors, including amplification refractory mutation system, digital polymerase chain reaction, next generation sequencing, western blot, electrochemical, and mechanical biosensors, have been studied in recent years. Specifically, field effect transistor (FET) biosensors, are attractive pocketable devices with short detection time capabilities. Because FET biosensors have outstanding electrical and mechanical properties, FET biosensors have been studied for their efficacy in the early detection of cancer. Traditional detection methods of cancer biomarkers include the use of FET biosensors for the detection of cancer biomarkers, especially gene, antigen, and protein characteristics. This review presents the latest strategies in FET applications in cancer biosensing and compares their advantages and disadvantages regarding sensing principle, configuration, and performance. Especially, FET biosensors for the detection of cancer biomarkers, which include antibodies, nucleic acids, proteins are highlighted. Mechanical and electrical properties of FET devices and their effect on performance is discussed. This review provides a guiding role in the design and development of FET-based biosensors.

Keywords: field effect transistor, biosensor, cancer, detection, application

(Some figures may appear in color only in the online journal)
1. Introduction

Diseases of malignant tumors seriously affect human health and have a high mortality rate that threatens human lives. Its early detection and diagnosis can reduce patient mortality and improve the effect of the treatment [1–4]. Cancer biomarkers are a valuable tool for staging certain cancers, monitoring cancer development, and assess the prognosis of treatment [5–7]. After the formation of tumor, changes in the levels of several biomarkers can be detected in blood samples or other body fluid samples [8, 9]. In order to distinguish subtle changes in levels of biomarkers in complex clinical blood samples or other body fluid samples, therefore, diagnostic analysis must be rapid, sensitive and selective. Traditional cancer detection technologies often involve multiple steps such as more complicated pretreatment, time consuming nucleic acid amplification, and target detection, which are not suitable for clinical practical applications.

With the high development of microelectromechanical system (MEMS) technology, micro device with clinical sample detection functions can be manufactured and integrated with a mini-chip [10]. MEMS such as carbon nanotube field effect transistor (CNT-FET) and nanowire FET (NW-FET), have received much attention because of their ability to directly convert interaction of the receptor with target molecules immobilized on the surface of the FET channel into electrical signals [11]. Sensing performs sample detection by detecting changes in the conductivity of the FET channel, which is caused by an interaction of analyte molecules from sample with the receptor on the device channel. The change in the effective charge of the molecule causes a change in the threshold voltage and current of the FET sensor [12]. To the best of our knowledge, the conductivity of the FET channel is highly sensitive to the detection of analyte-receptor binding.

Therefore, the FET sensor provides a comprehensive and effective method for detecting various biomolecules [13]. FET-sensing technology enable many processes that are important to human life, such as environmental monitoring [14–16], medical diagnostics [17–20], food safety [21–23], gas detection [24–26], etc. FET biosensors are similar to complementary metal oxide semiconductor circuits. Furthermore, they can be fabricated at a very small size for a low-cost using MEMS technology [24].

The nano-scale cancer FET biosensor is a versatile and multiphasic technological tool that can achieve early and rapid cancer detection [27]. FET biosensing in Indirect detection of drain current (I_D) by controlling the gate electrode voltage (V_G). The FET response is determined by a change in the channel surface potential of the biological sample, which is affected by charged molecules [28, 29]. In recent years, FET biosensors have been described as ideal candidates for early detection of different cancers [30]. FET devices enhanced with nanomaterials have been used for early detection of cancer [31]. Typical biomarkers for early detection of cancer are deoxyribo nucleic acid (DNA), protein, and antibodies, although there are other useful biomarkers [32–34]. Measurement of cancer biomarkers can provide important information that supports: (a) making a diagnosis, assessing disease severity, and determining the efficacy of treatment, (b) indexing organ or tissue function, and (c) determining risk biomarkers for the prediction of cancer, which guides future development of high-performance biosensors.

2. Structure and working principle of FET biosensor

FET biosensors primarily consist of two parts—a sensitive film composed of semiconductor material used for biomolecule recognition and a signal conduction component, which is the traditional FET device [35–37]. The manufacturing process of FET biosensor involves preparing the source (source, S) and drain (drain, D) on the silicon substrate via an etching process and then preparing the gate (gate, G) between S and D [38, 39]. Between the S and D of the FET, a sensitive film is prepared and biological functional substances are fixed on its surface. A measurement circuit is added to form a complete FET biosensor [40, 41]. When the fixed biological functional substance comes into contact with the substance to be tested, a specific reaction occurs, causing the electrons of the sensitive membrane to move, thereby indicating the amount of the substance to be tested (figure 1). Bias voltage detection methods of FET biosensors are usually divided into top, back, or solution gate.

2.1. Top-gate biosensor

The top-gate biosensor can be used as an extremely effective detection method; however, the preparation method of the biosensor is relatively simple. The top gate can be used as a sensing component, and a piezoresistive effect can be used to alter the signal emitted from the FET. Consequently, the strain in the cantilever reduces the mobility of electrons in the base, thereby reducing the leakage current. As shown in figure 2(A), Chalklen et al [42] used a top-gate biosensor to detect the deflection of the cantilever and the adsorption of the analyte. Bungon et al [43] used a top-gate biosensor to detect the deflection of the cantilever and the adsorption of the analyte. Bungon et al [43] demonstrated the use of evaporated chromium and sputtered gold on a p++ Si/SiO2 substrate.

The contact lithography patterning and metal lift-off technology fabricated the top-gate FET biosensor for Alzheimer’s disease protein biomarker clusterin detection. Jeseung et al [44] developed a metal-semiconductor FET biosensor with a CNT film. A gold top-gate is placed in the middle of the CNT channel, and the probe antibody is fixed on a gold top-gate with antibody binding protein G or an Escherichia coli outer membrane with the Z domain of protein A. This biosensor has high sensitivity (figure 2(B)).

2.2. Back-gate biosensor

The back-gate biosensor has maximum detection area. A silicon substrate is used as a common back gate, and a silicon dioxide is used as a gate dielectric layer of this type of FET.
biosensors [45]. The source and drain are formed via sputtering deposition and depositing patterned metal layers such as titanium. Second, the preparation of CNTs needs to be grown in an oxygen plasma atmosphere, and the vapor deposition growth of the electrode part needs to be coated with photoresist and patterned. Then, the photoresist was removed with organic solvents. Finally, annealing the device in vacuum (figure 3(A)) [46].

Figure 3(B) shows the Debye shielding effect in a back-gate graphene-FET [47]. Positive ions in the solution are attracted to the channel of FET. Antibody is a larger biomarker, when using face of FET channel in response to the back-gate this method to detect antibodies, if it is larger than the Debye length of the FET biosensor, the analyte will not attracted to the biological receptor, and thus the recognition reaction is less likely to occur. If we do not
consider other testing reasons, the detection method using back-gate biosensor of maximum detection area is relatively simply.

2.3. Solution-gate biosensor

The most common method of preparation produces a solution-gate FET biosensor, which can better simulate the human physiological environment. A reaction chamber made of polydimethylsiloxane is fixed on the substrate using silicone. The miniaturized Ag/AgCl electrochemical reference electrode is immersed in the reaction chamber as a gate electrode for sample functionalization (figure 4(A)). Then, drain-source voltage \( V_{ds} \) and gate-source voltage \( V_{gs} \) is applied to force the device to operate \([48, 49]\) bio-sensor devices that use graphene or reduction Graphene Oxide (rGO) as active materials in solution-gated FETs are superior to those that use other kinds of active materials \([50]\). Due to the nano electric double layer (EDL) at the graphene-solution interface, these devices exhibit high sensitivity to various analytes and operate at low-gate potentials \([51]\).

Ag/AgCl is the most common liquid gate electrode. Zeimpekis et al \([52]\) provided a comprehensive evaluation of pH and protein sensing when using Ag/AgCl as the gate electrode (figure 4(B)). Most FETs are unstable under water-based conditions, have low sensitivity, and require traditional Ag/AgCl electrodes for gating. Han et al \([53]\) proposed a solution-gated graphene FET for real-time monitoring of microscale loop-mediated isothermal DNA amplification. The source, drain, and gate of the sensor all use gold electrodes (figure 4(C)).

3. Biomarker for traditional cancer detection and analysis

Biomarkers are considered to be indicators of various diseases (including cancer, viral infections, and autoimmune diseases) \([54, 55]\). Recently, a large number of specific biomarkers were discovered, which has led to the rapid development of biode-tection sensors to detect DNA, protein, antibody, and other biomarkers for traditional cancer detection \([56, 57]\).

3.1. Gene

DNA biomarker detection have been developed and evaluated for the tumor genotyping in liquid biopsy samples, their performance in clinical detection has been accepted \([58, 59]\). The range of potential gene detection biomarkers includes but is not limited to ribonucleic acid (RNA) transcripts, DNA and epigenetic changes \([60, 61]\).

Among them DNA methylation biomarker detection is considered to be an important part of epigenetic modification and has become a hot research topic in recent decades \([62]\). It usually occurs when a methyl group is added to the fifth carbon atom of cytosine while the base sequence of DNA remains unchanged \([63]\). With the development of analysis technology to deepen DNA methylation research, DNA methylation detection strategies based on biosensing technology have been developed \([64]\). Larsen et al \([65]\) reviewed the latest advances in DNA methylation-based biomarkers for the detection of bladder, prostate, kidney, and upper urinary tract cancer, and explained the clinical application potential of biomarkers of DNA methylation (figure 5).
3.2. Antigen

Antigen refers to all substances that can induce an immune response in the body. When individuals suffer from cancer, the level of cancer antigen in the blood will increase greatly [66]. The detected antigen can be used as a biomarker of primary cancer or metastatic cancer, meanwhile, the growth rate and invasiveness of the tumor can be evaluated by the antigen level correspondingly. For instance, carcinoembryonic antigen (CEA) is a typical biomarker for colon cancer and rectal cancer [67].

T-cell receptor gamma chain alternating reading frame protein (TARP) was first discovered in human prostate cancer and androgen-sensitive prostate cancer [68, 69]. Since then, TARP has been found in breast cancer and endometrial cancer, salivary gland tumors, and acute myeloid leukemia in children and adults [70]. Interestingly, TARP promotes tumor cell proliferation and migration, reflected in the poor survival rates [71, 72]. Expression of TARP in malignant cells and its role in tumorigenesis while having limited expression in normal tissues have aroused interest regarding its potential use as a therapeutic target, which has led to the development of immunotherapy target strategies [73].

As a traditional method of early cancer detection, electrochemistry is a laboratory method that can effectively and quickly diagnose early cancer lesions. Cotchim et al [74] used graphene/methylene blue-chitosan/antibody and bovine serum albumin on indium tin oxide glass electrodes to create a new type of multiple label-free electrochemical immunosensor for the simultaneous measurement of three types of tumors markers, including CEA, cancer antigen 153, and cancer antigen 125 (figure 6).
3.3. Protein

Protein is the main working substance of the human body, and it involves in all molecular signaling pathways in human cells. When cancer occurs, cells start growing out of control and secreting abnormal proteins in the cancer tissue. Such as, the dormant pancreatic stellate cells in normal tissues will be only activated in pancreatic cancer tissues, secrete proteins, and deliver stimulating signals to tumor cells to promote the development and progression of pancreatic cancer [75].

Secreted extracellular protein induced by transforming growth factor β (TGFβ1 or β1IGH3) regulates many biological functions during embryonic development and the pathogenesis of human diseases, including cell adhesion and bone formation [76, 77]. TGFBI is most studied in hereditary corneal dystrophy, wherein mutations in TGFBI cause it to accumulate in the cornea [78]. In cancer, early research focused on TGFBI as a tumor suppressor, partly by improving chemotherapy sensitivity. However, in established tumors, TGFBI promotes tumor progression to a large extent, and its elevated levels are associated with poor clinical outcomes [79]. The mechanism of targeting TGFBI has potential clinical application in the treatment of advanced cancer, and assessment of the TGFBI expression level can be used as a biomarker of resistance to chemotherapy and progression of tumor [80, 81].

Western blot analysis is a traditional method for early detection of cancer protein biomarker that involves the presence of UNIVmAb reactive antigens in circulation. Huang et al [82] used Western blot assay to perform analysis on cervical cancer serum samples. The experiment was confirmed that miR-193b regulates the expression of CCND1 mRNA in cervical cancer cells (figure 7).

3.4. Other

Exosomal microRNA (miRNA) detection based on double-stranded specific nuclease-triggered rolling circle amplification is used for the detection of cancer cells. Among them, exosomal miRNA is a promising noninvasive biomarker for liquid biopsy [83]. Electrochemical impedance spectroscopy is used to detect interleukin-6 biomarkers as an immunosensor for the detection of cancer [84] Through functional processing of ordinary organic FET (OFET) devices to detect cancer, the proposed OFET-based biosensor provides more extensive analysis, and thus can be used in clinical applications for the diagnosis of early liver cancer [27, 85].

Confocal fluorescence imaging is one of the most important methods for detecting cancer biomarkers. He et al [86] used fluorescent probes to perform confocal fluorescence imaging of HeLa cancer cells (figure 8), KB cancer cells, and V79 normal cells. Although this work successfully proved that biomarkers can be used to detect cancer cells, the cost of confocal fluorescence imaging is extremely high,
and the biomarkers need to be labeled to obtain accurate results.

4. Bioreceptors used for FET cancer biosensors

Various advantages of the aforementioned biomarkers have laid a good foundation for the development of FET biosensors. To reduce the cost of samples to be tested, low-cost portable in vitro biosensors are in urgent need of development. Therefore, development of FET biosensors for rapid label-free detection have become a hot research topic. Rapid diagnostics utilizing a free-label system have enabled many opportunities in modern medicine for the clinical detection, cancer diagnosis, and treatment of infectious diseases [49, 87]. In addition, the recent global epidemic of the novel coronavirus (COVID-19) illustrates that the demand for rapid and flexible nucleic acid detection technology for the detection and diagnosis of diseases has not been met [8, 88]. The detection capability of biosensors is essential for a wide range of diagnostic applications [89].

4.1. Antibodies

Antibody is a protective protein produced by antigen stimulation. In order to achieve the early diagnosis of cancer and choose better targeted drugs to treat cancer, the detection of cancer-specific antibodies is of great significance [90].

A typical heterogeneous immunoassay includes multiple steps of antibody modification, cultivate, and washing cycles, as well as data readout and biological signal amplification [91]. From the initial antibody modification step to the final data analysis stage, immunoassay results usually take days to weeks to obtain. Various cancer cell detection technologies have been developed, including cytological detection, fluorescence imaging, magnetic resonance imaging, computed tomography, x-ray photography, and ultrasound [92, 93]. However, disadvantages of these detection method include high cost and the long time required to perform the experimental procedures or operate the instruments. Therefore, to reduce the mortality of certain cancers, it is necessary to develop a simple to use, rapid detection, and cost-effective early detection method for cancer patients in preclinical diagnosis. In this regard, point of care handheld devices provide a promising alternative to existing laboratory-based immunochemical analysis [94].

This prompted us to explore whether we can further improve sensitivity by using CNT FETs tightly coupled with engineered antibody components. Lerner et al [95] transformed the 23C3 monoclonal antibody into a single-chain variable fragment antibody. They observed that the 23C3 single-chain antibody retains its ability to bind to osteopontin (OPN), which will make it an effective diagnostic alternative to the Hu23C3 therapeutic antibody. They observed the antigen-specific, concentration dependent sensor response to OPN in the buffer and determined that the measured responses collected from 10 to 15 devices can be used to reliably distinguish between pure buffers and buffers containing OPN at a concentration of 1 pg ml$^{-1}$ or 30 fm liquid (figure 9(A)).

Figure 9. (A) Functionalization scheme for OPN attachment. Reprinted with permission from [95]. Copyright (2012) American Chemical Society. (B) Schematic specific detection process of the prostate specific antigen (PSA). Reprinted from [96], Copyright (2018), with permission from Elsevier.

Sungkyung et al [96] reported a cheap and simple FET biosensor, which uses paper combined with multiwalled CNTs as a substrate. The PSA antibody is fixed on the surface of the sensor channel, and the binding levels of PSA and PSA antigens are indirectly detected via changes in resistance to detection. Furthermore, the maximum detection limit is $\sim$50 times higher than that of enzyme linked immunosorbent assay (figure 9(B))

4.2. Aptamers

Aptamers are oligonucleotides or peptides, which have high specificity and affinity for their associated targets in cells. Aptamers serve as a mediator between targeted therapy method and its targeted disease site, selectively delivers drugs to the cancer site to kill cancer cells. Compared to antibody, aptamers are easier to obtain and modify, moreover, they have lower immunogenicity. In such manner, aptamers can be anchored on the biosensor to specifically capture small molecules, proteins such cytokines [97].

As the basic response of the immune system to disease, inflammation can eliminate the source of infection [98, 99].

However, certain diseases, such as middle east respiratory syndrome, COVID-19, and other diseases, may cause excessive and long-term inflammation [100, 101]. This reaction is called a ‘cytokine storm’, and it leads to higher mortality due to serious damage of human organs, developing rapidly of the patient’s condition, or acute respiratory distress syndrome. Simultaneously, cytokines are important markers of biological trauma, sepsis, cancer, and rheumatism [87, 102]. Therefore, there is an urgent need to develop a sensor that can be worn instantly for the continuous detection of cytokine levels in patients, which can distinguish deterioration of the condition of patients with acute infectious diseases and monitor their health status in daily life.
The sensor can be used for clinical noninvasive detection of cytokines in human saliva and other biological fluids. Wang et al. [103] developed a sensitive and renewable aptamer graphene-Nafion FET (GNFET) biosensor that can rapidly and consistently detect cytokine biomarkers in undiluted human biological fluids. The experimental results show that the sensor has high consistency and sensitivity in detecting the representative inflammatory cytokine biomarker interferon gamma (IFN-γ) in undiluted sweat containing a variety of impurities under various conditions. The detection range is 0.015–250 nm, and the detection limit is 740 fm. The biosensor repeatability and sensitivity detects cytokine biomarkers in human biological fluids (figure 10).

### 4.3. DNA

Among these detectors, electronic detectors can achieve rapid and real-time DNA signal readout because of the transduction elements (such as nanoparticles [104, 105], organic conductive materials [106], and carbon-based materials [107, 108]). The microresponse to the readable signal can be amplified within a few seconds. Advancements such as miniaturization and improved portability make electronic-based DNA detectors a promising technology to exploit for further commercial applications.

The ideal choice for personalized medicine is an electronic DNA biosensor with single-nucleotide resolving power. Hwang et al. [109] used DNA tweezers with graphene FET for detection of single-nucleotide polymorphism (SNP) and wirelessly transmitted data for analysis. By observing Dirac point displacement and resistance change, the picomolar sensitivity of quantitative SNP detection can be obtained. Implementing DNA tweezer probes and high-quality graphene field effect tubes increases the sensitivity of SNP detection by >1000 times and significantly improves the analysis characteristics of detection of SNP (figure 11).

Although DNA recognition has been achieved by many biosensors and various sensing probes, there have been few reports on the use of biological interactions between DNA and biomolecules for DNA detection. Li et al. [45] reported a peptide-based CNT thin film transistor biosensor, which achieved detection of sensitive sequence-independent DNA (figure 12). In that study, they used polypeptides as natural molecules, which have the special binding ability to bind to universal DNA and achieve excellent selectivity to DNA after functionalization. In the presence of DNA, can be observed within a few minutes of ions, which may be due to the van der Waals force adsorption that occurs between DNA and peptides with opposite zeta potential. With the gradual increase of DNA concentration, the $\Delta V_{ON}$ signal conforms to the Hill–Langmuir model ($R^2 = 0.98$), which indicates that there is a negative synergy between peptide and DNA.

### 5. Considerations in choosing a bioreceptor material

Due to the high degree of specificity and sensitivity of biosensor detection, this technology has a wide range of applications in the field of diagnosis. Latest advancements in the use of nanomaterial-mediated bioaffinity sensors for disease biosensing, point of care testing, and medical management have been previously described [110–112]. The sensor material is one of the most important components to consider in the manufacture of FET biosensors [47, 113, 114]. Many popular nanomaterials have attracted the special interest of scientists as sensors [115, 116]. By applying corresponding molecular functionalized FET sensors to specific target molecules and nonspecific molecules, the specificity and selectivity of the FET sensor array can be studied.

#### 5.1. Specificity

Highly specific molecular recognition is a key capability of biosensors. Affinity sensors rely on selective binding interactions between analytes and biological components (such as antibodies, nucleic acids, or receptors). Bao et al. [117] reported a silicon nanoribbon FET biosensor for CEA detection. To eliminate other unexpected factors that may affect the time-lapse relationship, a bovine albumin solution was allowed to be used simultaneously (figure 13(A)). Cheung et al. [49] used label-free FETs to detect short oligonucleotides and distinguish sequences with different individual bases. Their study demonstrated the ability of single-stranded DNA FET biosensor to detect complementary RNA sequences and distinguish single nucleotide variant RNA sequences. The development and implementation of FET biosensors that can quickly detect and distinguish oligonucleotides has brought developments for the diagnosis of disease and precision medicine (figure 13(B)). Yang et al. [118] reported a MoS$_2$ FET sensor array for the detection of bladder cancer biomarkers. The MoS$_2$ FET sensor functionalized with antibody molecules exhibited a high current response to specific target protein molecules but not to nontarget proteins. The sensor response of the molecule is extremely low, which indicates that the MoS$_2$ FET sensor they designed has high selectivity.
Figure 11. Schematic of DNA-tweezers probe with high-quality graphene FET probe design. [109] John Wiley & Sons. [Copyright © 2018 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim].

Figure 12. Schematic representation of the novel-peptide-based CNT biosensor. Reproduced from [45] with permission of The Royal Society of Chemistry.

Figure 13. (A) Different concentrations of CEA (red curve) and bovine serum albumin (BSA) (black curve) 0.01 × phosphate-buffered saline solution flowed through the microfluidic channel. Reprinted with permission from [112]. Copyright (2019) American Chemical Society. (B) Sequences of DNA used for FET biosensor measurements with different types of mismatches from the attachment location. Reprinted with permission from [49]. Copyright (2020) American Chemical Society.
5.2. Sensitivity

The field effect mobility \( \mu_{\text{FET}} \) and drain current \( I_D \) can be measured when the sensors are exposed to the target biomarker. Among them, field effect mobility \( \mu_{\text{FET}} \) is usually derived from the equation as follows:

\[
\mu_{\text{FET}} = \frac{g_m L}{W C_{\text{tot}} V_{ds}}
\]

where \( L \) is the channel length, \( W \) is the channel width, \( C_{\text{tot}} \) is the gatel capacitance per unit of channel area, \( V_{ds} \) is the source–drain voltage, and \( g_m \) is the differential transconductance [119]. The higher the mobility the FET biosensor has, the better conductivity will be.

Different materials have different detection limits for the same biomarker. PSA has been proved to be an extremely useful biomarker for early detection of prostate cancer. Wang et al. [120] reported that the MoS\(_2\) field effect biosensor achieved clear signals to the PSA solution, with the concentration down to 375 fm.

Differences in the detection of the same biomarker have also been reported. An FET configured with a silicon NW-based structure can perform ultrasensitive, label-free, and real-time detection of PSA. Kim et al. [121] reported that the conductance changes depending on PSA concentrations and pH values in the solution according to the isoelectric point of the PSA, which provides evidence that supports the real-time detection of 1 fg ml\(^{-1}\) PSA. Rani et al. [122] demonstrated silicon NW ionic-sensitive FET (Si NW-ISFET) arrays. Concentration-dependent measurements were performed in a wide range (1 pg ml\(^{-1}\)–1 \( \mu \)g ml\(^{-1}\)), which covers the clinical range of interest. The aforementioned tests were performed under relatively harsh conditions. As serum proteome is very complex, containing high levels of salts and other interfering compounds, Huang et al. [123] employed a poly-Si NW FET device to detected PSA. The results indicated that the sensor could detect trace PSA at <5 fg ml\(^{-1}\) in a microfluidic channel.

6. Current challenges and outlook

In summary, FET biosensors enable consistent specific and sensitive detection of cytokines in human biological fluids for label-free analysis to achieve real-time monitoring of wearable devices. The advantage of nanomaterials in tumor marker detection lies in the presence of magnetic, optical, or special structures in nanoparticles. When these materials are combined with specific tumor-targeting ligands, including small molecules, peptides, and monoclonal antibodies, these nanomaterials can target biomarkers and vasculature to tumors with high sensitivity and specificity. But there are certain challenges in clinical applications, and the environmental adaptability of nanomaterials remains unsolved.

Moreover, the cavity length and oxide thickness of nanomaterials have been affecting the sensor’s performance of \( I_{ON}, I_{OFF}, I_{ON}/I_{OFF}, V_{th}, \) and sensitivity. This affects the detection limit of the FET biosensor. At present, the detection limit of a large number of biosensors has far exceeded clinical needs. Therefore, the focus should now shift to practical implementation of these sensors, which can lead to improved testing and diagnosis.

The design of next-generation cancer FET biosensors should focus on rapid detection, implantability, and portability and should provide the following features: (a) precise positioning and treatment; (b) dose monitoring; (c) simultaneous monitoring of multiple and diverse tumors. Improving the technology for early screening of patients with cancer will lead to an improvement in their survival rate. In addition, cancer FET biosensors are being integrated wirelessly into microdevices for early detection of cancer. Theoretically, FET biosensors can detect any tumor marker or physiological abnormality and wirelessly transmit monitoring data to electronic equipment attached to the surface of the body. The electronic device programmed with an algorithm can then determine a suitable treatment plan, including the appropriate dosage, method, and duration of therapy.

Due to the global challenge of the COVID-19 pandemic, we recommend that biomarker-specific probes be modified with FET biosensors to achieve convenient and rapid monitoring of COVID-19 infection in human patients. This kind of sensor has the potential to play a critical role in providing rapid information about the condition of patients with acute infectious diseases, which can assist hospitals in stratifying COVID-19 patients of Suffering from different mutant viruses for prioritization and optimization of treatment.

Data availability statement

The data that support the findings of this study are available upon reasonable request from the authors.

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