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Original Article

Design and Comparative Analysis of Biosensing Devices with Different Dielectric Materials for Blood Cancer Detection

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Abstract *- The healthcare industry is constantly changing due to technological breakthroughs that spur new methods of diagnosing and treating illnesses. In this study, we suggested a novel structure for a label-free biosensor that senses both charged and neutral bioanalytes: the dielectric modulated dual-dielectric Ion-Sensitive Field Effect Transistor. Compared to Nanosheet FET (NSFET), the ISFET device shows better bio-sensing ability. Al2O3 oxide is substantially more sensitive than other oxides when pH 7.4 is considered. The resulting 2D-ISFET has the potential to be a rapid blood cancer screening tool due to its exceptional blood electrolyte sensitivity. The findings demonstrate that the ISFET has reduced Subthreshold Swing (SS), Increased ON-current (ION) and switching ratio, and drain-induced barrier lowering. The recommended apparatus and the pH sensor's sensitivity may identify blood cancer indicators as high as 30 fg/mL. A significant advancement in technology-driven healthcare is using ISFET sensors for DNA-based blood cancer detection. This creates new opportunities to enhance patient outcomes and cancer diagnosis. Its excellent sensitivity, selectivity, low detection limit, thermal stability, biocompatibility, and affordability make it a promising material for a wide range of flexible sensing applications in the future. In our work, we have mainly focused on blood cancer detection. The proposed biosensors signify a significant advancement in technology-driven healthcare, offering new possibilities for enhancing cancer diagnostics and patient outcomes.*

Keywords *- ISFET sensors, NSFET, Blood cancer, Dielectric materials, Al2O3, PVP.*

1. Introduction

Biosensing instruments are now indispensable tools for keeping an eye on foodborne and environmental diseases and healthcare systems. Early diagnosis and analysis can effectively avert serious consequences for human health. They are widely used in the diagnosis of cancer cells, DNA detection, microbe identification, glucose monitoring, and medication delivery [1-3]. It bridges the gap between the biological and technological realms by offering a fast and precise analysis [4, 5]. Considerable research is conducted on the subject of bioelectronics employing two different methodologies.

While the second strategy uses an artificial device to detect biological emulation [9, 10], the first approach relies on sending an electrical signal for corresponding biomolecular immobilization at the sensor surface [6-8]. Labeled and label-free methods are the biosensor's two ways to recognize the target analytes. At a reasonable price, one of these label-free methods can reliably and quickly detect biomolecules without the need for labels. Nonetheless, they have comparable material needs, such as biocompatibility, stability, and biological system adaptability [11, 12].

Field-Effect Transistors (FETs) have been the basis for researchers' successful development of many label-free biosensors. Transparent gate recessed channel FinFET [15], ISFETs [16], and Tunnel Field-Effect Transistors (TFET) [13] are a few examples of these biosensors. The ion-sensitive FET-based biosensor can identify biomolecules based on charge fluctuations in ionic solutions and dielectric characteristics. It can detect charged biomolecules with good sensitivity, but because of the unstable ionic concentration, it gradually deteriorates with time. They have trouble finding neutrally charged biomolecules, though. While inorganic FET-based biosensors use costly fabrication procedures at higher temperatures, they are compatible with essential CMOS processing technologies for macro production. Furthermore, several drawbacks affect FET-based biosensors, such as short channel effects, a reduced ION/IOFF ratio, higher power consumption due to leakage current, and the consequences of drain-induced barrier lowering [16].

Leukemia, lymphoma, and multiple myeloma are blood cancers that are among the most common and deadly cancers. Patient survival rates can be greatly impacted by quick intervention and individualized treatment plans, which depend on the early and correct identification of blood cancer. Traditional diagnostic approaches, like biopsies and imaging technologies, have been essential in the identification of cancer. However, a growing demand exists for novel and more considerate methods to support early diagnosis, allow real-time monitoring, and offer individualized treatment choices.

Given this, DNA-based analysis methods have drawn much interest due to their potential to transform how cancer is diagnosed thoroughly. DNA-based methods present a promising avenue for sensitive and specific diagnosis by utilizing the distinct genetic signatures linked to cancer cells. ISFET sensors have become a potential instrument for molecular detection among the different technologies used in DNA analysis. Solid-state ISFET sensors can identify pH shifts brought on by interactions between DNA strands. These sensors have several benefits over conventional detection techniques, such as their small size, high sensitivity, quick reaction times, and label-free detecting capability. Because of their characteristics, ISFET sensors are exceptionally well suited for point-of-care diagnostics, tailored treatment, and real-time monitoring.

This study intends to investigate the emergence of ISFET sensors for DNA-based blood cancer detection and its consequences for technologically advanced healthcare. Specific genetic biomarkers linked to blood malignancies can be found by combining DNA analysis methods with ISFET sensors. Improvements in early cancer identification can let doctors intervene in the earliest stages of the illness, resulting in more potent treatment plans and better patient outcomes. This work emphasizes the potential of DNA-based blood cancer diagnosis utilizing ISFET sensors in transforming healthcare practices through an extensive assessment of existing literature and presenting experimental results. Healthcare workers may anticipate breakthroughs in cancer diagnosis by utilizing technology-driven methods, ultimately leading to better patient care and higher survival rates.

Developing Ion-Sensitive Field-Effect Transistor (ISFET) sensors have drawn interest as a technique that could improve DNA-based cancer detection. Solid-state ISFET sensors measure pH variations brought on by interactions with DNA molecules. These sensors' tiny size, high sensitivity, quick response time, and label-free detection capabilities have shown them many advantages over traditional detection techniques. ISFET sensors are appealing for healthcare applications because they can also be used for “point-of-care diagnostics and real-time monitoring”.

The potential for improving cancer diagnoses is significant when technology-driven healthcare and DNA-based analysis with ISFET sensors come together. This study paper examines the possibilities of this novel strategy and how it might affect healthcare. Clinicians and researchers can envision a time when early diagnosis of blood malignancies becomes more accessible, improving patient outcomes and significantly lowering the burden of these diseases. This can be achieved by utilizing the power of ISFET sensors and DNA analysis. Figure 1 shows the blood cancer therapy.

Recently, incorporating ISFET sensors in DNA-based analysis has demonstrated significant potential for healthcare applications, namely cancer detection. ISFET sensors provide label-free and real-time monitoring capabilities by detecting changes in pH levels brought on by interactions between DNA strands. Point-of-care testing and tailored treatment can benefit from these sensors' high sensitivity, quick reaction time, and potential for downsizing.

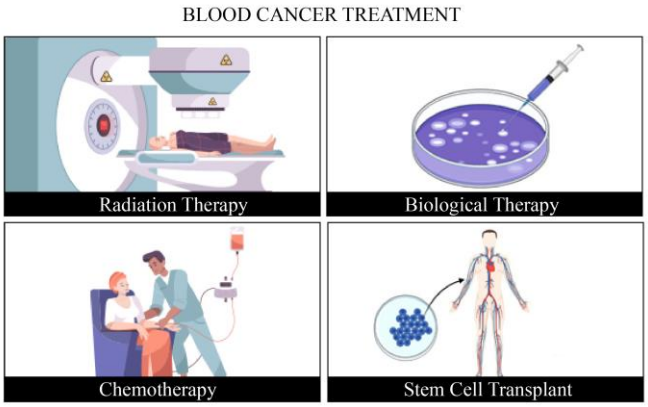

Fig. 1 Typical blood cancer treatments [3]

ISFET sensors have been investigated in several studies for use in blood cancer detection and other cancer diagnostics. For example, the study showed how to use ISFET sensors to detect genetic abnormalities specific to leukemia, highlighting the technology's potential for early diagnosis and disease progression tracking [17].

A study utilized ISFET sensors to identify circulating tumor DNA (ctDNA) in the blood of patients suffering from lymphoma. The researchers attained high sensitivity and specificity in ctDNA detection, underscoring the potential of ISFET-based technologies for real-time, non-invasive monitoring of genetic alterations linked to cancer.

Furthermore, how to combine ISFET sensors with microfluidic platforms to identify numerous DNA alterations linked to myeloma was investigated. The study proved that the combined strategy was feasible for the sensitive and precise detection of genetic biomarkers, opening up a possible path for early diagnosis and individualized treatment plans. Furthermore, Wang et al.'s study from highlighted the development of DNA-based analysis methods for cancer

diagnosis. It highlighted the function of ISFET sensors in enhancing sensitivity and enabling real-time monitoring. The review emphasized how ISFET-based technologies may help with blood cancer and other malignancies by providing early diagnosis, precise treatment selection, and therapeutic monitoring [18].

It is imperative to recognize the existing constraints and difficulties within this domain. These include the requirement for additional validation research, sensor performance enhancement, detection procedure standardization, and interaction with current clinical workflows. It will be imperative to address these issues in order to fully utilize the potential of ISFET-based technologies in clinical settings. The research on ISFET sensors-based DNA-based blood cancer detection emphasizes how important this new technology is to improving healthcare. The presented experiments demonstrate the potential of ISFET sensors for real-time, sensitive, and specific genetic biomarker detection related to blood malignancies. Researchers and clinicians have the chance to create technology-driven healthcare, which will lead to early identification, individualized treatment approaches, and improved outcomes for patients with blood malignancies by utilizing the strengths of ISFET sensors and DNA-based analysis methodologies. Researchers and clinicians have the chance to create technology-driven healthcare, which will lead to early identification, individualized treatment approaches, and improved outcomes for patients with blood malignancies by utilizing the strengths of ISFET sensors and DNA-based analysis methodologies. The study by Wang et al. also emphasized the advancement of DNA-based analysis techniques for cancer diagnosis. It emphasized how ISFET sensors improve sensitivity and make real-time monitoring possible.

The experiments presented display the promise of ISFET sensors for the specific, sensitive, and real-time detection of genetic biomarkers linked to blood cancers. By leveraging the benefits of ISFET sensors and DNA-based analysis tools, researchers and clinicians can establish technology-driven healthcare, resulting in early identification, personalized treatment methods, and improved outcomes for patients with blood cancers. The use of ISFET sensors in DNA-based blood cancer detection is a significant advancement in technology-driven healthcare, as it provides new opportunities for enhancing cancer diagnosis and patient outcomes.

2. Design of Biosensing Platform and Simulation Methodology

Initially, we designed a basic Nanosheet FET device. Afterwards, the gadget is designed and simulated using the Visual TCAD -3D Cogenda application [19]. A 16 nm gate length characterizes the NSFET. Doping silicon with N-type impurities at concentrations of 1020 cm-3 and 1015 cm-3 results in NSFET channel terminals. The gate tunneling effect is prevented by maintaining the EOT of 0.78 nm. Throughout the experiment, the work function of the constant metal gate remains at 4.6 eV. Direct tunneling is managed by means of a "5 nm nitride spacer" having a dielectric constant of 7.5. The NSFET's 3D perspective is displayed in Figure 2.

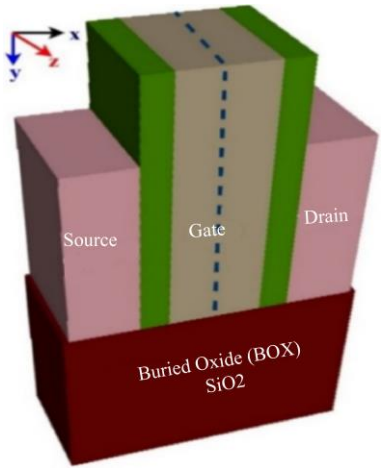

Fig. 2 NSFET's 3D structure

Table 1. NSFET device parameters during simulation

Parameter	Value used
Terminal Doping	10^{20} /cm^3
NS thickness	5-9 nm
work function (Gate)	4.6 eV
Length of the Gate	22 nm
Terminal Pad length	15 nm
Effective oxide Thickness	0.73 nm
Height of the Gate	74 nm
Terminal underlap length	7 nm
Doping of the channel	10^{18} /cm^3
NS width	30 nm
Underlap material	Nitride

Here, the interfacial oxide and HfO_2 with a thickness of 1.5 nm and a dielectric constant of around 20 are utilized to produce an overall EOT of 0.78 nm. In addition, the application that uses 5 nm nitride spacers on both sides of the gate also uses the spacer's benefit. To lower SCEs, spacer technology in sub-nm devices is crucial. The spacer's imposition, however, may increase the risk of a rise in series resistance, which would lower drain current. As a result, the fringing effect of a high dielectric spacer can dominate the effect, causing field coupling and raising the switching ratio. The simulated device parameters are shown in Table 1.

Many models and techniques have been applied to simulation and device construction. The simulation makes use of models such as Schenk's bandgap shrinking, Shockley-Read-Hall, and Lombardi's mobility. The Lombardi mobility model is used when carrier degradation processes occur as a result of surface roughness. Carrier recombination and generation are governed by the SRH model. The transfer property calibration of the NSFET was accomplished using the Visual TCAD simulation method, as shown in Figure 3 [14].

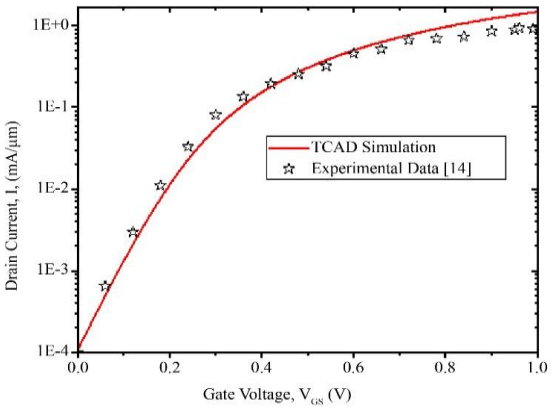

Fig. 3 Correlating suggested NSFET simulation results with experimental results [14]

The designed NSFET was then studied for blood cancer with sensitivity, selectivity, low detection limit, thermal stability, and biocompatibility. Then, the biocompatible ISFET device was designed and compared with NSFET.

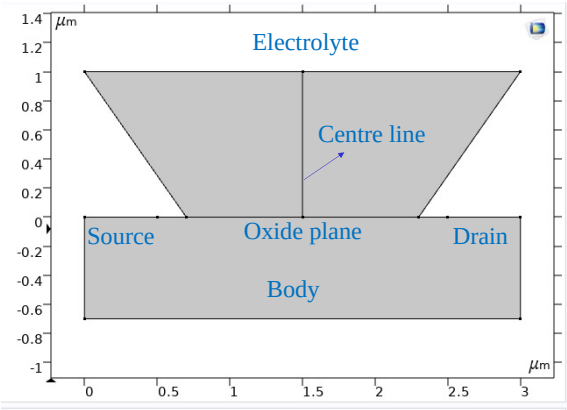

Fig. 4 A 2D-ISFET sensor device

It is possible to build and implement a 2D-ISFET under specific circumstances. The reference electrode receives the gate voltage. During the device design process, the electrolyte is applied to the oxide surface. A drain voltage of 10 mV is provided when the source is grounded. We initially assessed the sensitivity after adding water to the electrolyte tank. The surface electric potential of the structure is visible once the pH of the bulk electrolyte (pHb) has been adjusted and the drain voltage is steady. Since there is a correlation between pHb changes and doping concentrations, doping concentrations at the source and drain locations are proportionate to pHb variations. A two-dimensional ISFET designed with the COMSOL Multiphysics tool is shown in Figure 4. All of the simulated device's dimensions and properties are listed in Table 2.

Table 2. All of the simulated device's parameters during simulation

Device Parameter	Dimension
Sheet_resistance	1.7 Ω⁄square
Device_Length	20 μm
Lateral diffusion	0.96μm
Doping of the substrate	1.3E+15 cm-3
Device_Width	500 μm
GAMMA	0.3
Depth of the junction	1.2 μm
Gate_dielectric_thickness	150

3. Gate Oxide Materials

In biosensing devices, the choice of gate oxide material is crucial as it directly influences the sensitivity and performance of the sensor. The choice of gate oxide material depends on factors such as desired sensitivity, stability, fabrication compatibility, and targeted pH measurement range. Each material has advantages and limitations, and researchers continue exploring new gate oxide materials to improve biosensing performance, as shown in Table 4.

4. Results and Discussion

4.1. DC Performance Study of Biosensing Devices

The I_D-V_{GS} characteristics of NSFET at V_{DS} = 0.7 V. Drain current displays the transfer characteristics in logarithmic and linear scales, as shown in Figure 5. V_{th}, I_{ON}/I_{OFF}, DIBL, and other relevant parameters are required to evaluate the device's performance, and various spacer dielectrics are considered at V_{DS} = 0.7 V. A critical metric for evaluating the electrical performance of FET devices is the ratio of I_{ON} to I_{OFF}. When the FET is turned on, the device's ability to control power is measured by the on-state current or I_{ON}.

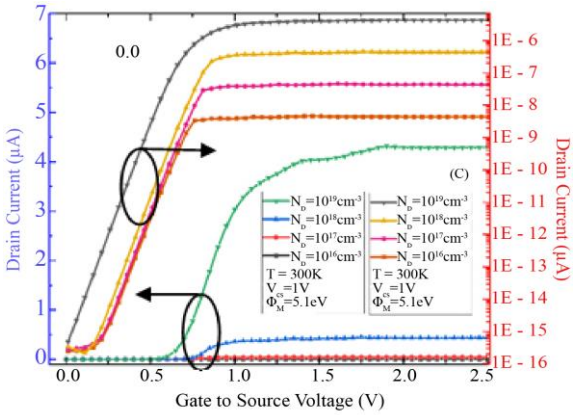

Fig. 5 Transfer properties of the proposed NSFET with varied spacer dielectric and VDS =0.7 V

Similarly, the transfer characteristics of the ISFET device are evaluated with various doping concentrations and a constant threshold voltage and temperature of 300K. Figure 6 displays the transfer characteristics of the proposed ISFET.

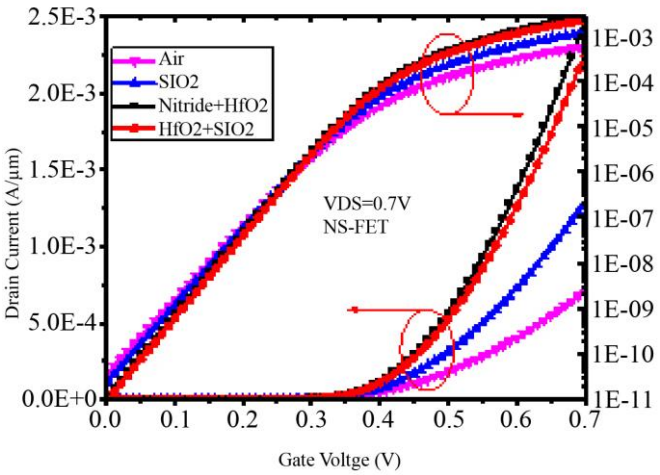

Fig. 6 Transfer properties of the proposed ISFET with different doping concentrations

SS and DIBL are the major DC measures for lower technology node subthreshold performance. Equations 1 and 2 show the equations for DIBL and SS, respectively [17].

$$DIBL\ (mV/V) = \left|\frac{V_{th1}-V_{th2}}{V_{DS1}-V_{DS2}}\right| \quad (1)$$

$$SS = \left[\frac{\partial log_{10} I_D}{\partial V_{GS}}\right]^{-1} \quad (2)$$

The constant current technique is used to obtain the DIBL using eq. 1, "where N is the number of channels and V_{th1} and V_{th2} are the threshold voltages extracted at VDS of 0.7 V and 0.04 V, respectively, at $N\times(Weff/L_G) \times 10^{-7}$ A". Table 3 displays the primary performance characteristics of the recommended ISFET device and NSFET device.

Table 3. NSFET device parameters during simulation

Parameter	Simulated ISFET results	Simulated NSFET results
Threshold Voltage	0.36 V	0.3 V
On Current	2.26 x 10^{-6} A	1.3 x 10^{-7} A
Off Current	1.04x10^{-11} A	2.9x10^{-12} A
On / Off Current Ratio	2.17 x10^5	0.45 x10^5
SS	57 mV/dec	64 mV/dec
DIBL	68 mV/V	73 mV/V

4.2. Transfer Characteristics of both the Devices with Blood as an Electrolyte

The ISFET design model's front gate receives the gate voltage. The drain current determines the effective gate voltage.

The suggested arrangement uses the conductor as the electrolyte and delivers gate voltage across its oxide surface. The graph shows oxide transport in blood as an electrolyte solution.

The transfer characteristic of Al_2O_3 shows it has a higher drain current than other oxides. However, the drain current of traditional SiO_2 oxide exhibits a noticeable rise.

Other oxides, such as magnesium peroxide (MgO_2), Zinc Oxide (ZnO), Tantalum oxide (Ta_2O_3), and Polyvinylpyrrolidone (PVP), exhibit very modest drain currents with variable gate voltages, as seen in Figure 7.

Table 4. Gate oxide materials

Material	Advantages	Limitations	Description
Silicon Dioxide (SiO_2)	Good electrical insulation properties. High stability. Compatible with standard silicon fabrication processes.	Limited sensitivity compared to high-k dielectrics. Lower dielectric constant.	The most commonly used gate oxide material in ISFETs. It is grown through thermal oxidation of the silicon substrate.
Titanium Dioxide (TiO_2)	The high dielectric constant for increased sensitivity. pH-sensitive properties. Potential for biofunctionalization.	Lower stability compared to SiO_2 and high-k materials. More complex fabrication process	Titanium dioxide gate oxides can be prepared using techniques like sol-gel deposition or ALD. They exhibit unique properties suitable for ISFET applications.
Silicon Nitride (Si_3N_4)	Higher dielectric constant compared to SiO2. Improved sensitivity. Good	Slightly lower stability compared to SiO2. More challenging fabrication	Silicon nitride gate oxides are typically deposited using techniques like CVD or PECVD.

	electrical insulation properties	process	
Hafnium Dioxide (HfO2)	The high dielectric constant for enhanced sensitivity. Improved signal-to-noise ratio. Suitable for advanced CMOS fabrication processes	Requires specialized deposition techniques (ALD). Potential reliability issues.	Hafnium dioxide gate oxides are deposited using techniques like ALD. They offer high-k properties and have gained attention in recent years
Magnesium peroxide (MgO_2)	The high dielectric constant for improved sensitivity. Enhanced electrical properties. Compatible with standard silicon fabrication processes	Limited stability at extreme pH ranges. Potential issues with moisture absorption	Magnesium peroxide gate oxides can be deposited through electrophoretic techniques.
Aluminium oxide (Al_2O_3)	The high dielectric constant for improved sensitivity. Enhanced electrical properties. Compatible with standard silicon fabrication processes	Limited stability at extreme pH ranges.	Aluminum oxide gate oxides can be deposited through techniques like ALD or PVD. They offer high-k properties and are widely used in ISFETs.

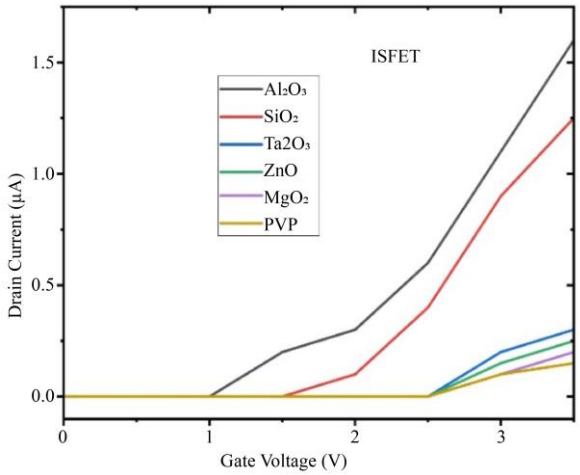

Fig. 7 Transfer characteristics of 2D- ISFET with blood as electrolyte

Similarly, the transfer characteristic of NSFET with blood was studied using electrolytes with the same dielectric materials. Figure 8 shows the transfer characteristic curve of NSFET with different dielectric oxides. The current drain trend is similar but much less than that of the ISFET devices.

4.3. Output Characteristics with Varying Oxide for Blood Electrolyte

The output characteristics of the designed 2D ISFET were studied using blood as the electrolyte. A SiO_2, Ta_2O_3, ZnO, MgO_2, Al_2O_3, and PVP oxide-varying ISFET was simulated for drain voltage fluctuations between 0 and 1.4 volts. Figure 9 illustrates that the I_d v/s V_d curve shows Al_2O_3 has a higher drain current than other oxides. SiO_2 also indicates a significantly greater drain current for the variable drain voltage V_d when blood is employed as the electrolyte. Al_2O_3 is, therefore, a better electrolyte for ISFET devices, it can be concluded.

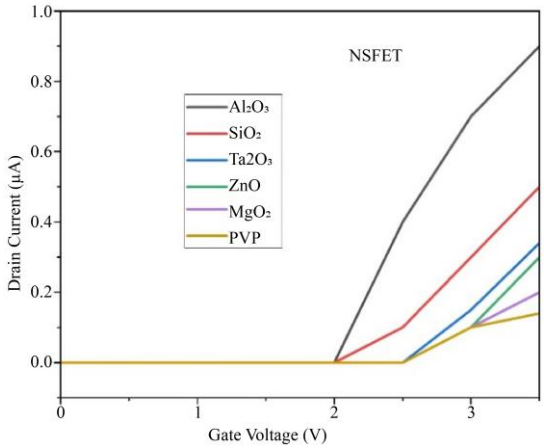

Fig. 8 Transfer characteristics of NSFET with blood as electrolyte

PVP shows a very negligible drain current. Similarly, the NSFET output characteristic shows a similar trend but negligible drain current. Hence, it cannot be a correct choice for detection of blood cancer. Figure 10 shows the output characteristics of the NSFET device with blood as an electrolyte.

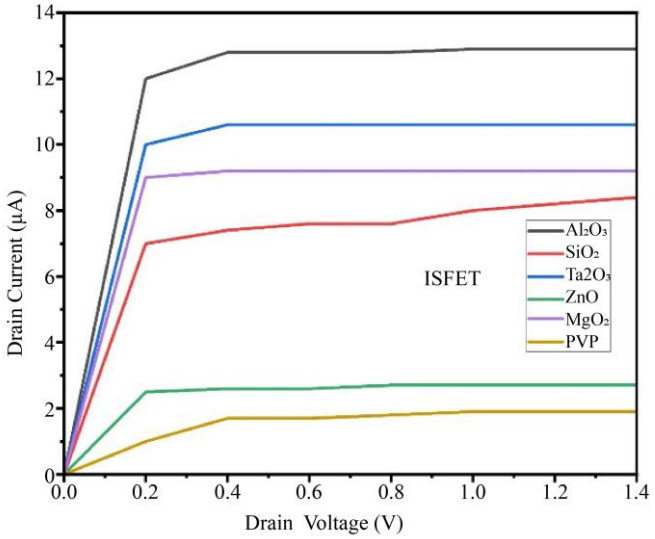

Fig. 9 Output characteristics of 2D-ISFET for blood as electrolyte

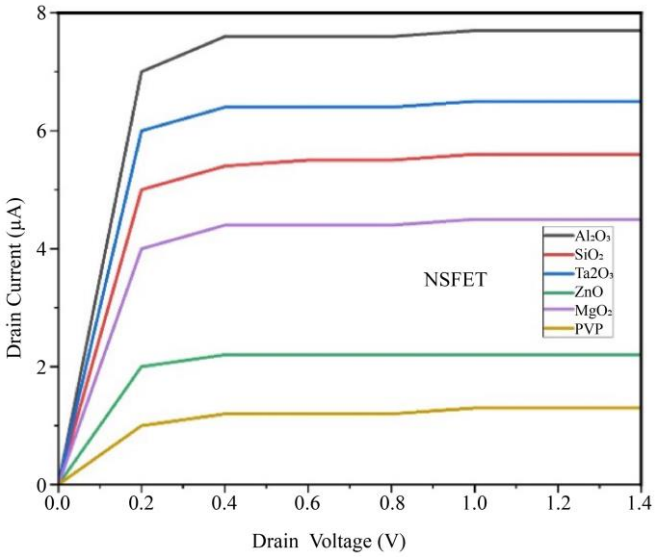

Fig. 10 Output characteristics of NSFET for blood as electrolyte

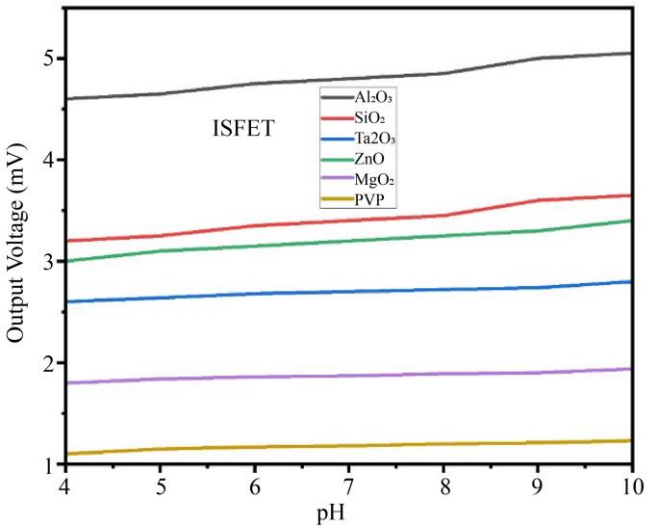

Fig. 11 Sensitivity of pH sensor with ISFET device

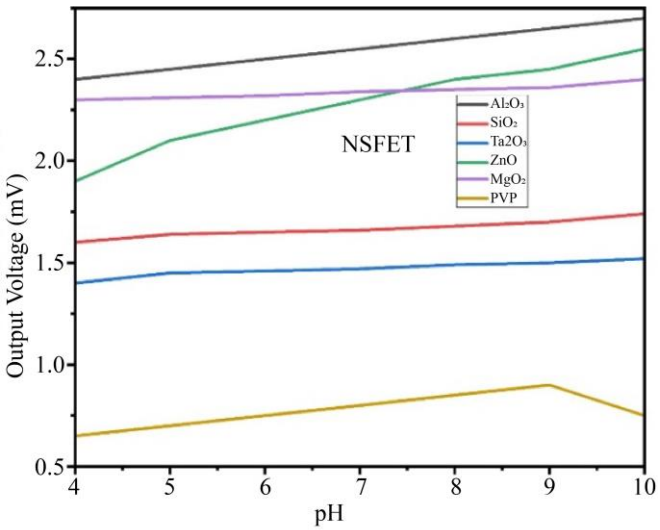

Fig. 12 Sensitivity of pH sensor with NSFET device

4.4. Output Sensitivity Study for Varying pH

Sensitivity is one of the prime performance measures for detecting any cancer. As the oxide surface varies, so does the sensitivity of the simulated 2D-ISFET. Our experiment has different oxide layers: Al_2O_3, Ta_2O_3, SiO_2, ZnO, MgO_2, and PVP. When using an ISFET as a biosensor in medicine, this is the most critical component to take into account for its proper operation. We accounted for blood as electrolyte solutions in our computation of the proposed model.

The output voltage, or the ISFET sensor's sensitivity, is displayed in Figure 11 for various pH values. Additionally, it is evident from the sensitivity testing that Al_2O_3 oxide is more sensitive to pH changes than other oxides. Comparatively speaking, Al_2O_3 oxide's output voltage of 4.7 mV is substantially higher than other oxides simulated for the intended ISFET.

Similarly, the NSFET device was studied with varying pH values for different oxide layers, as shown in Figure 11. Figure 12 displays the very minute output voltage with Al_2O_3 oxide of 2.2 mV. One can easily infer from this that the sensitivity to the varying pH value is double when using 2D-ISFET compared to the NSFET device. Hence, NSFET is not the correct choice for blood cancer detection.

4.5. Blood Cancer Detection with 2D-ISFET vs NSFET

The proposed devices establish an antigen and antibody reaction with leukaemia, lymphoma, and myeloma. The various steps of the recommended technique include patient sample collection, preservation in cold storage, and application of the samples on the ISFET-designed biosensors and NSFET-based biosensors. The main objective of this investigation is to find blood cancer cells in human blood. The main concept behind myoglobin detection with a device is as

follows: a sensor that uses the electrolyte plane of the device can detect molecules attached to or detached from a surface.

The attachment and dissociation of one electron from the oxide plane results in changes to the surface resistance of the biosensor. Resistance from the output characteristic for different biomarkers ranging from 0 to 30 fg/mL can be used to identify blood cancer.

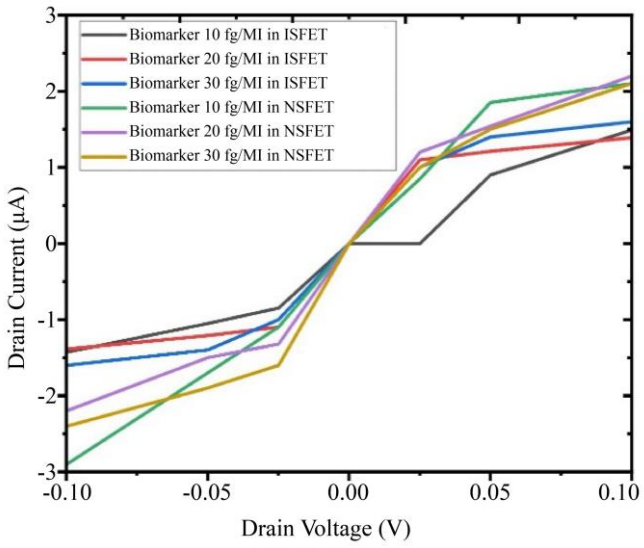

Fig. 13 Limit of detection of blood cancer biomarker with 2D-ISFET vs NSFET

The lowest biomarker solution's ability to recognize cancer cells is known as the limit of detection. To do that, device response for antibody modification was researched. The detection study's limit is illustrated in Figure 13 by gathering device replies. Plotting this device's response drain current (ID) involves changing the drain voltage between -0.1 and +0.1 volts. According to the plot, the biomarker's blood cancer cell detection level is 30 fg/mL for both the proposed devices. However, one can quickly realize that 2d-ISFET has better sensitivity than NSFET with the same detection limit. Hence, 2D-ISFET is a potential candidate for blood cancer detection up to 30fg/Ml with a very high detection limit.

5. Conclusion

This research presents the creation of a Nanosheet FET and a two-dimensional ion-sensitive field-effect transistor for the diagnosis of blood cancer. Blood from two electrolyte solutions is used to study the characteristics of transfer and concentration changes with various oxides. It is possible to evaluate how the modelled device can be utilized as a pH sensor or a biosensor in healthcare applications by looking at how the pH changes for different oxides. The output properties of simulated devices were also analysed for different oxides. The sensitivity of the devices is examined for various oxides, with blood serving as the electrolyte. Al_2O_3 oxide is far more sensitive than other oxides when pH 7.4 is considered. The resultant 2D-ISFET shows exceptionally high blood electrolyte sensitivity compared to NSFET and promises to be a rapid blood cancer diagnostic tool.

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