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Nanomaterial FET-based biosensor for Medical Applications

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Abstract

For distinct properties and advantages like easy integration, high sensitivity, portability, and good selectivity, FET (Field-effect transistors) find application in varied fields and research areas. Especially, in biomedical applications, a drastic improvement is seen with the evolution of FET where Nanomaterial-based Bio-FET is an outstanding performer for their biosensing ability. In medical field, such Nanomaterial FET-Biosensor is carried out for performing label-free biomolecule sensing to screen out different diseases. Including infectious disease detection like virus infection, and bacterial infection, glucose, and diabetic levels can be screened as well with the aid of FET-based biosensor. This paper concentrates on the basic concepts, working principle of Bio-FET, recent research of FET in medical area, challenges and future scope of Nanomaterial-based Bio-FET.

Keywords: FET, biosensor, Nanomaterial, Nanomaterial-biosensor, medical, biosensing, nanotransducer

1. Introduction

Biosensor devices have gained huge attention in marine sector, sports, environment, clinical diagnosis, agriculture, food analysis, and toxicity surveillance [1] since its introduction by Clark in 1962. These analytical devices convert the biological response into electrical signals that can be used for further processes [2]. Various biosensors are available at present like enzyme-based sensors, PH biosensors, and immunosensors that are used to perform specific operations like detection of glucose, oxygen, and other biomolecules. One great example for the popularity of such biosensor is the antigen testing kit that was developed for detecting the SARS-CoV-2 virus [3]. Although there are countless sensing techniques like surface plasmon resonance (SPR), colorimetric, chemi-resistive and micro-

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cantilever that are available in the market, there is need for a powerful alternative for long-term healthcare monitoring. Hence, Field-effective Transistors (FET) based biosensors, and ion-sensitive field-effective transistors (ISFET) were introduced, with unique characteristics like low-cost fabrication, sensitivity, and selectivity, FET-based biosensor gained importance.

FET or Field-Effect Transistor is a semiconductor device component that consists of three electrodes—Gate (G), Source (S), and Drain (D) whereas a Bio-FET comprises of a bio-recognition layer (made up of semiconductors like Zinc Oxide (ZnO), Indium Gallium Zinc Oxide (IGZO)), and transducer. In Nanomaterial FET-based biosensor, one-dimensional nanostructured components like carbon nanotubes, graphene, black phosphorous, are used. Gradually, with enhancement in the field of very-large integration, different assembly mechanisms like contact assembly, Langmuir-Blodgett assembly, field-assisted electrospinning, and so on were introduced [4]. With the use of such nanomaterial in FET sensors, the disadvantages like chemical instability, high surface-to-volume ratio, and bio incompatibility found in conventional metal-oxide semiconductor (MOS) based devices are irradiated. Also, Nanomaterial-based FET biosensor is highly suited for the detection of biomolecules like cancer biomarkers, proteins, and neurotransmitters [5].

While designing a FET biosensor, selection of the main biosensing element serves to be a critical factor. Antibodies, DNA/RNA being the important parameters to find out the virus infection or other diseases, the DNA and RNA probes sometimes can lead to weakening signals in physiological environments [6]. In recent days, efforts were taken to improve such sensitivity of FET devices in terms of probe design, and nanotransducers and hence the present strategy targets on exploiting compact-structured recognition elements, and probe density [7].

Various research works were carried out concerning the Nano FET-biosensor like graphene-based FET, PEDOT: PSS Bio-FET for DA detection, and SiNW-based FET dopamine detection [8]. When it comes to FET-based biosensor, Graphene comes out as the first convenient nano material that is been highly preferred yet continuous improvements are being done still. In different fields, graphene is used for sensing biomolecules as it is ultrasensitive and possess label-free electrical detection capabilities. In the form of graphene nanoribbons, it can solve the zero gap energy problems and hence is utilized in the fabrication of FET-based biosensor [9]. A new type of Graphene FET was then invented by China in which the graphene foam was used as an electrical channel. Research group in America introduced another GFET structure that used Al_2O_3 with the help of atomic layer deposition

(ALD). To produce higher molecular throughout, Nanopore-extended FET (nexFET) was developed by Ren's group with an enhanced signal-to-noise ratio [10]. Advantages of both nanopore platform and FET were well enough to immobilize the elements to facilitate in molecular detection.

For the purpose of improving the probe immobilization, nucleic- FET sensor with indium-tin oxide nanowires acting as a nano-transducer was invented by Mohsen Shariati. With inductive conductance of ITO nanowires, these nucleic-FET devices can detect Hepatitis B virus (HBV) [11]. For high sensitivity, CNT and SiNW are best examples suitable for detection of single virus particles. But still, they lag behind the present materials due to factors like high cost and fabrication complexity. When it comes to flexible biosensor fabrication, TMDC is recommended for its sensitivity, and selectivity [12]. When it comes to the immobilization technique, adsorption, cross linking, encapsulation, covalent bonding, and entrapment are the widely used ones. Such Nanomaterial FET-based FET's find application in DA sensor, Glucose sensor, DNA sensor, and Cancer biomarker sensor. For detailed analysis of the different transducer types and their target molecule, we have framed Table.1 for better understanding.

Table 1. Different transducer materials used in Nano-FET-based biosensor

Transducer material	Bio-probe	Target molecule	Analyte	LOD
Graphene	Human anti-EGP	EGP	0.01*PBS	1 ng/mL
Graphene Foam	ATP Aptamer	ATP	0.1*HS	0.5pM
Indium Tin Oxide Nanowire	DNA	HBV DNA	100mM PBS	ifM
Zinc Oxide Nanoribbon	GOx	Glucose	10mM PBS	3.8uM
Black Phosphorous	Anti-IgG	Human IgG	0.01*PBS	10ng/mL

2. Related Works

Well known for the purpose of label-free biomolecules sensing of different diseases, FET sensors is the highlight with miniature capability, and low minimum limit of detection (LoD) [13]. However, improvement and enhancement is still required in the detection phase of FET as infectious disease detection needs to highly précised with respect to integration, realization, diagnosis, and Point of Care (PoC). At the time of Covid-19 pandemic, these FET-based biosensors gained huge demand for their extraordinary LoD down to femtomolar and fast response time [14]. Also, they are found as novel PoC devices helpful in early diagnosis of infectious diseases [15].

Bergveld et.al [7] discussed in detail about pH-sensitive ISFET that is clinically investigated for intravascular blood pH recording. The operation of ISFET was completely explained and the performance was compared with the electronic analogue, MOSFET. In the project, SiO_2, Ta_2O_5, and Al_2O_3 were used as the insulators for the ISFET process technology [16]. As these oxides consist of hydroxyl groups, they act as discrete sites for chemical reactions. Also, to achieve stable ISFET operation, a feedback circuit is used that results in drain-source voltage. This original work of the author was started at Twente University, and the actual clinical product was carried out at research group of Cordis [17].

In reference [18], the Chen et.al has explained the design of FET-biosensor with graphene nanoribbons of high resolution. Graphene being a single layer of graphite, is discovered as the eligible nanomaterial for carbon-based electronic application, and biosensing devices [19]. Characterized to be a zero-gap semiconductor or semi-metal, graphene isn't used directly in the integration with FET's but intricate in the form of nano-ribbons patterned with nanometer size and quasi-one dimensional system [20]. If bio applications are to be used as hybrid devices, GNR is coated with lipid membranes or composite polymers.

Followed by Chen et.al, Dong et.al [21-22] carried out label-free electrical DNA detection with graphene-based FET device. With the evaluation of Dirac point shift, the process was evaluated .Similarly, Kim et.al [23] studied GFET devices for pH changes and also the working of graphene-Ag nanowires hybrid FET model in detecting protein.

3. Proposed Methodology

3.1 Nano Bio-FET

Biosensor is a device that estimates the amount of analyte present in the received signal (electrical, thermal, and optical signals). It consists of three elements: a) a transducer, b) a bio-recognition component, c) an amplifier. The first phase consists of a biocompatible layer that consists of immobilized biological sensing membranes. This channel is in contact with the electrolyte solution. The layer is then connected to the Transducer that receives or sends electrical or optical or physical signals. There are surplus transducer types like electrochemical, electrical, optical, thermal, acoustic and gravimetric [24]. The electrochemical type is further categorized into: Amperometric, potentiometric, voltammetry, conductometric, and impedometric biosensor. The transducer is in turn connected to amplifier and the signal is sent to the micro-electronics phase for the signal processing. The typical schematic of a biosensor is shown in Figure.1 that serves as an example for the DNA detection.

In FET-based biosensor, the sensitivity is calculated using the below equation:

$$\frac{dI_D}{I_D} = \left(dc\ \frac{d\rho}{dc}\right)\left(\frac{dv_{EG}}{d\rho}\right)\left(\frac{d_{ID}}{dv_{EG}}\frac{1}{I_D}\right)$$

In the above equation,

$d\rho$= Change in drain-source current,

dv_{Eg}= Change in effective gate voltage,

dI_D= Change in drain current.

dc= Change in analyte concentration

d_{ID}- Change in current without target analyte

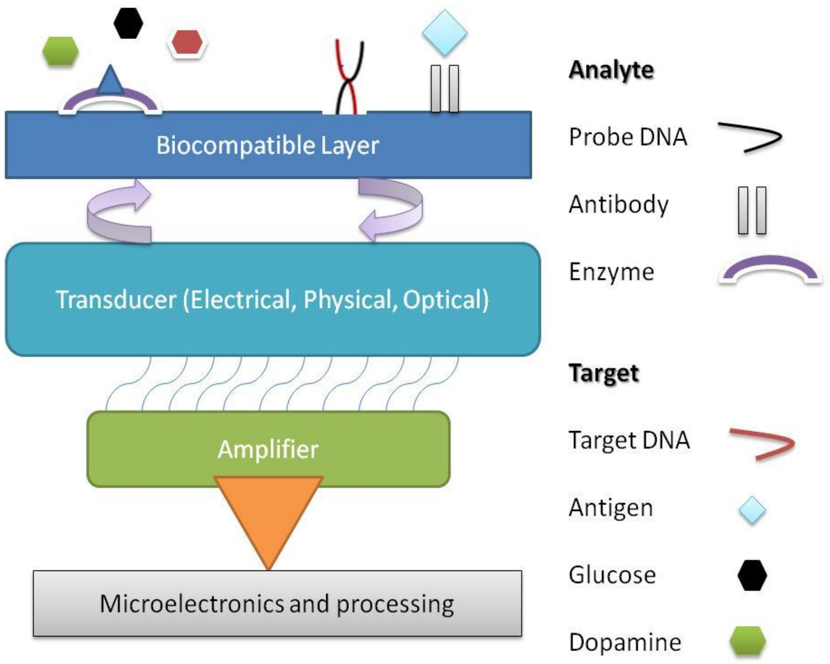

Figure 1. Schematic diagram of working mechanism of a biosensor

3.2 Detection by Nano FET-biosensor

As discussed above, Bio-FET is used in detecting various infectious diseases, neurotransmitters, and hormone regulation. At present, Bio-FET's are popularly used in the detection of DA, and the glucose levels. With the selectivity and sensitivity characteristics of Nano Bio-FET, abnormal levels of DA is easily identified and neurological disorders like Parkinson's disease, and Alzheimer's disease are diagnosed at the early stage [25]. Also, Bio-FET is used in detecting metabolic disorders. One such example is the glucose level monitoring that plays a vital role for people affected with Diabetes Mellitus. Causing blindness, kidney failure, and heart-related issues, this insulin deficiency in blood glucose is to be monitored continuously where FET-based biosensors are advantageous with small sensing chip, and low-power operation. The outlook detection process of detection of glucose in Bio-FET is illustrated in Figure.2.

In the past, glucose sensors where enzyme-based and their performance purely depends on reaction of the Catalyst. With drawbacks like functionality degradation, instability, and high cost, Bio-FET was introduced as an alternative [26]. The above outlook or model was devised with nanostructured materials like metal oxides, 1D and 2D nanomaterials following the SGGT architecture.

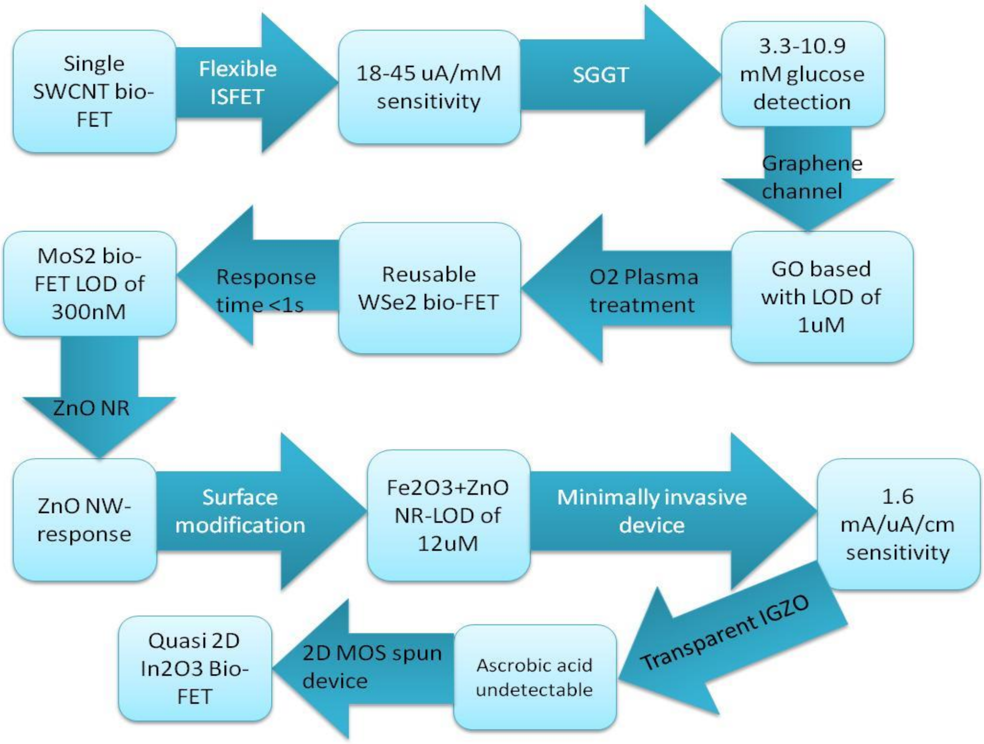

Figure 2. Outlook detection of glucose using nanomaterials in Bio-FET

4. Results and Discussion

This section discusses about the results and inferences made out after the entire review over the Nanomaterial-based FET biosensor. The below Figure.3 represents the glucose sensing performance obtained by WSe_2nano-based Bio-FET. The first graph represents the response against drain current & gate voltage, later one of gate voltage & sensitivity, and final one with concentration against sensitivity. It can be seen that the destined FET configuration performs well in terms of I_d-V_G characteristics, and average sensitivity.

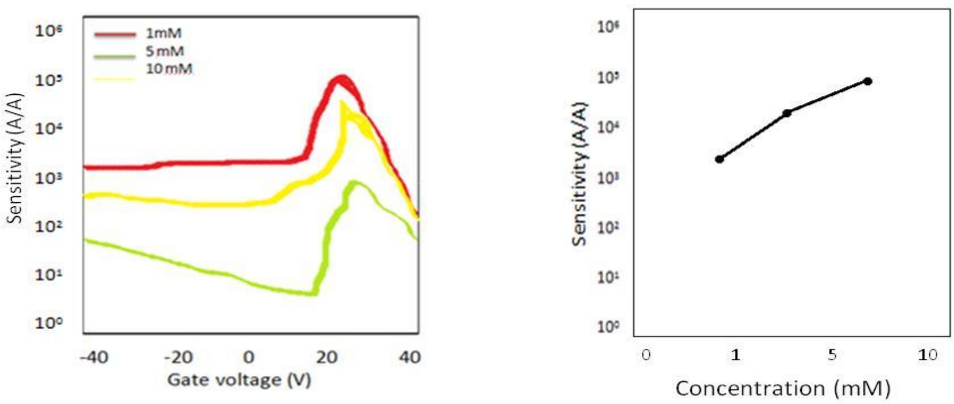

Figure 3. Glucose sensing performance WSe_2 Bio-FET

Similarly, if a TMDC-based FET biosensor is examined, the below characteristics are observed from [27-29] as shown in Figure.4. The graph represent the electrical characterization and the simulation response of the sensing response of TMDC-based FET sensors. Likewise, if carbon nanowires are used as the fabrication transducer material, then the characteristic leakage and transfer curves obtained as the result is depicted in Figure.5.

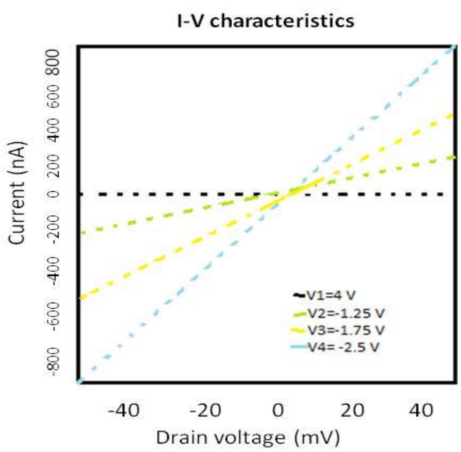

Figure 4. Performance of TMDC-based Bio-FET

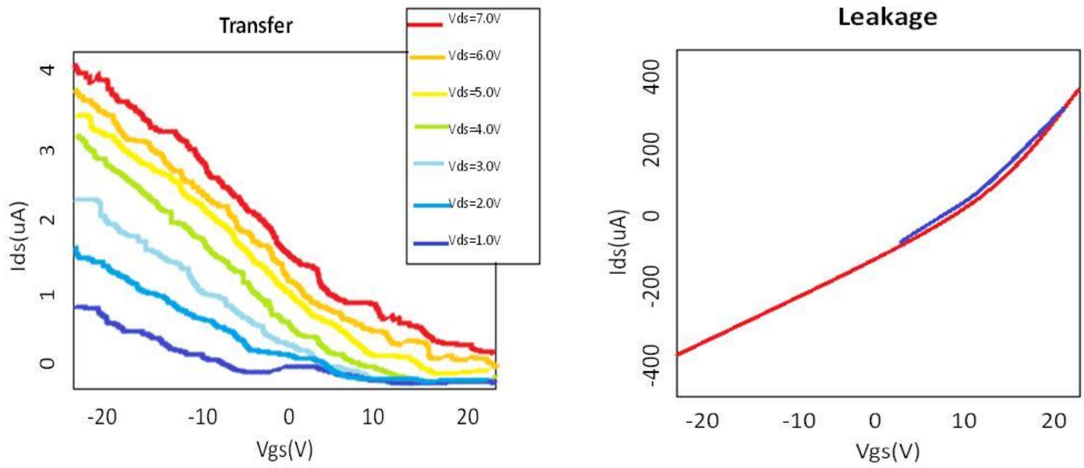

Figure 5. Simulation of transfer and leakage curves of a CNT-FET

5. Conclusion

In biomedical applications, FET-based biosensors play a vital role in the detection of infectious diseases, DNA, glucose, and diabetes level. Starting from ISFET, drastic changes and evolution occurred in the history of FET-based biosensor which was interpreted in detail in respective sections. Transducers or nanomaterials being the prime factor of the FET operation, was analyzed in detail as well. With discussion over a wide range of concepts like Nanotransducers, essential constituents of FET biosensors, review on the recent surveys, working mechanism, and comparison of conventional and FET-based devices, this paper has come to an end. While the present Nanomaterial FET-based biosensor concept suits well for the biosensing applications in medical field, the future scope extends for the enhancement of FET-based devices in the detection of upcoming infections period like the one encountered during the Covid-19 pandemic.

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