Advances in Bioresearch
Adv. Biores., Vol 6 (6) November 2015: 01-08
©2015 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
ICV 7.20 [Poland]

Advances in Bioresearch

REVIEW ARTICLE

A Review of Field-effect Transistors for Nucleic acid-based Medical Diagnosis

Sayed Mostafa Hosseini[1], Mahmoud Tavallaei[1], Ehsan Hosseini[2]
1- Human Genetic Research Center, Baqiyatallah University of Medical Science, Tehran, Iran.
2- Young Researchers and Elite Club, Central Tehran Branch, Islamic Azad university, Tehran, Iran
Email: smhosseini@bmsu.ac.ir

ABSTRACT
In last decade, field effect transistors (FETs) have growing forward application in electrical biosensing technology of medical diagnosis as well as electronic circuits. In biomedical diagnosis, they can be applied as transducing component of biosensors.These biosensors are equipped with immobilized bioreceptor probes (e.g., nucleic acids, antibodies, enzyme substrate) which targeted specific molecule. Owing the fact that nucleic acids have smaller size than the other bioreceptors, researchers are interested in fabrication and development of FET-based biosensors. Herein we overview and introduce the various various FETs and FET-based biosensors in terms of building blocks and working procedure. The following FETs are included in this study: Ion-sensitive field effect transistors (ISFET), silicon nanowire field effect transistors (SiNW-FETs), carbon nanotube (CNT)-based field effect transistor, graphenefield effect transistors (GFET), molybdenum disulfidefield effect transistors (MoS_2-FET), and organic field effect transistors (OFET).Finally, we discuss the recent advances in application and fabrication of FET-based biosensors for nucleic acid-based detection in medical diagnosis devices.
Keywords: *Field Effect Transistor; DNA; Hybridization; Nanowire; Carbon Nanotube.*

Received 24/02/2015 Accepted 29/05/2015

How to cite this article:
Sayed M H, Mahmoud T, Ehsan H. A Review of Field-effect Transistors for Nucleic acid-based Medical Diagnosis. Adv. Biores., Vol 6 [6] November 2015: 01-08**.** DOI: 10.15515/abr.0976-4585.6.6.18

INTRODUCTION

Early diagnosis leads to early medical intervention and improves the patient survival rates. In order to make a medical diagnosis, history, diagnostic techniques and other information are considered. There are a variety of disease diagnosis techniques from anatomic pathology to noninvasive techniques such as electrograms(e.g. electrocardiogram and electroencephalogram) and medical imaging (e.g. magnetic resonance imaging). Among them, molecular diagnostic techniques have experienced a rapid development during the last years [1]. Molecular diagnostics is used to analyze biomarkers in the proteome and genome by applying molecular biology to medical testing. It has been used in a variety of applications such as viral and bacterial pathogens detection [2], cancer detection [3], and pharmacogenomics [4].

Molecular diagnostics based on nucleic acids have become important tools in disease detection because nucleic acids are used as genetic material in all living organisms. In addition, nucleic acids are easy to purify, amplify, label and sequence. Nowadays, nucleic acid extraction, purification, amplification, hybridization and sequencing have been facilitated by the use of the lab on chip (LOC) technology [5].An important step in LOC-based medical diagnosis is the detection of hybridization events. This detection is performed by use of biosensors.

A biosensor is an analytical device incorporating a bioreceptor element and a transducer [6]. The bioreceptor can be an enzyme, antibody, nucleic acid (DNA, RNA, PNA, aptamer(artificial oligonucleotides) and etc.), antigen, etc. When the bioreceptors bind to the target analyte, a specific biological event take places. The transducer converts the recognition event (hybridization detection) into a measurable signal. Depending on various transducing mechanism such as electrochemical, optical, and

piezoelectric, several transducing elements have been proposed and fabricated. Among several transducers, surface plasmon resonance (SPR) [7], quartz crystal microbalance (QCM) [8], and modified field effect transistors (FET) are in the advent of current science.

For a medical diagnosis LOC platform, a digital microfluidic device is combined with a biosensor part capable of target material analysis. Because the sensors based on FET have small size and feasibility for label-free chip-based detection, they are more ideal than other types of biosensors for coupling to microfluidic devices [9].

This survey paper is organized as follows: The fundamental mechanisms of the nucleic acid sensors based on FET are described is section 2. Recent advances in the application of nucleic acid FET biosensors to medical diagnosis are reviewed in section 3.We have chosen to focus mainly upon developments occurring during the last ten years. Conference proceedings and patents are not included in this survey. Concluding remarks and future outlooks of FET biosensors are discussed in section 4.

FIELD EFFECT TRANSISTORS (FET)

Basic concepts of FET

A field effect transistor (FET) is a type of transistor which commonly used in electronic circuits for several applications [10]. It consists of three terminals (electrodes): the source, the gate, and the drain. The device consists of a channel through which electrons or holes flow from the source to the drain.A minimum voltage (the threshold voltage) between the gate and source is needed to create the channel. In the n-channel FETs the carriers are electrons while in the p-channel FETs the carriers are holes.A FET also consists of a substrate. For example, an n-channel FET consists of two n-type semiconductors as source and drain, and a p-type substrate.

The effective electrical diameter of the channel, which is related to the conductivity of the FET, is varied by application of a voltage to the gate. That is, the applied voltage imposes an electric field in to the FET.A positive gate voltage causes free holes to be repelled from the substrate under the gate. It also pulls electrons from substrate into the channel. Applying a voltage between the drain and source with the created channel causes current flows through the channel.

In the metal-oxide-semiconductor FET (MOSFET), the gate electrode is a piece of metal whose surface is oxidized. The oxide layer electrically insulates the gate from the main current carrying channel. This layer acts as a dielectric. Hence, the MOSFET has extremely high in put impedance. The basic structure of an n-type MOSFET is shown in Figure 1.

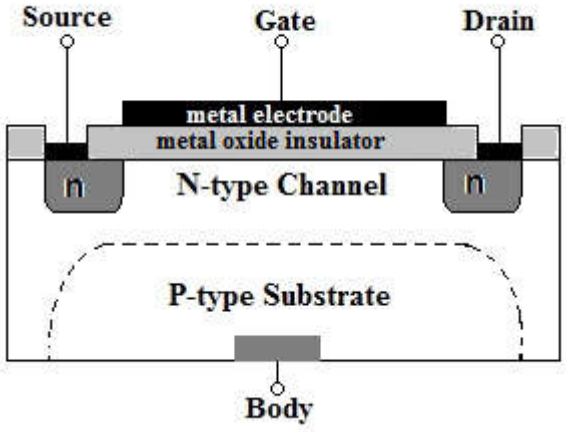

Figure 1.Cross section of an n-type MOSFET.

Ion-Sensitive Field Effect Transistors (ISFET)

The ISFET biosensor was introduced by Bergveld in 1970 [11]. The ISFET is a device that operates in a way similar to the way the MOSFET works. In the ISFET, the metal gate is replaced by the metal of a reference electrode. Then, the gate oxide is placed directly in an aqueous electrolyte solution.The basic structure of an n-type ISFET is shown in Figure 2.

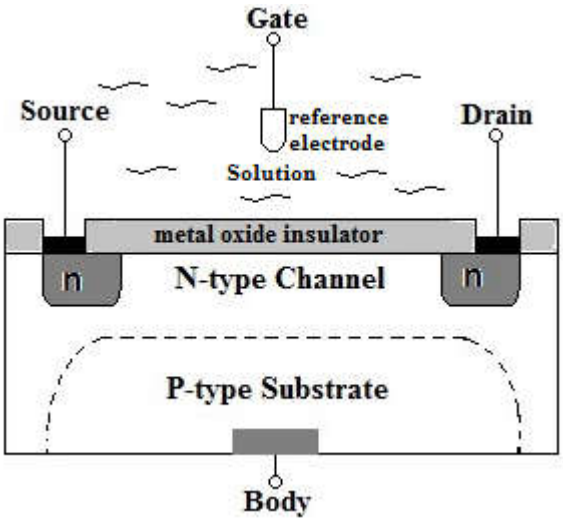

Figure. 2. The basic structure of an ISFET.

In ISFET, the source-drain current flow is influenced by the interface potential at the oxide/aqueous solution. The current also influenced by the charge of biomolecules interacting on the ISFET's dielectric. The ISFET is capable of detecting biomolecular interactions through a change in conductance [12].

DNA-based ISFET

A DNA-based ISFET (DNA BioFET) can be constructed according to the basic principle of the biosensors. That is, ISFETs are applied as signal transducer andthe DNA strands immobilized on to the oxide surface of ISFET's act as bioreceptor elements [13]. The block diagram of such biosensors is depicted in Figure. 3. When the unknown single-stranded DNA (ssDNA) forms a double-stranded DNA (dsDNA) with its complementary immobilized probe, the hybridization reaction is occurred. This reaction is detectable by processing the output signal of the applied ISFET (source-drain current or channel conductance variation signals).

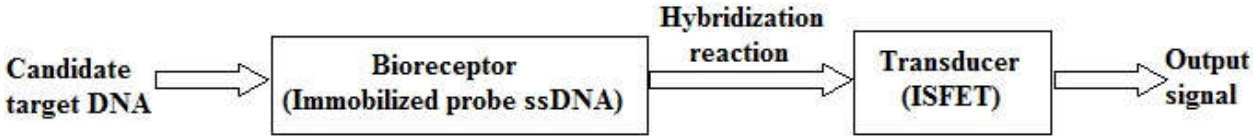

Figure 3.The block diagram of a DNA-based ISFET.

There are a variety of strategies for immobilization of the probe ssDNA on the gate oxide. Two major strategies are electrostatic immobilization and covalent immobilization [14]. In a commonly used strategy, the gate oxide is cleaned and activated in an acid step. Then the gate oxide is silanized with 3-aminopropyltriethoxysilane (APTES). The purpose of silanisation is to introduce positive charges to the gate surface for a more stable and faster immobilization. The immobilization is performed by electrostatic attraction between the negatively-charged probe DNA backbone (one negative charge per base) and the positively-charged transducer surface.The efficiency of the resulted hybridization can be improved by using suitable cross-linker molecules to covalently attach the amino-end functionalized probe ssDNA molecules to transducer surface [14].

Hom et al, [15] reported a DNA sensor based on an ISFET with protein a modification for characterization of DNA hybridization. Protein A originally found in the cell wall of the bacterium *Staphylococcus aureus*. Protein A was used to modify the ISFET surface instead of a complicated silanization technique. The antibiotin antibody was immobilized to protein A and a single-strand biotinylated DNA probe was added to bind to a specific antibiotin antibody. The detection limit of 0.08 μM for the DNA hybridization was reported.

Nanowire-Based Field Effect Transistors

Nanomaterials are comparable in size with nucleic acids [16] making them excellent interfaces for biosensing applications. Different nanomaterials such as quantum dots, nanowires (NW), nanogaps, and nanotubes have been used as sensing elements. In FET nanosensors, the semiconductor channel is made of nanomaterials such as NW and carbon nanotubes (CNT).

The basic structure of a nanowire FET (NW-FET) is illustrated in Figure. 4. The NW channel is placed between the source and drain electrodes. The gate electrode modulates the conductivity of the channel. In the biosensing applications, the bioreceptors are anchored to the surface of the channel.

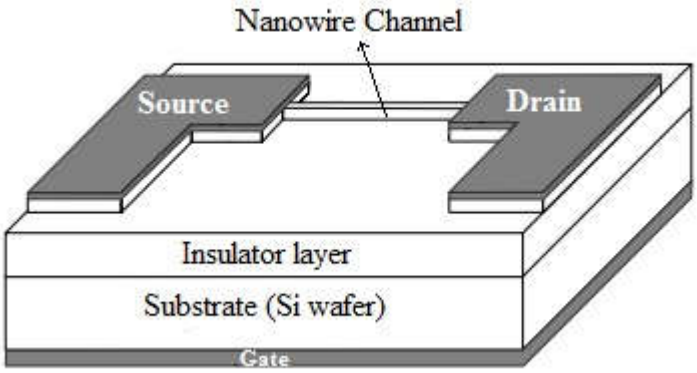

Figure.4. The basic structure of a NW-FET.

The NW is a semiconductor such as Ge, Si or metal oxides such as In_2O_3 and ZnO. The wire size can affect the sensitivity of the NW-FET. The interior areas of thick wires could be unaffected while approaching charged particles [17]. The smaller FET device diameter leads to the larger conductance changes.

Immobilization of bioreceptors on the NW surfaces may involve different linker molecules. For example, 3-(trimethoxysilyl) propylaldehyde (APTMS) and APTES can be used for Si NWs [16]. Besides, aphosphonate derivative like 3-phosphonopropanoic acid is an optimum linker for metal oxide NWs.In order to homogenize the orientation of the linkers on silica NWs, Chu et al. [18] proposed the use of an external voltage on a metal plate above the surface while grounding the gate electrode.

Nanotube-Based Field Effect Transistors

Carbon nanotubes may be composed of a single shell (wall) or of several walls. Singled-walled carbon nanotubes (SWNTs) are one-dimensional nanostructures. All carbon atoms of SWNTsare located on the surface making them an ideal material for biosensing applications [19]. Fahad and Hussain concluded that the nanotube architecture is more advantageous than the nanowire architecture for FET [20]. In SWNT-FET the conducting channel is made of a SWCNT. A schematic cross section of a SWNT-FET is shown in Figure.5. The SWNT is typically located on the surface of the supporting substrate and bridges the gap between the gold electrodes.In contrast to SWNTs, nanotube networks (with a random array of nanotubes between source and drain) are much easier to fabricate but they take up more space than SWNTs [21].

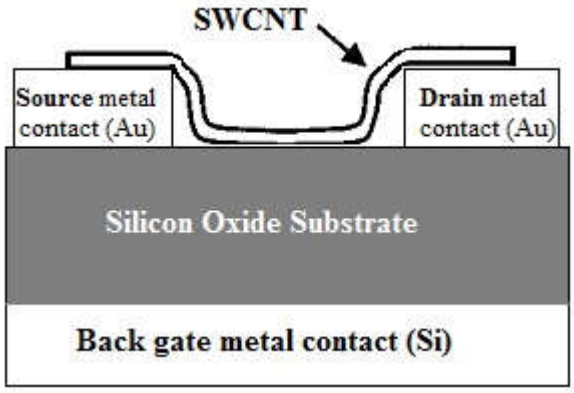

Figure 5.The basic structure of a SWNT-FET.

The SWNT-FETs can be used to detect DNA hybridization. RNA and ssDNA can disperse SWNTs in water. ssDNA can interacts non-covalently with SWNTs and forms a hybrid with them by wrapping around them by means of interactions between SWNT sidewalls and nucleotide bases [19]. DNA sensing has also been explored by attachment of DNA molecules at different device segments such as gold electrodes, SWNT sidewalls, and gate surface [21].

Graphene-Based Field Effect Transistors

Graphene is a 2-dimentional carbon material, a natural match to biomolecules. In graphene, layers of carbon atoms are arranged in six-membraned rings. Carbon nanotube, graphite, and fullerene can be

formed from grapheme [22].Graphene conductivity is strongly dependent on ionic strength, the type of ions present and the pH [23].

In graphene-Based FET (GFET), grapheneis used as conducting channel material between source and drain. In a typical configuration of GFET, SiO_2 layer is usually selected as substrate, and graphene is deposited on the substrate surface through chemical vapor deposition method (CVD). There are also top-gated and back- and top-dual gated GFETs [24].Dontschuk et al. [25] have demonstrated that GFETs are capable of detecting distinct coverage-dependent conductance signatures upon adsorption of DNA nucleobases (ie, adenine, thymine, cytosine and guanine).

Molybdenum Disulfide (MoS_2)-Based Field Effect Transistors

Molybdenum disulfide (MoS_2) is a 2-dimensional inorganic compound. A monolayer of this biocompatible material is only around 0.65 nm thick. In MoS2-FET, $MoS_2$is used as the channel material. The dielectric layer covering the channel is functionalized with bioreceptors. The source and drain terminals are also covered with a dielectric layer to protect them from the electrolyte [26].High-quality MoS_2 films do not possess π electrons for covalent attachment of probe molecules [27]. However, in order to detect hybridization between the target and probe DNA, DNA probe molecules can be immobilized on MoS_2 surface through vander Waals interactions [28].

Sarkar et al [26], compared MoS2 with Si nanowire, carbon nanotube, and graphene in terms of sensitivity, device fabrication and large-scale integrability, device scalability, and flexibility and transparency for FET-based biosensing. They concluded that MoS2 had the potential to overcome the shortcomings of these materials.

Organic Field Effect Transistors

An organic field effect transistor (OFET) uses an organic small moleculeor a polymer as its channel semiconducting material. In contrast to CNT-FETs and Si-based FETs, OFETs are superior in flexible, light-weight, and low-cost switching components [24]. In addition, organic materials are biocompatible.Four different OFET architectures are possible: bottom-gate bottom-contact, bottom-gate top-contact, top-gate top-contact, and top-gate bottom-contact [29].

Some of the materials used in OFETs are rubrene, tetracene, pentacene, and poly (3-hexiothiophene). Kergoat et al, proposed an OFET which its gate dielectric was replaced by a simple water droplet [30]. The water-gated OFET benefits from very low operation voltage and easy fabrication, and appears very pertinent for DNA detection.

The Application of BioFETs in Genetic Medical Diagnosis

In order to provide biosensors with high sensitivity and selectivity for medical diagnosis, researchers are continuously developing several nucleic acid-based BioFETsto detect disease agents and biomarkers.In following we will review the most recent advances in detection of pathogens (viral pathogens in particular) and cancer biomarkers by utilizing FET Biosensors.

Dastagir et al, have reported an unambiguous detection of a sequence of Hepatitis C Virus (HCV) by using SWNT-FET [31]. The target sequence was a 12-base RNA oligonucleotide, based on a specific sequence of HCV RNA. They have observed that the transconductance of the FET was increased only when PNA-functionalized SWNTs were exposed to complementary RNA. A detection limit down to 0.5 pM was reported. A back-gated NW-FET with the 60-nm wide NW has been fabricated by Wu et al, for real time sensing of Hepatitis B Virus (HBC) X gene [32].A 15-mer capture DNA strand with a sequence which was fully complementary to the target DNA was used for DNA immobilization. The detection range of HBV X gene was from 1 fM to 1 pM, and the detection limit could be down to 3.2 fM.

Lin et al, [33]have demonstrated poly-crystalline Si NW-FET to achieve detection of high pathogenic strain virus (H5 and H7 subtypes) DNA of avian influenza (AI). The width of NW channel was 80 nm. They have observed the electric response of DNA/DNA hybridization as soon as the target DNA was loaded on the nano device. The sensitivity in the femtomolar (fM) concentration range was obtained. In another paper, Lin et al, [34] have proposed a DNA recovery system that could easily be adapted to DNA biosensor for detection of target DNA. The method was based on the re-hybridization of DNA target with a recovery DNA to free the DNA probe. NW-FET with silicon-on-insulator wafers was demonstrated to monitor such DNA-DNA interaction using high pathogenic strain virus H1 DNA of AI as target.

Thu et al, [35] have reported a label-free DNA biosensor based on SWCNT-FET for selective DNA sequence hybridization detection of H5N1 virus. A random network of SWCNTs was used as the conductor channel. The channel lengths were 20, 50, and 100 μm. The DNA biosensor could detect full-complementary DNA with detection limit of 1.25 pM. The approximate sensitivity of 0.28 nM/nA was reported.

Zhang et al, [36] demonstrated a Si NW-FET for sensitive and rapid detection of reverse-transcription-polymerase chain reaction (RT-PCR) product of Dengue serotype 2virus. The PNA-DNA hybridization was verified by measuring the resistance change of Si NW channel before and after binding of the RT-PCR product to a PNA sequence which covalently attached to NW surface. The detection limit of 10 fMwithin 30 min was reported.

Croce Jr et al, [37] have reported a successful electrochemical detection of the protein thrombin utilizing a thrombin aptamer functionalized SWCNT-FET. A 15-mer aptamer which binds to the blood clotting factor thrombin was employed as bioreceptor in the fabricated device. The drain current of the FET was linearly related to thrombin concentration with sensitivity of 33 μA/(μM mm^2). Hammock et al, [38] presented a thorough study of various parameters (spacing between receptors, buffer pH, buffer ionic strength) affecting biosensing using OFET decorated with gold nanoparticle binding sites. They employed the thrombin protein and its DNA aptamer. The aptamers were preferred over antibodies because of small size of the thrombin aptamer. The detection limit of 100 pM was reported.

Kim et al, [39] fabricated a pentacene OFET for label-free detection of DNA from pathogenic organisms. The bacteriophage lambda virus (λ-phage) genomic DNA was chosen as a model organism and its presence was successfully detected by probe DNA hybridization on the pentacene layer. The sensitivity of 0.28 μA/pM was reported.The feasibility of the device as a disposable sensor for DNA hybridization was demonstrated.

Farid et al, [40] have developed a DNA aptamer-based GFET for detection of Interferon-gamma (IFN-γ). IFN-γ is an inflammatory cytokine associated with the tuberculosis susceptibility. Aptamer immobilization was verified by using unique structural approach by Atomic Force Microscopy. Change in drain current appeared to be highly sensitive to the IFN-γ concentrations ranging from nM to μM range. The detection limit of 83 pM was reported.

So et al, [41] used a RNA-based aptamer-functionalized SWCNT-FET for detection and titer estimation of *Escherichiacoli* in water. The device showed a conductance decrease of more than 50% after binding with *E.coli*. Moreover, the device did not show a noticeable conductance change when exposed to high-density *Salmonella* solution. The required time for detection was less than 20 min.

Wu et al [42] have developed a Si NW-FET (with line width of 60 nm) that allows DNA biosensing. As the target DNA sequence, they have employed the $BRAF^{V599E}$ mutation gene, which correlates to the occurrence of several cancers such as lung cancers, breast cancers, liver cancers, melanomas, gliomas, sacromas, ovarian carcinomas, papillary thyroid carcinomas, and colorectal cancers. The threshold voltage of the device increased when the mutation gene was hybridized with the 30-mer ssDNA capture probes on the NW and decreased to the original level after de-hybridization of the gene. Detection limit in sub-femtomolar level was reported.Chen et al, [43] usedfunctionalized Si NW-FET for detection of the breast cancer serum biomarker protein CA15.3. CA15.3 is a mucin-associated antigen, specific for the protein core of the MUC1 gene product. The detection limit of around 20 pM was reported.

Mutation of the p53 gene is one of the frequent alterations in human cancer. Han et al, [44] by using a MOSFET biosensor have assessed the abilities of wild p53 and mutant p53 proteins to interact with the consensus DNA-binding sequence. The cognate DNA was immobilized onto the gate electrode. The sequence-specific-DNA-protein interactions were successfully monitored by drain current measurement.

Cai et al [45] have reported a gold nanoparticle-decorated GFET biosensor for label-free detection of MicroRNAs. MicroRNAs (miRNAs) are a family of short endogenous non-coding RNA molecules that as ideal biomarkers can identify cancer in the early stage. After PNA probe immobilization, the detection was carried out via PNA-miRNA hybridization. The detection limit of 10 fM was reported.

CONCLUDING REMARKS AND FUTURE OUTLOOKS

In this survey report we have discussed constructions and working principle of various field effect transistors and DNA-based FET biosensors. In addition, recent developments in nucleic acid BioFETs for disease detection have been reviewed.The small size of nucleic acids in contrast to other bioreceptors makes them ideal for applying with microfluidic devices. Since nanoBioFETs and GFETs offer a sensitive tool for disease detection, there are growing researches for fabrication and optimization of such devices. Further advances in medical diagnosis can be obtained by utilizing the BioFETs in lab on chip systems. In future, the application of sensor fusion methods to FET devices could improve the sensitivity and selectivity of biosensors.

REFERENCES

1. Cobo, F. (2012). Application of molecular diagnostic techniques for viral testing.Open. Virol. J., 6:104-114.

2. Nolte, F.S. (2008). Molecular diagnostics for detection of bacterial and viral pathogens in community-acquired pneumonia.Clin. Infect. Dis., 47 (supplement 3):S123-S126.
3. Nikiforova, M.N.&Nikiforov, Y.E. (2009). Molecular diagnostics and predictors in thyroid cancer.Thyroid., 19(12): 1351-1361.
4. Francia, R.D, Berretta M., Catapano O., Canzoniero L.M.T &Formisano L. (2011). Molecular diagnostics for pharmacogenomic testing of fluoropyrimidine based-therapy: costs, methods and applications. Clin.Chem Lab. Med., 49(7): 1105-1111.
5. Li, P.C.H. (2010). Fundamentals of microfluidics and lab on a chip for biological analysis and discovery, CRC Press, p.249.
6. Turer, A., Karube, I. & Wilson, G.S. (1987). Biosensors: fundamentals and applications.Oxford University Press.
7. Van der Merwe, P.A. (2001). Surface plasmon resonance (Eds. Harding, E. &Chowdhry, B.Z.) Protein-ligand interactions: hydrodynamics and calorimetry. Oxford University Press, New York, pp. 137-184.
8. Marx, K. A. (2003). Quartz crystal microbalance: a useful tool for studying thin polymer films and complex biomolecular systems at the solution-surface interface. Biomacromolec., 4(5): 1099-1120.
9. Choi, K., Kim, J.Y., Ahn, J.H., Choi, J.M., Im, M., & Choi, Y.K. (2012). Integration of field effect transistor-based biosensors with a digital microfluidic device for a lab-on-a-chip application.Lab Chip., 12: 1533-1539.
10. Neamen, D.A. (2001). Electronic circuit analysis and design.McGraw-Hill.
11. Bergveld, P. (1970). Development of an ion-sensitive solid state device for neurophysiological measurements.IEEE.Trans. Biomed. Eng., 17: 70-71.
12. Lee, C.S., Kim, S.K. & Kim, M. (2009). Ion-sensitive field-effect transistor for biological sensing.Sensors., 9: 7111-7131.
13. Schöning, M.J. &Poghossian, A. (2002). Recent advances in biologically sensitive field-effect transistors (BioFETs).Analyst., 127: 1137-1151.
14. Ingebrandt, S. &Offenhäusser, A. (2006). Label-free detection of DNA using field-effect transistors.Pys. Stat. Sol., 203(14): 3399-3411.
15. Hom, N.M., Promptmas, C. &Wat-Aksorn, K. (2015). Detection of DNA hybridization using Protein A modified ion sensitive field effect transistor. Aalytic.Lett., 48(7): 1128-1138.
16. Curreli, M., Zhang, R., Ishikawa, F.N., Chang, H.K., Cote, R.J., Zhou, C & Thompson, M.E. (2008). Real-time, label-free detection of biological entities using nanowire-based FETs.IEEE. Trans Nanotechnol. 7(6): 651-667.
17. Grieshaber, D., MacKenzie, R., Vörös, J. &Reimhult, E. (2008).Electrochemical biosensors - sensor principles and architectures.Sensors., 8: 1400-1458.
18. Chu, C.J., Yeh, C.S., Liao, C.K., Tsai, L.C., Huang C.M., Lin, H.Y., Shyue. J.J, Chen, Y.T. & Chen, C.D. (2013).Improving nanowire sensing capability by electrical field alignment of surface probing molecules.Nano.Lett., 13(6): 2564-2569.
19. Hu, P., Zhang, J., Li, L., Wang, Z., O'Neill, W. & Estrela, P. (2010). Carbon nanostructure-based field-effect transistors for label-free chemical/biological sensors.Sensors., 10: 5133-5159.
20. Fahad, H.M. &Hussain, M.M. (2012). Are nanotube architectures more advantageous than nanowire architectures for field effect transistors?. Sci. Rep., 2: 475. DOI: 10.1038/srep00475.
21. Kichambare, P.D. & Alexander, S. (2007). Biosensing using carbon nanotube field-effect transistors. Nanotechnologies for the Life Sciences., DOI: 10.1002/9783527610419.ntls0082.
22. Geim, A.K.&Novoselov, K.S. (2007).The rise of graphene. Nat. Mater. 6(3): 183–191.
23. Liu, S. &Guo, X. (2012). Carbon nanomaterials field-effect-transistor-based biosensors.NPG Asia Materials., 4(e23). DOI:10.1038/am.2012.42.
24. Zhan, B., Li, C., Yang, J., Jenkins, G., Huang, W. & Dong, X. (2014). Graphene field-effect transistor and its application for electronic sensing.Small., 10(20): 4042-4065.
25. Dontschuk, N., Stacey, A., Tadich, A., Rietwyk, K.J., Schenk, A, Edmonds, M.T., Shimoni, O., Pakes, C.I., Prawer, S. &Cervenka, C. (2015). A graphene field-effect transistor as a molecule-specific probe of DNA nucleobases.Nature Commun. 6. DOI: 10.1038/ncomms7563.
26. Sarkar, D., Liu, W., Xie, X., Anselmo, A.C., Mitragotri, S. & Banerjee, K. (2014).MoS_2 field-effect transistor for next-generation label-free biosensors.ACS Nano., 8(4): 3992-4003.
27. Lee, D.W., Lee. J., Sohn, Y., Kim, B.Y., Son, Y.M., Bark, H., Jung, J., Choi, M., Kim, T.H., Lee, C. & Lee, N.E. (2015).MoS_2 sensing channel for label-free and highly sensitive electrical detection of DNA hybridization.Nano.Res., DOI 10.1007/s12274-01 5-0744-8.
28. Zhu, C., Zeng, Z., Li, H., Li, F., Fan, C. & Zhang, H. Single-layer MoS2-based nanoprobes for homogeneous detection of biomolecules. (2013). J. Amer. Chem. Soc., 135(16): 5998-6001.
29. Wang, C., Dong, H., Hu, W., Liu, Y. & Zhu, D. (2012) Semiconducting π-conjugated systems in field-effect transistors: a material odyssey of organic electronics. Chem. Rev., 111(4):2208-67.
30. Kergoat, L., Herlgsson, L., Braga, D., Piro, B., Pham, M.C., Crispin, X., Berggren, M. & Horowitz, G. (2010). A water-gate organic field-effect transistor. Adv. Mater., 22(23): 2565-2569.
31. Dastagir, T., Forzani, E.S., Zhang, R., Amlani, I., Nagahara, L.A., Tsui, R. & Tao, N. (2007). Electrical detection of hepatitis C virus RNA on single wall carbon nanotube-field effect transistors.Analyst., 132(8): 738-40.l.
32. Wu, C.Y., Cheng, H.Y., Ou, K.L. & Wu, C.C. (2014). Real-time sensing of hepatitis B virus X gene using an ultrasensitive nanowire field effect transistor. J. Polym. Eng., 34(3):273-277.

33. Lin, C.H., Hung, C.H., Hsiao, C.Y., Lin, H.C., Ko, F.H. & Yang, Y.S. (2009). Poly-silicon nanowire field-effect transistor for ultrasensitive and lab el-free detection of pathogenic avian influenza DNA.Biosens.Bioelectron., 24(10): 3019-3024.
34. Lin, C.H., Chu, C.J., Teng, K.N., Su, Y.J., Chen, C.D., Tsai, L.C. & Yang, Y.S. (2012). Recovery Based Nanowire Field-Effect Transistor Detection of Pathogenic Avian Influenza DNA. Jpn. J. Appl. Phys., 51(2S): 02BL02-1-02BL02-5.
35. Thu, V.V., Tam, P.D. & Dung, P.T. (2013). Rapid and label- free detection of H5 N1 virus using carbon nanotube network field effect transistor. Cur.Apl. Phys., 13(7): 1311-1315.
36. Zhang, G.J., Zhang, L., Huang, M.J., Luo, Z.H.H., Tay, G.K.I.T., Lim, E.J.A., Kang, T.G & Chen, Y. (2010). Silicon nanowire biosensor for highly sensitive and rapid detection of Dengue virus.Sens. Actuator. B-Chem., 146(1): 138-144.
37. Croce Jr, R.A., Vaddiraju, S., Chan, P.Y., Seyta, R. & Jain, F.C. (2011).Label-free protein detection based on vertically aligned carbon nanotube gated field-effect transistors. Sens. Actuator. B-Chem., 160: 154-150.
38. Hammock, M.L., Knopfmacher, O., Naab, B.D., Tok, J.B.H. &Bao, Z. (2013).Investigation of protein detection parameters using nano-functionalized organic field-effect transistors.ACS.Nano.,DOI: 10.1021/nn305903q.
39. Kim, J.M., Jha, S.K., Lee, D.H., Chand, R., Jeun, J.H., Sin, I.S. & Kim, Y.S. (2011). Rapid pathogen detection using an organic field effect transistor.Micro.Nano.Lett., 6(9): 745-748.
40. Farid, S., Meshik, X., Choi, M., Mukherjee, S., Lan, Y., Parikh, D., Poduri, S., Baterdene, U., Huang, C.E., Wang, Y.Y., Burke, P., Dutta, M. &Stroscio, M.A. (2015). Detection of Interferon gamma using graphene and aptamer based FET-like electrochemical biosensor. Biosens.Bioelectron., 71: 294-299.
41. So, H.M., Park, D.W., Jeon, E.K., Kim, Y.H., Kim, B.S., Lee, C.K., Choi, S.Y., Kim, S.C., Chang, H. & Lee, J.O. (2008). Detection and titer estimation of Escherichia coli using aptamer-functionalized single-walled carbon-nanotube field-effect transistors. Small, 4(2): 197-201.
42. Wu, C.C., Ko, F.H., Yang, Y.S., Hsia, D.L., Lee, B.S. & Su. T.S. (2009).Label-free biosensing of a gene mutation using a silicon nanowire field-effect transistor.Biosens.Bioelectron., 25(4): 820-825.
43. Chen, Y., Wang, X., Hng, M.K., Rosenberg, C.L., Reinhard, B.M., Erramilli, S. &Mohanty, P. (2010). Nanoelectronic detection of breast cancer biomarker. Appl. Phys. Lett., 97:(233702), DOI: 10.1063/1.3519983.
44. Han, S.H., Kim, S.K., Park, K., Yi, S.Y., Park, H.J., Lyu, H.K., Kim, M. & Chung, B.H. (2010). Detection of mutant p53 using field-effect transistor biosensor.Analyt.Chim.Act.,665: 79-83.
45. Cai, B., Huang, L., Zhang, H., Sun, Z., Zhang, Z. & Zhang, G.J. (2015).Gold nanoparticles-decorated graphene field-effect transistor biosensor for femtomolar MicroRNA detection.Biosens.Bioselectron., 74: 329-334.