UDC 621.3.084

Clinical Applications of Biosensors Based on Field-Effect Transistors with Carbon Nanotubes or Nanowires

D.S. Bodilovska
National Technical University of Ukraine “Kiev Polytechnic Institute”,
pr. Peremogy, 37, Kyiv-56, 03056, Ukraine.

In this paper we describe recent advances in the rapidly developing area of analyte detection using field-effect transistors (FETs) based on carbon nanotubes or nanowires. In this article behavior and advantages of one-dimensional nanomaterials for biosensing application is depicted. Among one-dimensional nanometer-scale materials, carbon nanotubes and nanowires offer unique electronic and mechanical properties that make them extremely attractive for the task of biosensing.

The structures and work principles of FET-biosensors based on carbon nanotubes/nanowires is discussed. Carbon nanotubes/silicon nanowire field-effect transistors have recently attracted great attention as promising tools in biosensor design because of their biocompatibility, size compatibility, ultrasensitivity, selectivity and label-free and real-time detection capabilities. In addition, interaction mechanisms between transducer elements of FET-biosensor (carbon nanotubes or nanowires) and target entities is also reviewed. Finally, applications of FET-type biosensors for measurement of different analytes is highlighted in this review. Proteins interaction, antibody–antigen reactions including prostate-specific antigen detection, DNA hybridization and enzymatic reactions involving glucose is shown. Reference 36, figures 5.

Keywords: *nanobiosensor, field-effect transistor, carbon nanotubes, nanowires, FET-based biosensor.*

Introduction

Modern medical diagnosis is mainly based on laboratory tests that require the involvement of highly skilled and experienced staff and a large amount of laboratory instruments and devices. Laboratory diagnostic techniques provide highly accurate results, but the main disadvantages of these diagnostic methods are great waste of time, high cost and use of huge devices. Quick, cheap and easy-to-use real-time “point-of-care” systems for testing in near patient locations, without the need for sample transport and delays associated with dedicated central laboratories, can significantly improve the quality of health care service. [9]

Label-free electrical monitoring of biorecognition events provide a promising platform, which is simpler, cheaper and requires less energy. Rapid testing of various analytes is required in various applications ranging, including the chemical analysis, clinical diagnosis/monitoring and drug discovery, environmental monitoring, food analysis, the bioterrorism detection technologies and many other fields.

For the last years the number of articles describing advantages in FET-based biosensors’ development has increased at times. Research reports describing the new biosensors for the detection of analytes in a clinical setting continues to increase, but the movement of the biosensor research laboratory to the clinical laboratory remains slow. Great necessary of such biosensors will be felt at “point-of-care” testing locations without laboratory support. Integration of biosensors in a reliable, easy-to-use and rugged instrumentation will be required to ensure the success of biosensor-based systems at the “point-of-care” testing systems. To create highly sensitive biosensors, applications of nanoscience will be required. Nanotechnology can be used to enhance the performance of biosensors using electrochemical, optical, mechanical and physical modes of transduction and to allow arrays of biosensors to be constructed for parallel detection.

Dimensions of nanomaterials (1—100nm) provide a perfect study opportunities of most biological entities, such as nucleic acids, proteins, viruses and cells [9]. Also, the high surface-to-volume ratio of nanomaterials allows a large number of the constituent atoms in the material to be located close to the surface. This feature permits the surface atoms play important role in determining the physical, chemical or electronic properties of nanomaterials. In addition, some particular nanomaterials with surfaces, which are easy chemically modify, are good candidates for nanoscale sensing applications.

Biosensors, described in this paper, are used mainly to detect cancer biomarkers, cardiac biomarkers, biomarkers for autoimmune diseases, infectious diseases, DNA/RNA, etc.

One-dimensional nanomaterials for biosensing application

One-dimensional (1D) nanomaterials have found applications as building blocks for nanodevices such as transistors, probes, biological and chemical sensors. 1D nanomaterials, such as carbon nanotubes (CNTs), nanowires (NWs), etc., have unique electronic and mechanical properties, that make them extremely attractive for the task of biosensing. In particular, 1D nanomaterials are directly comparable to the size of most biological substances, such as molecules, nucleic acids, proteins, viruses, cells, carbohydrates and aptamers (Fig.1) [9]. Several experiments have confirmed the applicability of nanomaterials in biosensors by demonstrating sensor systems for different types of biomolecules [34]. However, the interaction mechanisms had not been clearly identified.

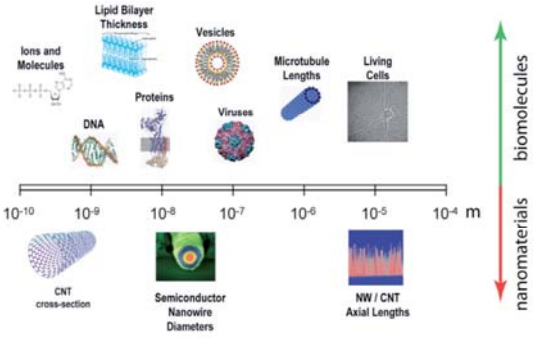

Fig. 1. Size of several nanomaterials is compared to the size of some biological entities, such as nucleic acids, proteins, virus and cells. Reprinted from [23]

1D nanomaterials possess unique physical and chemical properties because of their size. They have high sensitivity to molecular adsorption on the tube wall. These properties make CNTs/NWs well suitable for electronic detection of biomolecules or other analytes for a wide range of electrochemical biosensors application (Fig.2). The detection of the substances occurs with high accuracy, selectivity, stability, degree of immobilization, specificity, sensitivity, directly. NWs and CNTs can be used for direct, label-free and real-time detection of biomolecule binding by taking advantage of their properties. Thus, among different 1D nanomaterials, CNTs and NWs have a great potential for biosensing applications [1]. Biosensors based on CNTs/NWs can provide a promising platform for quick and inexpensive chemical and biological analysis of substances in biological fluids. The usage of sensors based on CNTs/NWs in medicine is rapidly evolving and favor the significant expansion of diagnostic capabilities.

Recent biosensing literature has reported the use of either CNTs or NWs as transducer for a number of biological analytes. However, combining these two nanomaterials may offer an interesting comparison and also novel sensing strategies [20].

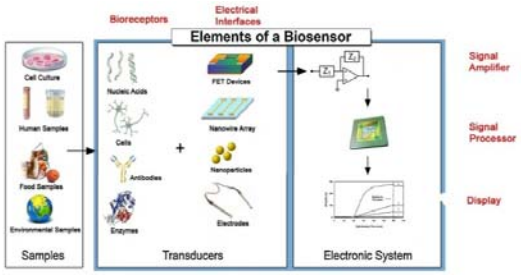

Fig. 2. The construction of typical biosensors with elements and selected components. Reprinted from [5]

Carbon nanotubes are allotropes of carbon with a cylindrical nanostructure. Nanotubes have been constructed with length-to-diameter ratio of up to 132.000.000:1.

CNTs can be realized as graphite sheets that have been rolled into cylinders. These sheets are rolled at specific ("chiral") angles and the combination of the rolling angle and radius defines the nanotube properties. The properties of CNTs depend strongly on physical properties, such as their diameter, their length, the presence of residual catalyst and chirality. In addition, carbon nanotubes may have properties either metallic conductors or semiconductors, based on the chirality of the structure.

Since CNTs have been discovered by S. Iijima [17] in 1991, they have become the most promising nanostructured 1D materials.

Most of CNTs are synthesized by carbon arc methods, laser evaporation or chemical vapor deposition (CVD) method.

Semiconductor nanowires are nanostructures, such as solid semiconductor rods, beams or ribbons that have a thickness or diameter in the range to tens of nanometers. Typical nanowires show length-to-width ratio of 1000 or more. At these scales, quantum mechanical effects are important and NWs have the behavior of "quantum wires". NWs have many properties that cannot be observed in bulk. This is because electrons in nanowires are quantum confined laterally and thus occupy energy levels that are different from the traditional continuum of energy levels or bands found in bulk materials.

Many different types of NWs exist, including metallic (e.g., Ni, Pt, Au), insulating (e.g., SiO2, TiO2) and semiconducting (e.g., Group IV – Si and Ge nanowires, Group III-V InAs, GaAs, GaN nanowires, Group II-VI CdS, CdSe, ZnS, ZnSe nanowires and metal oxide nanowires such as In2O3 [20], ZnO, SnO2, etc.) These semiconductor materials have been used as field-effect transistors or nanoelectrode materials for biosensing. [23]

NW can be synthesized by several common laboratory techniques, including suspension, electrochemical deposition, vapor deposition, Ion track technology and VLS growth.

Biosensors based on field-effect transistors with 1D nanomaterials

Field-effect transistors can be suitable candidates for biological sensors, due to their ability to directly convert the interaction with target molecules taking place on the FETs' surface into electrical signal [25]. FET is a type of transistor commonly used for weak-signal amplification. FETs show potential for very high sensitivity since the depletion or accumulation of charge carriers, which are caused by the binding of charged biological entities on the surface of NWs or swCNTs, can affect the entire cross-sectional conduction pathway of these nanostructures.

FET-biosensor has the structure of typical three-electrode transistor (Fig.3), where NWs or networks of swCNTs placed between a source and a drain electrode on a SiO2/Si substrate and the gate electrode modulates the channel conductance [9], the physical diameter of the channel is fixed, but its effective electrical diameter can be varied by the application of a voltage to gate electrode. The Si layer can act as back gate, which is separated by an insulating layer of SiO2. Since the work function of CNTs/NWs is higher than that of most metals, the contact barrier between CNTs/NWs and metals is usually a Schottky barrier. The height of the Schottky barrier in the FET-biosensors contact is determined by the work function of the electrode metal.

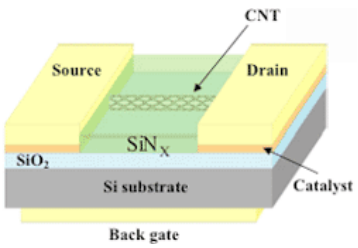

Fig. 3. Structure of FET-type nanobiosensor

The conductivity of the FET depends on the electrical diameter of the channel. The conductance of CNTs/NWs-based FET can be modulated by applying a potential to the gate electrodes with a constant drain-source bias voltage. A small change in gate voltage can cause a large variation in the current from the source to the drain by which the FET amplifies signals. Because of its high sensitivity, FETs have been widely used in biosensor application. [31]

Biosensors based on carbon nanotube field-effect transistors

Semiconducting swCNTs play a central role in the operation of swCNTs-based field-effect transistors (swCNTs-FETs). Biosensors based on swCNTs field-effect transistors [1] were first obtained in 1998 by the groups of both Dekker at Delft University [30] and Avouris at IBM [22]. The first biological application of swCNTs-FETs was proposed by the Dai group in 2003 while investigating specific protein–protein interactions [6]. FET-type biosensors have attracted great attention because of high selectivity and sensitivity, real-time response and label-free detection capabilities.

There are two classical types of biosensor device design regarding swCNTs-FETs. The first design uses a single CNT to act as an electron channel between the source and drain electrodes [22, 30]. The second type of structure uses a network of CNTs serving as a collective channel between the source and drain.

Semiconducting CNTs can be used to fabricate swCNTs-FETs, which can operate at room temperature and in ambient conditions.

In scientific reports various mechanisms of swCNTs-FETs-based sensors operation such as electrostatic gating, changes coupling, carrier mobility changes and Schottky barrier effects were shown.

Recognition mechanisms between CNTs/NWs and analytes

In the case of biosensors based on field-effect transistors, the semiconductor channel is made of a nanomaterial (CNTs, NWs) and used as the extremely sensitive transducer element of the device. In order to provide selectivity towards a unique analyte, a specific recognition group (biological receptors) fixtures to the surface of the semiconductor channel.

The specific biological receptors are cramped to the CNTs/NWs-based FET surface of the semiconductor channel for recognition and binding

of the target biomolecules through their high specificity and strong binding affinity in the buffer environment. When the target molecules bind to the receptor molecules in solution, the surface potential of the semiconductor channel changes (Fig.4) [9], because of the charges of the target molecules affect to the conductance of the CNTs/NWs. This lead to channel conductance modulating and the signal is collected by a detection system. Thus, CNTs/NWs-based FET can detect specific target molecules in real time by monitoring the change of electrical characteristics. [5, 19]

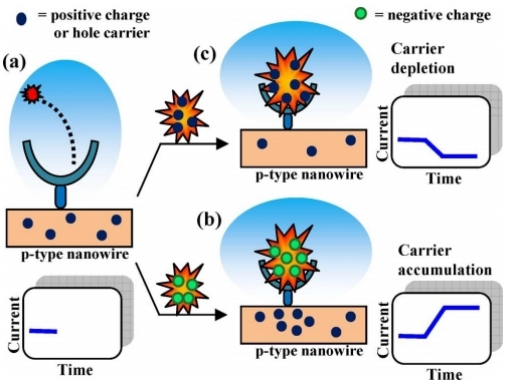

Fig. 4. Mechanism to modulate the conductance of a p-type NW FET. Reprinted from [9]

Antibodies are ideal receptors for recognition and binding due to their specificities and strong affinities for cognate antigens. Antibodies have numerous successful applications in the area of diagnostics with antibodies and they were successfully used in many types of biosensors.

The sensing could be controlled by the interaction of molecules with metal contacts or the contact interfaces. Adsorbed molecules can change the metal work functions, and thereby the Schottky barrier.

The interaction between analyte and CNTs may have one of two effects. The first effect involves charge transfer from molecules to the carbon nanotubes. I this case, the threshold voltage will become either more positive (electron withdrawing from the target analyte to the CNTs) or more negative (electron donation from the analyte to the CNTs). In the second type of mechanism, the analyte acts as a scattering potential across the carbon nanotube. It is possible to distinguish two mechanisms by taking measurements. In addition, a scattering mechanism may be observed from an overall drop in conductance. This is because of the scattering effect induced by the target analyte absorbed on the sidewalls of swCNT. [11]

Other authors describe interaction between analyte and NWs as following. The charge transfer between the analyte and NWs shifts the source-drain current towards more positive (electron donation from the analyte to the NWs) or towards more negative (electron withdrawing from the target analyte to the NWs) gate voltages. Also molecules on the surface of the NWs may also act as scattering centers, which means these molecules, can decrease the mobility of electrons in NWs, thus decreasing the current without shifting. [34]

Heller's group [14] identified four different mechanisms for biosensing proteins with CNTs-based FETs, although they concluded that electrostatic gating and Schottky barrier effects are the two most relevant mechanisms. The mechanisms for gas sensing in CNTs-based FETs are differ from other entities biosensing. Peng's group [24] identified two main mechanisms for NH3 detection depending on temperature (Schottky barrier effects for temperatures below 1500C and charge transfer for higher temperatures). CNTs-based FETs sensors have shown sensitivity to gases such as NH3, NO2, H2, CH4, CO, H2S and some organic vapors such as ethanol and methanol. A completely different mechanism was proposed for the detection of mercuric ions in solution.

But the exact mechanism of molecule detection by CNTs/NWs-based FET is still a subject of intensive debate in the literature and response mechanisms depend on the type of detected molecule.

Applications of CNTs/NWs - FETs biosensors

Several recent articles have reviewed biological detection of variety of analytes [6,16], such as proteins [1] (antibody-antigen interactions [6] and enzymatic glucose detection [3]), nucleic acids [10, 29], bacteria or higher cells [7] (e.g.,Salmonella infantis, Escherichia coli or Candida albicans), viruses, aptamers, etc.

Lieber's group showed the usage of Si NWs-based FET for detecting proteins [8], DNA hybrids [10] and cancer markers [36]. This biodetection approach may allow selective detection at the single-particle level. This group was also able to push the sensitivity of Si NWs for the purpose of demonstrate their ability for single viruses detection.

Protein detection

The immobilization of proteins on CNTs provides a straightforward biological detection. The

majority of research reports towards biosensing application of FET-biosensors describe the interactions of CNTs and NWs with proteins. These papers show some general detection mechanisms, conductivity measurements based on interactions, antibody–antigen interactions and enzymatic glucose detection. [1]

The difference of proteins can be bound to the CNTs' surface via nonspecific adsorption. Protein such as streptavidin crystallizes in a helical fashion, resulting in ordered arrays of proteins on the nanotube surface. It was observed that protein adsorption is associated with the amino affinity of CNTs and demonstrated by monitoring the conductance change in a CNT. The intermolecular interactions involving aromatic amino acids (i.e., histidine and tryptophan) in the polypeptide chains of the proteins can help to the observed affinity of the peptides to CNTs.

Star's group [4] has fabricated CNTs-based FETs sensor which is sensitive to streptavidin by using individual biotin-functionalized CNT arrays. These CNTs in the CNTs-FETs sensor device was coated with a mixture of two polymers: poly(ethylene imine) (PEI) and poly(ethylene glycol) (PEG). These polymers prevented the nonspecific adsorption of proteins on the functionalized CNT. The experiments point at the specific binding of streptavidin, which occurs only at the biotinylated interface. [1]

Experiments made by Cui's group [8] demonstrated the real-time detection of streptavidin binding to biotin-modified Si NW-FETs. They also explored the ability of biotin-modified Si NW-FET to detect streptavidin at the concentration of 10pM, which is much lower than the detection level obtained from other techniques.

It is well known that the interaction between CNTs and protein molecules can be described as nonspecific. Several research groups have found that proteins adsorb onto the surface of a CNT without any favour. Balavoine's group [2] found that the protein streptavidin binds strongly to the wall of a CNT in a helical fashion. Other groups of Kam and Dai [18] have shown other interaction between proteins and CNTs. They discussed the nonspecific binding after researching nanotubes as protein intercellular transporters. They have found that imparting hydrophilicity was not enough to block this type of binding. Haddon's group [35] also found nonspecific binding between the cell and the carbon nanotubes.

But in most cases, CNTs can be suitable to specifically bind protein to the wall. There are a lot of reports that demonstrate the ability to chemically functionalize nanotubes for this purpose.

Two approaches to this kind of attachment involve covalent and noncovalent. In terms of covalent attachment, the CNTs are oxidized to have free carboxyl groups that coupling with amino groups in protein molecules. While covalent modifications are often effective at introducing functionality, they decrease the mechanical and electronic properties of swCNTs.

But on the other hand, noncovalent modifications, not only increase the solubility of swCNTs in water, but also constitute nondestructive processes, protection the primary structures of the swCNTs along with their unique mechanical and electronic properties. There are two main schemes to noncovalent functionalization of CNTs. The first type of noncovalent functionalization involves bi-functional molecules that exhibit π-π stacking on the CNTs' wall. For instance, pyrene moiety, commonly used for graphite functionalization, is typically used for noncovalent functionalization. The second scheme involves the use of a polymer addition. Dai's group [108] used polymer scheme to achieve protein binding. [1]

Dai's group [6] has investigated specific antigen–antibody interactions using NWs-based FETs devices. They have successfully performed the affinity binding of antibody to human auto antigen.

Lee's group [26] suggested the use of aptamers for biomolecule recognition, instead of antibodies. Aptamers are classified as artificial oligonucleotides that are capable of a wide range of detection of specific biomolecules with aptamer configuration. The aptamer application is very attractive because of their low cost and capability of reversible denaturation, meaning that the biosensor can be reused continuously. [1]

Antibody modification of CNTs/NWs-based FETs sensors allowed detecting of pig serum albumin and prostate-specific antigen (PSA) (Fig.5) [20].

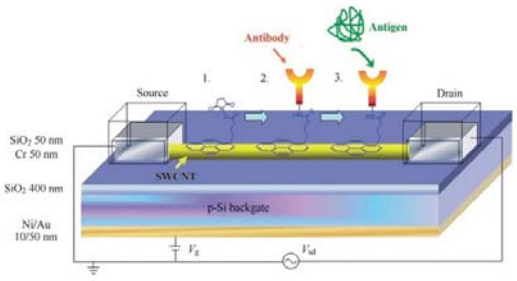

Fig. 5. Schematic representation of CNTs/NWs-based FETs sensors including the surface modification and molecular recognition procedures. Reprinted from [5]

CNTs/NWs-based FETs sensors can be utilized for PSA detection using so-called "biomarkers". The biomarkers are defined as indicators of a biological state. It is a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention. In this reason, the detection of specific biomarkers can be applied to disease screening. For instance, prostate-specific antigen (PSA) has been applied to prostate cancer diagnosis [15]. However, these biomarkers usually exist in the blood in extremely low concentrations. Finding a method to rapidly and precisely detect these biomarkers is an important task of clinical diagnoses. PSA is often used as a model cancer marker for demonstration of biosensor measurement principles.

Zheng's group [36] has applied a Si NWs-based FETs sensor for the detection of multiple cancer markers. The main advantage of the ultrasensitive Si NWs-based FETs sensor is the detection limit for these cancer markers, which is in pg/mL scale. There are some problems regarding to using the Si NWs-based FETs sensor to detect biomarkers from a whole blood sample. The reasons are in the ionic strength of the whole blood; it could cause a very short Debye length to severely limit the FET signals.

Stern's group [28] has developed a microfluidic purification chip system to pre isolate the target molecules, followed by using NWs-based FETs sensor to analyze the pre-purified sample.

CNTs-based FETs were applied to the real-time detection of a cancer marker for neuroendocrine tumors (chromo-granin A (CgA), released from embryonic cortical neurons. [32]

Li's group [20] has studied the detection of prostate-specific antigen by using a network of CNTs as FET-biosensor. They have found the sensitivity of CNTs' network is comparable to sensitivity of metal oxide NWs. They showed the interaction between prostate-specific antibody and antigen, and measured the electronic interaction. Functionalization of the swCNTs uses a π-π stacking method with a pyrene moiety. [1]

The diagnosis and treatment of diabetes mellitus requires a constant monitoring of blood glucose levels. Similar to other glucose sensors, CNTs-based FETs sensors for glucose detection is based on enzymatic glucose oxidation and subsequent hydrogen peroxide detection. The glucose oxidase enzyme binds to CNTs' surface of FET-biosensor and provides biomolecular diagnostic capabilities, such as pH sensing enzymatic activity monitoring. [33]

Dekker's group has studied the redox enzyme glucose oxidase (GOx) that catalyzes the oxidation of β-D-glucose ($C_6H_{12}O_6$) to D-glucono-1,5-lactone ($C_6H_{10}O_6$) [3]. The redox enzymes go through a catalytic reaction cycle, where groups in the enzyme temporarily change their charge state and conformational changes occur in the enzyme, which can be detected by using CNTs-based FETs sensors. These measurements indicate that the GOx activity is responsible for the measured increasing conductance upon glucose addition. [1]

Nucleic acids detection

There are a lot of reports on the electrochemical detection of DNA hybridization by using CNTs/NWs-based FETs. [33]

For instance, Li's group [21] was able to covalently link DNA onto the tips of CNTs for DNA detection. But other groups have focused on the covalent functionalization aspect of CNTs by DNA or other nucleic acids. Nucleic acids, such as ssDNA, short double-stranded DNA and some total RNA can disperse swCNTs in water. The charge differences among the DNA and swCNTs, which are associated with the negatively charged phosphate groups of DNA and the different electronic properties of swCNTs, have allowed postproduction preparation of samples in metallic and semiconducting swCNTs.

Strano's group [12-13] has found that the conformational rearrangement of a biomolecule could be transduced directly by a swCNTs. Staii's group [27] combined single-stranded DNA into a FET-biosensor for detection of a range of vaporous odors. Some of the vapors showed CNTs-based FETs detection was water, propionic acid, trimethylamine, methanol, dimethyl methylphosphonate and dinitrotoluene.

Most biological processes including DNA hybridization involve electrostatic interactions and charge transfer, which allows electronic detection using CNTs-based FETs sensor device. DNA molecules attached to the CNTs will influence FET's characteristics by electron depletion in the channel, while chemicals attachment to metal electrodes will influence only the metal/nanotube.

Tang's group [29] examined the sensing mechanism between the DNA and swCNTs. They found that DNA hybridization on gold electrodes is mainly responsible for the electrical conductance change because of the modulation of the energy level adjustment between swCNTs and the gold contact, that means that the Schottky barrier plays significant role in detection. [1]

Si NWs-based FETs were adapted for the detection of DNA or RNA. Due to the large amount

of negative charges in the phosphate backbones of DNA or RNA, FET-biosensor offers a good candidate for monitoring DNA or RNA hybridizations, because the hybridizations cause the accumulation or depletion of charge carriers in the Si NWs-based FETs. This leads to a conductance change. Peptide nucleic acid (PNA), an artificially synthesized polymer similar to DNA, is commonly used in biological research, especially in DNA or RNA hybridizations. Because PNA has no phosphate groups in its backbone, the binding of PNA/DNA or PNA/RNA strands is stronger than that of DNA/DNA or DNA/RNA duplexes due to the lacking of electrostatic repulsion. Hahm's group has reported about real-time and label-free detection of DNA with PNA-modified Si NWs-based FETs. [10]

Conclusion

In this review, we have described modern advances in the field of biomolecule detection using CNTs/NWs-based FETs biosensors. 1D nanomaterials, such as CNTs and NWs have unique semiconductor properties that make them extremely attractive and could supply new opportunities for CNTs/NWs-based FETs fabrication for the purposes of biosensing applications.

At the present time CNTs and NWs show excellent detection possibilities of proteins, nucleic acids, bacteria, higher cells, etc. These advantages are used for drug-delivery systems, cancer therapy, viral detectors and glucose sensors development.

Unfortunately, the movement of the FET-type biosensors from research laboratories to clinical laboratories is slow enough. But, it is important to continue work on a variety of biosensor technologies to permit a successful transition from the research laboratories to location of patients. The great impact of biosensor technology will be felt "point-of-care" testing devices, especially in places without laboratory support.

At the present time there are a lot of articles and research reports which describe kinds, structures, and work principles of biosensors based on CNTs/NWs-FETs. Despite all achievement in research institutes and laboratories, physics of FET-based biosensors is not completely clear yet. For example, the exact mechanism of molecule detection by CNTs/NWs is still a subject of intensive debate in the literature; it is only known that response mechanisms depend on the type of detected molecule.

There is extremely important to develop a general efficient approach that will be able to describe physical processes and improve characteristics of biosensors based on CNTs/NWs-FETs, because there is no general accepted model, which could completely describe the physics of FET-biosensors. For better understanding of physics of the FET-type biosensors and optimization of the structures of nano-dimensional biological sensor systems, mathematical model of this device have to be established and this will help to obtain accurate, selective, stabile and sensitive biosensor.

Current transport changes through the CNTs/NWs depending on the concentration of attached entities, charge configurations, detecting mechanisms, etc. have to be studied and depicted. The mathematical models of ballistic transport in the channel should be further improved and supplemented with such parameters as: scattering of charge carriers mechanism, velocity saturation effects, mobility of charge carriers in CNTs, the effect of the Schottky barrier, parasitic resistances, resistances due to scattering effects, etc. Simulations will help to understand the device physics, explain of experimental data and chose the optimal parameters for the high sensitivity and selectivity of biosensor.

References

1. *Allen, B.* Carbon Nanotube Field-Effect-Transistor-Based Biosensors / B. L. Allen, P. D. Kichambare, A. Star // Advanced Materials. – 2007. – Vol. 19, June 2007. – P. 1439–1451.
2. *Balavoine, B.* Helical Crystallization of Proteins on Carbon Nanotubes: A First Step towards the Development of New Biosensors / F. Balavoine, P. Schultz, C. Richard, V. Mallouh, T.W. Ebbesen, C. Mioskowski // Angew. Chem. Int. Ed. – 1999. - Vol. 38, №13/14, P. 1912 - 1915.
3. *Besteman, K.* Enzyme-coated carbon nanotubes as single-molecule biosensors / K. Besteman, J.-O Lee, F.G.M. Wiertz, H.A. Heering, C. Dekker // Nano Letters. – 2003. – Vol. 3, №6. – P. 727–730.
4. *Bradley, K.* Charge Transfer from Ammonia Physisorbed on Nanotubes / K. Bradley, J.-C. P. Gabriel, M. Briman, A. Star, G. Grüner // Phys. Rev. Lett. – 2003. – Vol. 91, №21. – P. 218301.
5. *Chen, K.* Silicon nanowire field-effect transistor-based biosensors for biomedical diagnosis and cellular recording investigation / Kuan-I Chen , Bor-Ran Li, Yit-Tsong Chen // Nano Today. – 2011. – Vol. 6, April 2011. – P. 131–154.

6. *Chen, R.J.* Noncovalent functionalization of carbon nanotubes for highly specific electronic biosensors / R.J. Chen, S. Bangsaruntip, K.A. Drouvalakis, N.W. Kam, M.Shim, Y.M. Li, W. Kim, P.J. Utz, H.J. Dai // Proc. Natl. Acad. Sci. U. S. A. – 2003. – Vol. 100, №9. – P. 4984–4989.
7. *Cohen-Karni, T.* Graphene and nanowire transistors for cellular interfaces and electrical recording / T. Cohen-Karni, Q. Qing, Q. Li, Y. Fang, C.M. Lieber // Nano Lett. – 2010. – Vol. 10. – P. 1098–1102.
8. *Cui, Y.* Nanowire Nanosensors for Highly Sensitive and Selective Detection of Biological and Chemical Species / Y. Cui, Q. Wei, H. Park, C.M. Lieber // Science. – 2001. – Vol. 293. – P. 1289–1292.
9. *Curreli, M.* Real-Time, Label-Free Detection of Biological Entities Using NW-Based FETs / M. Curreli, R. Zhang, F. N. Ishikawa, H.K. Chang, R.J. Cote, C. Zhou, M.E. Thompson // IEEE Transactions on nanotechnology. – 2008. – Vol. 7, №6. – P. 651–667.
10. *Hahm, J.* Direct Ultrasensitive Electrical Detection of DNA and DNA Sequence Variations Using Nanowire Nanosensors / J. Hahm, C. M. Lieber // Nano Letters. – 2004. – Vol. 4, №1, P. 51–54.
11. *Hecht, D.S.* Bioinspired Detection of Light Using a Porphyrin-Sensitized Single-Wall Nanotube Field Effect Transistor / D.S. Hecht, R.J.A. Ramirez, M. Briman, E. Artukovic, K.S. Chichak, J.F. Stoddart, G. Grüner //Nano Lett. – 2006. – Vol. 6, №9. – P. 2031–2036.
12. *Heller, D.* Optical Detection of DNA Conformational Polymorphism on Single-Walled Carbon Nanotubes / D. Heller, E. Jeng, T. Yeung, B. Martinez, A. Moll, J. Gastala, M. Strano // Science. – 2006. - Vol. 311, №5760. - P. 508-511.
13. *Heller, D.* Single-Walled Carbon Nanotube Spectroscopy in Live Cells: Towards Long-Term Labels and Optical Sensors / D. Heller, S. Baik, T. Eurell, M. Strano // Advanced Materials. – 2005. – Vol. 17, №23. – P. 2793–2799.
14. *Heller, I.* Identifying the Mechanism of Biosensingwith Carbon Nanotube Transistors / I. Heller, A.M. Janssens, J. Mannik, E.D. Minot, S.G. Lemay, C. Dekker // Nano Lett. – 2008. – Vol. 8, №2. – P. 591–595.
15. *Hernandez, J.* Prostate-specific antigen: A review of the validation of the most commonly used cancer biomarker / J. Hernandez, I.M. Thompson // Cancer. – 2004. – Vol. 101, №5, P. 894–904.
16. *Hu, P.A.* Carbon Nanostructure-Based Field-Effect Transistors for Label-Free Chemical/Biological Sensors / P.A. Hu, J. Zhang, L. Li, Z. Wang, W. O'Neill, P. Estrela // Sensors. – 2010. – Vol. 10, №5. – P. 5133–5159.
17. *Iijima, S.* Helical microtubules of graphitic carbon / Sumio Iijima //Nature. – 1991. – Vol. 354. – P. 56–58.
18. *Kam, N.*W.S. Functionalization of Carbon Nanotubes via Cleavable Disulfide Bonds for Efficient Intracellular Delivery of siRNA and Potent Gene Silencing / N.W.S. Kam, H. Dai // J. Am. Chem. Soc. – 2005. – Vol. 127, №36, P. 12492–12493.
19. *Kim, J.P.* Ultrasensitive carbon nanotube-based biosensors using antibody-binding fragments / J.P. Kim, B.Y. Lee , S. Hong , S.J. Sim // Analytical Biochemistry. – 2008. – Vol. 381, №2. – P. 193–198.
20. *Li, C.* Complementary Detection of Prostate-Specific Antigen Using In2O3 Nanowires and Carbon Nanotubes / Chao Li, M. Curreli , H. Lin, B. Lei, F. N. Ishikawa, R. Datar, R.J. Cote, M.E. Thompson, C. Zhou // J. Am. Chem. Soc. – 2005. – Vol. 127, №36. – P. 12484–12485.
21. *Li, J.* Carbon Nanotube Nanoelectrode Array for Ultrasensitive DNA Detection / J. Li, H. T. Ng, A. Cassell, W. Fan, H. Chen, Q. Ye, J. Koehne, J. Han, M. Meyyappan // Nano Letters. – 2003. – Vol. 3, №5. – P. 597–602.
22. *Martel, R.* Single- and multi-wall carbon nanotube field-effect transistors / T. Schmidt, H. R. Shea, T. Hertel, Ph. Avouris // Applied Physics Letters. – 1998. – Vol. 73. – P. 2447–2449.
23. *Noy, A.* Bionanoelectronics with 1D materials / A. Noy, A.B. Artyukhin, N. Misra // Materials today. – 2009. – Vol. 12, №9. – P. 22–31.
24. *Peng, N.* Sensing Mechanisms for Carbon Nanotube Based NH3 Gas Detection / N. Peng, Q. Zhang, C.L. Chow, O.K. Tan, N. Marzari // Nano Lett. – 2009. – Vol. 9, №4. – P. 1626–1630.
25. *Poghossian, A.* Label-free detection of charged macromolecules by using a field-effect-based sensor platform: Experiments and possible mechanisms of signal generation / A. Poghossian, S. Ingebrandt, M.H. Abouzar, M.J. Schoning // Appl. Phys. A. – 2007. – Vol. 87, №3. – P. 517–524.
26. *So, H.M.* Single-Walled Carbon Nanotube Biosensors Using Aptamers as Molecular Recognition Elements / H.M. So, K. Won, Y.H. Kim, B.K. Kim, B.H. Ryu, P.S. Na, H. Kim, J.O. Lee // J. Am. Chem. Soc. – 2005. - Vol. 127, №34, P. 11906–11907.
27. *Staii, C.* DNA-Decorated Carbon Nanotubes for Chemical Sensing / C. Staii, A.T. Johnson //

Nano Letters. – 2005. – Vol. 5, №9. – P. 1774–1778.
28. *Stern, E.* Label-free biomarker detection from whole blood / E. Stern, A. Vacic, N.K. Rajan, J.M. Criscione, J. Park, B.R. Ilic, D.J. Mooney, M.A. Reed, T.M. Fahmy // Nat. Nanotechnol. – 2010. - Vol. 5, №10, P. 138-142.
29. *Tang, X. W.* Carbon Nanotube DNA Sensor and Sensing Mechanism / X.W. Tang, S. Bansaruntip, N. Nakayama, E. Yenilmez, Y.L. Chang, Q. Wang // Nano Lett. – 2006. – Vol. 6, №8. – P. 1632–1636.
30. *Tans, S.* Room-temperature transistor based on a single carbon nanotube / Sander J. Tans, Alwin R. M. Verschueren, Cees Dekker // Nature. – 1998. – Vol. 393. – P. 49–52.
31. *Veetil, J.V.* Development of Immunosensors Using Carbon Nanotubes / J.V. Veetil, K. Ye // Biotechnol Prog. – 2007. – Vol. 23, №3. – P. 517−531.
32. *Wang, C.W.* In Situ Detection of Chromogranin A Released from Living Neurons with a Single-Walled Carbon-Nanotube Field-Effect Transistor / C.W. Wang, C.Y. Pan, H.C. Wu, P.Y. Shih, C.C. Tsai, K.T. Liao, L.L. Lu, W.H. Hsieh, C.D. Chen, Y.T. Chen // Small 3. – 2007. – Vol. 3, №8, P. 1350–1355.
33. *Wang, J.* Carbon-Nanotube Based Electrochemical Biosensors: A Review / J. Wang // Electroanalysis. – 2005. – Vol. 17, №1, P. 7–14.
34. *Wang, Y.* Performance Investigation for a Silicon NW FET Biosensor Using Numerical Simulation / Y. Wang, G. Li // IEEE Nanotechnology Materials and Devices Conference. – Monterey, California (USA), 2010. – P. 81–86.
35. *Zanello, L.P.* Bone Cell Proliferation on Carbon Nanotubes / L.P. Zanello, B. Zhao, H. Hu, R. C. Haddon // Nano Letters. – 2006. – Vol. 6, №3, P. 562–567.
36. *Zheng, G.* Multiplexed electrical detection of cancer markers with nanowire sensor arrays / G. Zheng, F. Patolsky, Y. Cui, W.U. Wang, C.M. Lieber // Nature Biotechnology. – 2005. - Vol. 23, P. 1294 – 1301.

УДК 621.3.084

Клінічні застосування біосенсорів на основі польових транзисторів з вуглецевими нанотрубками або нанопроводами

Д.С. Боділовська

Національний технічний університет України "Київський політехнічний інститут",

пр. Перемоги, 37, Київ-56, 03056, Україна.

В цій статті ми описуємо останні досягнення в стрімко розвиваній області детектування аналітів з використанням польових транзисторів (ПТ) на основі вуглецевих нанотрубок і нанопроводів. У цій статті відображено поведінку та переваги одновимірних наноматеріалів для використання в біосенсорах. Поміж одновимірних нанометрових матеріалів вуглецеві нанотрубки і нанопроводи пропонують унікальні електронні та механічні властивості, які роблять їх надзвичайно привабливими для задач біодетектування.

Проаналізовано структури і принципи роботи ПТ-біосенсорів на основі вуглецевих нанотрубок / нанопроводів. Польові транзистори на основі вуглецевих нанотрубок / кремнієвих нанопроводів останнім часом привертають до себе величезну увагу як перспективні інструменти для проектування біосенсорів, через їх біосумісність, сумісності за розміром, ультрачутливість, селективність, а також можливості без маркерного виявлення в режимі реального часу. Крім того, також проаналізовано механізми взаємодії між елементами трансдьюсера ПТ-біосенсора (вуглецевими нанотрубками або нанопроводами) та біооб'єктами. На закінчення, в цьому огляді основна увага приділяється застосуванню біосенсорів на основі польових транзисторів для вимірювання різних аналітів. Показано взаємодію білків, реакцію антитіло-антиген, включаючи реакцію виявлення простат-специфічного антигену, ДНК-гібридизацію і ферментативні реакції за участі глюкози. Бібл. 36, рис. 5.

Ключові слова: *нанобіосенсор, польовий транзистор, вуглецеві нанотрубки, нанопроводи, біосенсор на основі польового транзистора.*

УДК 621.3.084

Клинические применения биосенсоров на основе полевых транзисторов с углеродными нанотрубками или нанопроводами

Д.С. Бодиловская

Национальный технический университет Украины "Киевский политехнический институт",
пр. Победы, 37, Киев-56, 03056, Украина.

В этой статье мы описываем последние достижения в стремительно развивающейся области детектирования аналитов с использованием полевых транзисторов (ПТ) на основе углеродных нанотрубок и нанопроводов. В статье описаны поведение и преимущества одномерных наноматериалов для использовании в биодатчиках. Среди одномерных нанометровых материалов углеродные нанотрубки и нанопроводы предлагают уникальные электронные и механические свойства, которые делают их чрезвычайно привлекательными для задач биодетектирования.

Проанализированы структуры и принципы работы ПТ-биосенсоров на основе углеродных нанотрубок/нанопроводов. Полевые транзисторы на основе углеродных нанотрубок/кремниевых нанопроводов в последнее время привлекают к себе большое внимание как перспективные инструменты для проектирования биосенсоров из-за их биосовместимости, совместимости по размеру, ультрачувствительности, избирательности, а также возможностям без маркерного обнаружения в режиме реального времени. Кроме того, также проанализированы механизмы взаимодействия между элементами трансдьюсера ПТ-биосенсора (углеродными нанотрубками или нанопроводами) и объектами. В заключение, в этом обзоре основное внимание отводиться применению биосенсоров на основе полевых транзисторов для измерения различных аналитов. Показаны реакции взаимодействия белков, реакция антитело-антиген, включая реакцию обнаружения простат-специфического антигена, ДНК-гибридизацию и ферментативные реакции с участием глюкозы. Библ. 36, рис. 5.

Ключевые слова: *нанобиосенсор, полевой транзистор, углеродные нанотрубки, нанопроводы, биосенсор на основе полевого транзистора.*

Поступила в редакцию 18 марта 2013 г.