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ORIGINAL ARTICLE

THIN FILM BASED BIO-ELECTRONIC SENSORS: FUTURE GENERATION OF ELECTRONIC SENSOR TECHNOLOGY

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ABSTRACT: Development of Thin film based Biosensors (TBS) is new, interesting field of academic study in Bio Physics, Molecular electronics, Nanotechnology, Bio technology etc. The main objective of the study of TBS is to explore the new possibilities of fabrication of TBS devices where molecular level engineering can be done with ease and new devices with interesting functionality can be manufactured. This communication reports the development, market status of TBS. The article also gives brief details of fabrication, characterization, challenges and future prospects of TBS in different area of research and industrial applications.

Keywords: Thin Film based Bio-sensors (TBS), Molecular electronics, Bio technology.

INTRODUCTION

With the increase of intense research in the field of biotechnology (Baron *et al.,* 2005) and bio electronics (Martinoia *et al.,* 2001), the development of bio molecular electronics device fabrication has become increasingly important. Biosensor is a very important player of 21st century which caused a revolution to the traditional methods of bio electronics engineering. The development of biosensors at nano range holds enormous potential in the filed of drug delivery (Lehmann *et al.,* 2001), gene therapy (Zayats *et al.,* 2006), DNA sequencing (Besselink *et al.,* 2003) etc. Nano biosensors offer several opportunities for two reasons. The first is size compatibility due to recent advances in nano-scale materials and development of thin film technology; we are now able to construct electronic circuits in which the component parts are comparable in size to biological entities, thus ensuring appropriate size compatibility between the detector and the detected species. Figure 1 shows the range of bio molecular devices. Some length scales illustrate this observation: single cells are approximately 1 micron in size; viruses are approximately 100 nanometers, while individual proteins are on the order of 10 nanometers, and the diameter of the DNA duplex is approximately 1 nanometer. Optical lithography-based nano-wire fabrication reaches down to 100 nm, the size of a typical virus.

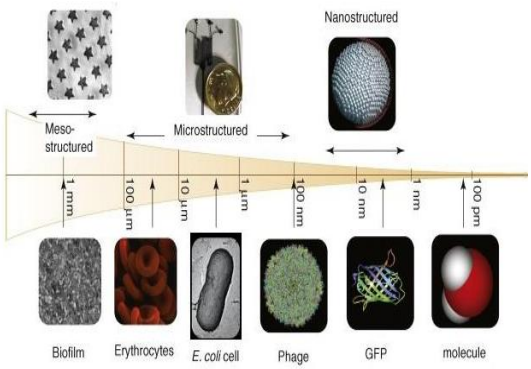

Figure 1: The range of bio molecular devices.

As the size of bio electronic devices went down to few nanometer over the last decade research in the field of tissue engineering, receptor cell regulation and other bio technological development excelled at a super fast rate. Accurate mass sensitive sensors for chemical and biological compounds and feasibility to detect particular gases (Qu *et al.,* 2009), enzyme (Feng *et al.,* 2006), protein (Hwang *et al.,* 2006), DNA (Hejazi *et al.,* 2007) biosensors have high potential of future Nano biotechnology.

In this communication, we systematically highlight different aspects of fabrication and characterization of Thin film based biosensors developed by thin film technology and there future prospects in the field of biotechnology and bio electronics.

DEVELOPMENT OF THIN FILM BASED BIOSENSORS

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The first description of a biosensor was an enzyme electrode for glucose designed by Clark in 1969 (Kalogianni *et al.*, 2006). In 1970 potentio-metric biosensor was developed in which urease was immobilized on an ammonia electrode to detect urea in living organism (Sun *et al.*, 2009). Thereafter, in 1972 invention of the Ion-Selective Field-Effect Transistor (ISFET) was done by Bergveld (Bogani *et al.*, 2009). Artificial pancreas, microbe-based biosensor, immune-sensor and glucose biosensor were developed during 1975-1980 (Urthaler *et al.*, 2005). In 1982 fiber optic-based biosensor for glucose and fiber optic pH sensor for in vivo blood gases were invented by Peterson (Liang *et al.*, 2007). From 1983-1990 blood glucose Biosensor and biosensor system was launched by the MediSense ExacTech. Mediated amperometric biosensor of ferrocene used with glucose oxidase for the detection of glucose surface plasmon resonance (SPR) immunosensor was also launched (Lee *et al.*, 2007). Hand-held blood analyzer was manufactured in 1992 by I SAT (Giakoumaki *et al.*, 2003). In 1998 first blood glucose biosensor was launched in the market by LifeScan (Iijima, 1991) there after Nano bioNMES, Quantum dots, Nano-particles, Nano-cantilever, Nanowire and Nanotubes were sequentially developed in the last decade of this millennium (Peng and Shi, 2005).

MARKET STATUS OF THIN FILM BASED BIOSENSORS

The economic impact of TBS has been enormous. It is found that TBS accounts about 40% of market share of the recent growth in biomedical engineering. It accounts to about 25.7 Billion $. TBS technology have also made sizable contributions to the filed of nanotechnology based consumer market. Figure 2 shows the economic status of TBS technology and Figure 3 shows the market share of TBS in each category of biomedical and consumer market. From figure 3 it is observed that the biomedical and consumer demand is booming day by day.

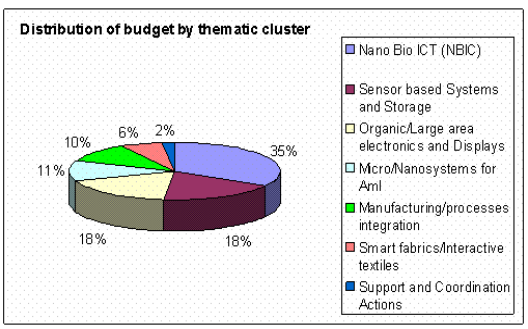

Figure 2: The economic status of TBS technology.

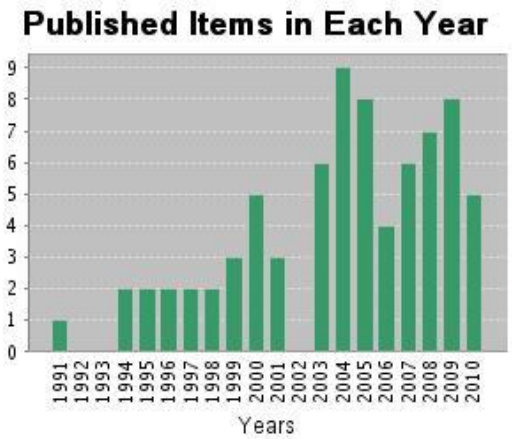

Figure 3: The market share of TBS in each category of biomedical and consumer market.

DESCRIPTION OF THIN FILM BASED BIOSENSORS

4.1. Principle

In general, a Transistor based Biosensor (TBS) consists of three terminals; the source, drain and the gate. The voltage between the source and drain of the transistor regulates the current flow in the gate voltage. Specifically, the current-control mechanism is based on an electric field generated by the voltage applied to the gate. The current is also conducted by only one type of carrier (electrons or holes) depending on the type of FET (n-channel or p-channel). A positive voltage applied to the gate causes positive charges (free holes) to be repelled from the region of the substrate under the gate. These positive charges are pushed downward into the substrate, leaving behind a carrier-depletion region. The depletion region is populated by the bound negative charge associated with the acceptor atoms. These charges are “uncovered” because the neutralizing holes have been pushed downward into the substrate. The positive gate voltage also pulls negative charges (electrons) from the substrate regions into the channel region. When sufficient electrons are induced under the gate, an induced thin n-channel is in effect created, electrically bridging the source and drain regions. The channel is formed by inverting the substrate surface from p-type to n-type (inversion layer). When a voltage is applied between the drain and source, a current flows through channel via the mobile electrons (n-type FET). In the case of a p-type semiconductor, applying a positive gate voltage depletes carriers and reduces the conductance, whereas applying a negative gate voltage leads to an accumulation of carriers and an increase in conductance (the opposite effect occurs in n-type semiconductors). The applied gate voltage

generates an electric field which develops in the vertical direction. This field controls the amount of charge in the channel, and thus it determines the conductivity of the channel. The gate voltage applied to accumulate a sufficient number of electrons in the channel for a conducting channel is called the threshold voltage (VTH). Note that VTH for an n channel (p-channel) FET is positive (negative).With all these properties, a transistor can be configured as a biosensor by modifying the gate terminal with molecular receptors or ion-selective membranes for the analyst of interest. The binding of a charged bio-molecule results in depletion or accumulation of carriers caused by change of electric charges on the gate terminal. The dependence of the channel conductance on gate voltage makes FETs good candidates for electrical biosensors because the electric field generating from the binding of a charged bio-molecule to the gate is analogous to applying a voltage to a gate. In general, the drain current of the FET-type biosensor is defined as follows:

IDS = 1/2μCW/L (VGS TTH) at saturation region
(VDS VGS – VTH)

Where,

μ is the electron mobility in the channel; W and L are the width and the length of channel, respectively; C is the net gate capacitance per unit area formed by the gate and the channel.

4.2. Fabrication Technique

There are two different architecture of TBS fabrication.

In one device architecture, the devices contain a random array of nano tubes functioning as the conducting channel, as shown in Figure 4. In another method a single nano tube channel connects the source and the drain, in a configuration that is shown in Figure 5.

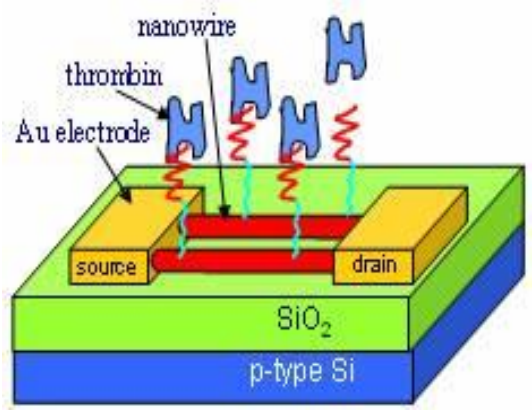

Figure 4: Devices contain a random array of nano tubes functioning as the conducting channel.

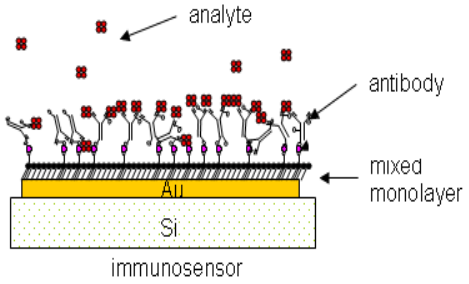

Figure 5: Single nano tube channel connects the source and the drain

In the both case carbon nano-tubes are used to connect the source and drain electrodes the source and gate electrodes have been developed Such devices have been utilized in the bio-sensing area but there is substantial variation between the different devices that are fabricated. Current flows along several conducting channels that determine the overall device resistance. The construction has several advantages. Device operation depends on the density of nano-tubes. For a dense array screening of the gate voltage by the conducting nano-tubes is important, in a fashion similar to gate voltage screening due to a metal layer deposited on the device. For a rarified array such screening is not important and the array can serve as the source-to-drain conducting channel. It is expected that arrays close to, and on the conducting side of the two dimensional percolation limit will have appropriate transistor characteristics. Under such circumstances screening effects are expected to be small, but conduction is still provided by the nanowire network. In both cases the parameter that is used for detection is the so-called device characteristic (DC), the dependence of the source-drain current, I_{sd} (for a fixed source-drain voltage Vsd) on the gate voltage VG, a typical DC is displayed on Figure 6. The most interesting property of the devices is found that the devices displayed a hysteresis, due mobile ions at the surface of the devices which has several potential applications in the field of bio electronics and bio sensors.

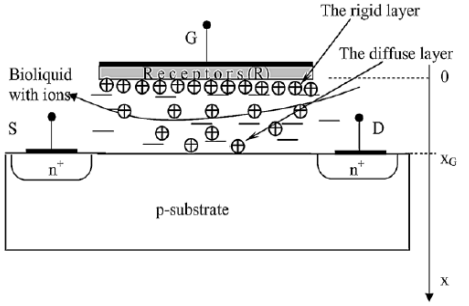

Figure 6: a scheme of typical device characteristic (DC).

4.3. Detection and Characterization of Thin Film Based Biosensor

4.3.1. Optical-detection Biosensors

The output transduced signal that is measured is light for this type of biosensor. The biosensor can be made based on optical diffraction or electro-chem luminescence. In optical diffraction based devices, silicon wafer is coated with a protein via covalent bonds. The wafer is exposed to UV light through a photo-mask and the antibodies become inactive in the exposed regions. When the diced wafer chips are incubated in an analyte, antigen-antibody bindings are formed in the active regions, thus creating a diffraction grating. This grating produces a diffraction signal when illuminated with a light source such as laser. The resulting signal can be measured or can be further amplified before measuring for improved sensitivity.

4.3.2. Thermal-detection Biosensors

This type of biosensor is exploiting one of the fundamental properties of biological reactions, namely absorption or production of heat, which in turn changes the temperature of the medium in which the reaction takes place. They are constructed by combining immobilized enzyme molecules with temperature sensors. When the analyte comes in contact with the enzyme, the heat reaction of the enzyme is measured and is calibrated against the analyte concentration. The total heat produced or absorbed is proportional to the molar enthalpy and the total number of molecules in the reaction. The measurement of the temperature is typically accomplished via a thermistor, and such devices are known as enzyme thermistors. Their high sensitivity to thermal changes makes thermistors ideal for such applications. Unlike other transducers, thermal biosensors do not need frequent recalibration and are insensitive to the optical and electrochemical properties of the sample. Common applications of this type of biosensor include the detection of pesticides and pathogenic bacteria.

4.3.3. Ion-Sensitive Biosensors

These are semiconductor FETs having an ion-sensitive surface. The surface electrical potential changes when the ions and the semiconductor interact. This change in the potential can be subsequently measured. The Ion Sensitive Field Effect Transistor (ISFET) can be constructed by covering the sensor electrode with a polymer layer. This polymer layer is selectively permeable to

APPLICATION OF NANO BIOSENSORS

One distinct merit of is their suitability for use in miniaturized measurement systems, thereby allowing its easy integration into the required electronics (Nikitina *et al.,* 2007). In this regard, a TBS device of small size and low weight might be appropriate for use in a portable monitoring system, i.e., a hand-held drug monitoring system. When it comes to sensitivity and specificity of biosensor, both the fabrication of a nano-scale device and elimination of nonspecific molecular adsorption would contribute to an improvement in the limit-of-detection (LOD) and selectivity of the biosensor. Currently, various kinds of bio-recognition materials for biological analysis such as DNA, proteins, enzymes, and cells are being applied to TBS measurements owing to the unique electrical and biological properties, thereby elevating the sensitivity and specificity of detection (Zhu *et al.,* 2005; Erdem *et al.,* 2006). Among a variety of types of biosensors, one of the most promising approaches and the focus of investigators' concerns are the TBS-based bio-sensors and their integration in biological components. In the TBS system based on different bio-contents for biological analysis, assorted concepts of biosensors like enzyme FETs, Immuno FETs, and DNA FETs that contain layers of immobilized enzymes, antibodies, and DNA strands respectively, have been reported in a large number of documents (Lao *et al.,* 2007; Hussain *et al.,* 2007; Dey *et al.,* 2008a; Dey *et al.,* 2008b; Li *et al.,* 2005; Ferreyra and Rivas, 2007).

There are very vast applications of TBS in different fields of these some are listed below:

a) Drug Development and drug delivery
b) In pathology and for other medical diagnosis
c) Study of interaction between bio-molecules and their interaction with other foreign elements
d) Bio-specific interaction analysis (BIA)
e) Environmental studies and field monitoring
f) Forensic and other scientific crime detection
g) Quality control in small food factory and Food Analysis
h) Gene therapy etc.

CHALLENGES OF NANO BIO SENSORS FABRICATION AND RESEARCH:

The main disadvantage of bio-circuits is the switching time or the response time. The typical switching time for an electrical inverter is a few nanoseconds (10^{-9}) whereas the typical switching time for the bio-inverter

is in minutes (Chen *et al.,* 2004). It is too early to consider the long switching time to be a deterrent from exploring bio circuits as an alternate technology. Future research may find ways to either reduce this time through genetic control or alleviate its effect through parallelism. The other main disadvantage is the need for a vast library of proteins and matching gates. No two proteins can be repeated in one logic circuit. These conditions severely restrict the number of gates that can be cascaded together to form a circuit. Another important concern is that the output concentration decays constantly. Hence the signal strength or concentration is another important factor to be considered when bio-circuits are cascaded. These issues have to be addressed when trying to build large circuits from the basic building blocks of bio-circuits. Finally there is no standard fabrication procedure or experimental standard defined for mass production of bio-circuits. These issues have to be addressed in order to make bio-circuits a viable alternate technology to replace silicon technology.

FUTURE PROSPECTS

TBS have been actively developed because of their specificity, speed, portability, and low cost. Recently, there has been considerable interest in using nano-materials for DNA biosensors. Because of their high surface-to-volume ratios and excellent biological compatibilities, nano-materials could be used to increase the amount of DNA immobilization; moreover, DNA bound to nano-materials can maintain its biological activity which may lead to development of future biosensors and other bio medical devices.

CONCLUSION

TBS biosensors have provided various opportunities for developing a new generation of biosensor technologies. Because of their simple and clear operation principles, TBS biosensors have a well-established position as a powerful sensing tool for detecting DNA, proteins, enzymes and cells. Although various types of TBS-based biosensors have been developed, they still suffer from a variety of fundamental and technological problems such as impurities of the semiconductor and instability of functional groups in the sensing layer. To overcome these problems, interdisciplinary cooperation from various research fields such as chemistry, biology, electrics, and physics must be required. In the future, TBS biosensors may have advanced performance and special properties, accompanying nano-materials such as nano-particles, nano-tubes, and nano-wires. The integration of TBS in micro systems such as micro-total-analysis-system (μ-TAS) or lab-on-a-chip (LoC) may also provide small packaged sensor systems with ultrahigh sensitivity. We believe that these TBS biosensors can be useful for biomedicine, clinical diagnosis, environmental monitoring, and other testing system.

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