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Synthesis, Characterization and Utility of Carbon Nanotube Based Hybrid Sensors
in Bioanalytical Applications

A Dissertation submitted in partial satisfaction
of the requirements for the degree of

Doctor of Philosophy

in

Electrical Engineering

by

Sushmee Badhulika

August 2011

Dissertation Committee:
    Professor Ashok Mulchandani, Chairperson
    Professor Roger Lake
    Professor Elaine D. Haberer

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Dedication

To My Parents.

ABSTRACT OF THE DISSERTATION

Synthesis, Characterization and Utility of Carbon Nanotube Based Hybrid Sensors
in Bioanalytical Applications

by

Sushmee Badhulika

Doctor of Philosophy, Graduate Program in Electrical Engineering
University of California, Riverside, August 2011
Professor Ashok Mulchandani, Chairperson

The detection of gaseous analytes and biological molecules is of prime importance in the fields of environmental pollution control, food and water - safety and analysis; and medical diagnostics. This necessitates the development of advanced and improved technology that is reliable, inexpensive and suitable for high volume production. The conventional sensors are often thin film based which lack sensitivity due to the phenomena of current shunting across the charge depleted region when an analyte binds with them. One dimensional (1-D) nanostructures provide a better alternative for sensing applications by eliminating the issue of current shunting due to their 1-D geometries and facilitating device miniaturization and low power operations. Carbon nanotubes (CNTs) are 1-D nanostructures that possess small size, high mechanical strength, high electrical and thermal conductivity and high specific area that have resulted in their wide spread applications in sensor technology. To overcome the issue of low sensitivity of pristine

CNTs and to widen their scope, hybrid devices have been fabricated that combine the synergistic properties of CNTs along with materials like metals and conducting polymers (CPs). CPs exhibit electronic, magnetic and optical properties of metals and semiconductors while retaining the processing advantages of polymers. Their high chemical sensitivity, room temperature operation and tunable charge transport properties has made them ideal for use as transducing elements in chemical sensors. In this dissertation, various CNT based hybrid devices such as CNT-conducting polymer and graphene-CNT-metal nanoparticles based sensors have been developed and demonstrated towards bioanalytical applications such as detection of volatile organic compounds (VOCs) and saccharides. Electrochemical polymerization enabled the synthesis of CPs and metal nanoparticles in a simple, cost effective and controlled way on the surface of CNT based platforms thus resulting in the fabrication of hybrid sensors which exhibited superior properties and improved performance when used for sensing applications using various modes of sensor configurations.

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Chapter 1: Introduction

1.1 Introduction

There is a growing public concern worldwide for increasing demands in the fields of environmental pollution control, food and water – quality and safety, clinical diagnostics and homeland security. This calls for monitoring and control using advanced and improved technology that is reliable and inexpensive. Hence chemical sensors form an integral part of research initiatives in a wide range of disciplines ranging from detection and control of environmental toxins, quality control in food and water and general healthcare and safety.

Chemical sensors come in a broad category depending upon their construct, properties and applications. But overall they can be defined as devices that detect or measure any chemical quantity by converting it into an analytically useful signal. The main requirements of a good sensor are high sensitivity, fast response, low cost, high volume production, and high reliability that can be operated on site and in situ.

With time, the need for miniaturization of these sensors has been realized to suite the ever changing market demands. Hence, the emergence of nanotechnology was felt with a purpose to have a strategic shift in sensor technology towards more sensitive recognition layers, increasingly complex architectures and reduced size and more so because of the fact that silicon-based semiconducting metal oxide technologies will reach its limit in the near future.

In the past few decades, several approaches have been put forward to fabricate simple, robust solid state sensors whose operation is based on the energy conversion of binding of an analyte at the active surface of the sensor to a measurable signal (resistance, capacitance, temperature etc.). However with the advent of nanotechnology, the current goal has been replaced to the fabrication and successful demonstration of nanosensor devices, which when integrated with modern electronic fabrication technologies will deliver faster, better, low cost and low power operations.

In order to meet specific requirements demanded for particular applications (e.g. biocompatibility for nanotube biosensors and interfacial strength for blending with polymers), techniques for chemical modification of nanostructures have been proposed and successfully implemented.

Rapid progress in the synthesis and fundamental understanding of surface phenomena of nanomaterials has enabled their incorporation into sensor architectures. Nanomaterials are strong candidates for analyte detection, because their reduced dimensions create an increase in environmental sensitivity. The reduced dimensionality also creates structures with exceptionally high surface area, and some materials, such as certain types of carbon nanotubes (CNTs) (Iijima, 1991) which are composed almost entirely of surface atoms. These two consequences of reduced size result in a class of materials that has the potential for unsurpassed sensitivity towards changes in its chemical environment.

This thesis mainly deals with the development and demonstration of nanogas sensors and nano biosensors towards gases; volatile organic compounds (VOCs) and biomolecules

whose detection and analysis plays crucial role in environmental pollution control and food safety respectively.

1.2 Nanomaterials based biosensors:

Biosensors are the class of chemical sensors in which the recognition system utilizes a biochemical mechanism or in other words, incorporates a biological sensing element connected to a transducer. Based on the analyte to be detected, typical analytical techniques are used for necessary detection and quantification. The transduction element of a biosensor performs the function of converting a specific biological reaction (binding or catalytic) into a response that can be processed into a useable signal. This element must also be suitable for the immobilization of the biological component at, or close to its surface. The integration of nanomaterials and biological molecules is very attractive and has gained tremendous attention to create new materials for biomedical and bioanalytical applications (Daniel and Astruc, 2004). Self-assembly of Au nanoparticles onto a cysteamine modified gold electrode resulted in an increased capacity for nucleic acid detection in a DNA sensor (Cai *et al.*, 2001). Boron-doped silicon nanowires (SiNWs) were used to create label free, highly sensitive, real-time electrically based sensors for detection of biological and chemical species (Lieber *et al.*, 2001). Fiber optic nanosensors coated with antibodies were fabricated to detect the presence of toxic chemicals within single cells (Cullum *et al.*, 2000). Nanomaterials like Au nanoparticles exhibit excellent biocompatibility while materials like CNTs and graphene possess unique chemical and optical properties electrical and heat conductivity and catalytic activity that is being widely used in the field of nano bioelectronics. Biomolecules tend to

bind through electrostatic interactions with nanoparticles by displacing the surrounding capping ions or forming a chemical bond with ligands such as thiols, amines, etc. Furthermore, the surface property of nanotubes and graphene can be modified using chemical (Niyogi *et al*., 2002), electrochemical, thermal, or plasma oxidation treatment techniques that open up avenues for further reactions to produce a large family of tailored materials that can easily bind or interact with biomolecules. In addition, to appeal the increasing demands of the biosensor industries for rapid and reliable detection and analysis, on the spot measurement devices are necessary which are target specific in their selectivity and can be subjected to miniaturization, mass production and possess improved transduction mechanisms at low cost. Since sensors based on nanomaterials meet all these criteria, this paved the way for realizing the potential of using nanosensors in biosensing applications.

1.3 Nanomaterials based gas sensors:

The interaction of various gases and chemical species with semiconductors has been studied extensively to develop useful sensing devices based on properties of the semiconductor materials. Examples include gas detectors using metal-oxide semiconductor field-effect transistor (MOSFET), metal-oxide semiconductor capacitors, as well as schottky barrier diodes (Göpel *et al*., 1989; Janata and Huber, 1985; Steele *et al*., 1976). Nanomaterials are promising candidates for fabrication of chemical sensors that can be used for detection of a wide variety of gases and volatile compounds including aromatic compounds, amines, alcohols and alkanes etc. They offer a wide diversity and versatility in their application owing to the fact that a slight surface

modification brings about a pronounced change in their sensitivity towards different chemical compounds. Recent reports on gas sensing properties of CNT (Dai *et al.*, 2000), SnO_2 nanoribbon or nanowire (NW) (Law *et al.* 2002; Moskovits *et al.*, 2003) and In_2O_3 nanowire (Li *et al.*, 2003) have shown that these nanostructures exhibit unique properties such as high sensitivity, fast response time, and room temperature detection, which are unattainable by the conventional sensor materials. Further enhancement in the sensitivity of nanostructure based gas sensors can be achieved by incorporating metals, metal oxides or different polymers on to them. The mechanism of detection of gases using nanomaterials based gas sensors primarily depends on the nature of interaction between the gases and VOCs. It could be in the form of variations in the physicochemical properties of the chemically interactive layers or changes in the surface morphology or charge transfer between the interacting components that results in a change in the signal generated. Molecules in the gas phase, which are adsorbed onto the surface of nanomaterials generally, modify the electrical, optical, or mass properties of the sensitive material thereby giving rise to a number of different kinds of chemical sensors based on different working principles.

In recent years, there has been a major focus on use of one-dimensional (1-D) nanostructures, such as nanowires, nanobelts, nanosprings and nanotubes, as transducer elements. Apart from having the essential transducing function that converts a non-electric quantity to an electric quantity with the help of a desired circuitry, these nanosensors possess the additional properties of high sensitivity and can be easily modified with the molecular recognition element. These nanostructures also provide the

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advantage of small size and portability along with low power consumption that form the prerequisites for any efficient sensor.

1.4 Importance of one-dimensional nanostructures for sensing applications:

In a conductometric sensor, when a charged/ionic analyte binds to the surface of the sensor it leads to addition/depletion in the number of charge carriers in the sensor element, leading to the change in the resistance/conductance of the sensing material. In a thin film based sensor however, only a fraction of the total cross-sectional area is affected by such modulation in the number of charge carriers. As a result, the current can shunt across such regions of modified conductance and leads to depletion in the sensing signal. On the other hand, one-dimensional nanostructures like nanowires/nanotubes show modification in the electrical properties across its entire cross-section due to their small sizes and allow surface chemistry to play a role as compared to in bulk state (fig. 1.1). This ballistic conduction of current through the nanostructures leads to increase in the signal and thus making them more sensitive than the thin film sensors.

(a) A large surface-to-volume ratio means that a significant fraction of the atoms (or molecules) in such systems are surface atoms that can participate in surface reactions.

(b) The Debye length λ_D (a measure of the field penetration into the bulk) for most nanowires and nanotubes is comparable to their radius, which causes their

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electronic properties to be strongly influenced by processes at their surface. This could result in better sensitivity and selectivity.

(c) Finally, nanowires and nanotubes can be easily configured as field-effect transistors (FETs) and can be potentially integrated with conventional devices and device fabrication techniques.

1.4.1 Carbon nanotubes as sensor element:

CNTs are one dimensional hexagonal networks of carbon atoms of approximately 1 nm diameter and 1 to 100 microns of length. A SWNT can be metallic, semimetallic or semiconducting depending on its chirality. Single walled carbon nanotubes (SWNTs) display excellent chemical stability, good mechanical strength and a range of electrical conductivity (Iijima 1991; Mintmire *et al*., 1992; Nardelli *et al*., 2000; Rinzler *et al*., 1998; Wong *et al*., 1997; Yakobson and Smalley, 1997a, b) that makes then ideal building blocks for electronic applications. Their properties of small size, high strength, high electrical and thermal conductivity and high specific area have been successfully explored and used in applications related to scanning probes, actuators and nanoelectronic devices. When compared with other conductance sensitive materials like metal oxide semiconductors and conducting polymers, CNTs offer advantages in terms of higher sensitivity, smaller sizes that facilitates fabrication of miniaturized sensors and massive nanosensor arrays, lower power consumption for wireless applications. They have proven to be less sensitive to variations in temperature (compared to silicon piezoresistors). This makes them perfect candidates for chemical sensors and also as highly sophisticated implantable sensors. The remarkable sensitivity of CNT conductivity

to the surface adsorbates permits the use of CNT as highly sensitive nanoscale sensors. The sensing behavior arises from the fact that changes in their local chemical environment has a direct impact on their electronic structure and hence provides unambiguous path for detecting interacting molecules that initiate the change.

1.4.2 Carbon nanotubes as biosensors:

Biosensors are the class of chemical sensors in which the recognition system utilizes a biochemical mechanism or in other words incorporates a biological sensing element connected to a transducer. They could be used to detect a wide variety of analytes ranging from detecting levels of acidity, alcohol, minerals, starch, toxins and vitamins in dairy, fish, meat and beverages. Based on the analyte to be detected, typical analytical techniques are used for necessary detection and quantification. The transduction element of a biosensor performs the function of converting a specific biological reaction (binding or catalytic) into a response that can be processed into a useable signal. This element must also be suitable for the immobilization of the biological component at, or close to its surface. Nanomaterials are promising candidates in the field of biosensors as they allow the use of new signal transduction technologies. In addition, their ultra high surface area makes it possible to enhance the amount of immobilized biomolecules in construction of a sensor thus improving the limit of detection of a sensor. The combination of excellent conductivity, good electrochemical properties, and nanometer dimensions has seen SWNTs being plugged directly into individual redox enzymes for better transduction in electrochemical enzyme biosensors. (Gooding *et al.*, 2003; Liu *et al.*, 2005; Patolsky *et*

al., 2004; Yu *et al*., 2003). The direct electron transfer ability of carbon nanotubes has been exploited cases (Guiseppi-Elie *et al*., 2002) wherein use of SWNT has made possible a direct electron transfer with the redox active centers of adsorbed oxidoreductase enzymes. SWNTs modified with biorecognition molecules, such as antibodies, aptamers or DNA, have been successfully used to detect various targets, including proteins (Dai *et al*., 2003; Lee *et al*., 2006; Mulchandani *et al*., 2010a; Mulchandani *et al*., 2010b), viruses (Yoo *et al*., 2009), bacteria, yeast, DNA/RNA (Mhaisalkar *et al*., 2008; Tang *et al*., 2006; Tao *et al*., 2007) ,mammalian cancer cells (Shao *et al*., 2008) and small and weakly charged molecules like glucose (Mulchandani *et al*., 2010a).

1.4.3 Carbon nanotubes as gas sensors:

The SWNTs consists solely of surface atoms such that every single carbon atom is in direct contact with the environment and this makes them highly sensitive to any surface adsorption event. SWNTS thus, could be ideal building blocks for making gas sensors. The earliest reports of gas sensors made from semiconducting SWNTs showed good sensitivities toward NH_3 and NO_2 at room temperature. (Dai *et al*., 2000). However, the less than ideal sensitivity and lack of selectivity to detect many types of analytes such as volatile organic compounds (VOCs) and hydrogen (Dag *et al*., 2005) due to weak binding energy of the nanotubes necessitated the modification of SWNTs with certain compounds like metals, oxides and polymers etc. When functionalized with Pt or Pd, which act as a catalyst for the adsorption of H_2, CNTs can be very sensitive to hydrogen (Kong *et al*., 2001; Sayago *et al*., 2005). Conducting polymer-SWNT based nanocomposite gas

sensors have also been demonstrated (Bartlett *et al.*, 1989; Feller *et al.*, 2009) which show enhanced response towards detecting gases. These approaches of sensing were based on chemiresistive mode of sensor configuration where the resistance of the sensor changes as a function of the concentration of the gaseous analyte. The resistance response of CNTs to gas adsorption can also be detected with field emit transistors (FETs) configuration (Dai *et al.*, 2000; Lee *et al.*, 2004; Someya *et al.*, 2003). If two metal contacts are connected to each end of an individual semiconducting SWNT, the metal/S-SWNT/metal device exhibits p-type transistor characteristics. Someya *et al.*, characterized the influence of alcohols adsorption on the resistance of SWCNTs using the same transistor structure. The responses were found to be reversible and reproducible over many cycles of vapor exposure.

1.5 Conducting polymers:

Conducting polymers (CPs) are an attractive group of materials which exhibit electronic, magnetic and optical properties of metals and semiconductors while retaining the attractive mechanical properties and processing advantages of polymers (Heeger 2001; MacDiarmid 2001; McQuade *et al.*, 2000). Their conductivity can be varied as high as fifteen orders of magnitude by varying the dopant level thus making them excellent flexible building materials for wide range of electronic applications (MacDiarmid 2001). CPs consist of repetitive sequences of monomer units that contain sp^2 hybridized backbones. Incorporation of dopants onto them results in change in their conductivity levels depending upon the dopant type and its concentration. This prominent feature of

CPs along with high chemical sensitivity, room temperature operation and tunable charge transport properties has made them ideal for use as tranducing materials in chemical sensors (Craighead *et al*., 2004; Dong *et al*., 2006).

1.5.1 Literature survey on conducting polymers as nanobiosensors:

CPs have attracted significant interest in the development of biosensors which are being used widely in fields of biotechnology, food and agriculture product processing for detection of food borne pathogens (Arshak *et al*., 2009; Ghosh *et al*., 1998; Minett *et al*., 2003), health care and medicine (Kajiya *et al*., 1991; Kumar *et al*., 2001). The electrically conducting polymers are known to possess numerous features in terms of stability and ease of processing. They can be synthesized by one-step electrosynthesis in the form of an adherent film deposited at the surface of the electrode with anionic species being included by doping. This doping reaction makes it possible to modulate the conductivity reversibly over several orders of magnitude via redox interactions. All these features allow them to act as excellent materials for immobilization of biomolecules and rapid electron transfer for the fabrication of efficient biosensors. Of the several generations of biosensors categorized depending upon their mode of operation, CP based biosensors come under the category of direct binding of the biocatalyst to an electronic device that transduces and amplifies the signal. Reports demonstrating use of electropolymerized polypyrrole films as electrochemical sensing devices for glucose sensors, both enzymatic and non enzymatic have been found vastly in literature (Bidan 1992; Zotti 1992).

Realizing the advantages of nano arrays in terms of miniaturization, greater sensitivity and less power consumption, efforts were also made to successfully demonstrate glucose sensor arrays based on polyaniline nanojunctions (Forzani *et al.*, 2004). These CP based nanosensor arrays were very specific and exhibited fast responses toward glucose without being affected by factors like need for oxygen and redox mediators that often plague conventional enzymatic sensors.

1.5.2 Literature survey on conducting polymers as nanogas sensors:

Over the past few years, CPs have been put to use in form of thin and thick film sensors for detection of a wide variety of components ranging from biomolecules to gas analytes (McQuade *et al.*, 2000; Myung *et al.*, 2010). Nanosensors based on CPs exhibit the property of bulk penetration of analytes thus making them highly sensitive. The earliest reports of conducting polymers and their utility in the field of gas sensing came in the form of thick/thin films of PPy, PANI, PT, and their derivatives with a clear understanding of the of interaction of the gases with the CPs structures. While in some cases swelling of the polymer film (Mayer *et al.*, 2008) occurred due to interaction with gas molecules thereby resulting in an increase in the average hopping distance between chains that led to an increase in the resistance of the sensor device, in other cases it resulted in a decrease in resistance caused due to change alignment (Svetlicic *et al.*, 1998; Tan and Blackwood, 2000) . The dopant dependent conductivity together with the porosity of the CP enabled electrochemical activity thus allowing redox control over conductivity. This facilitated ease of processing of CP using electrochemical techniques.

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Over the years, focus has been shifted to the fabrication of one dimensional nanostructure based gas sensors owing to the reasons cited in the preceding sections. Some of the first attempts involved single polymeric polyaniline nanowire based gas sensor which showed a rapid and reversible resistance change upon exposure to NH_3 gas at concentrations as low as 0.5 ppm (Craighead *et al.*, 2004). Template directed PPy nanowire; both drop casted and dielectrophoretically positioned between prefabricated microelectrodes were also synthesized and demonstrated for the detection of ammonia (Hangarter *et al.*, 2008; Myung *et al.*, 2007). Further enhancement in the structure of the polymer nanowires was achieved by synthesis of Au/PEDOT/Au nanowire (Dan *et al.*, 2007) which were then used for the detection of volatile organic compounds. These gas sensors showed low sample to sample variation and proved to exhibit excellent reproducibility.

Thus, taking into considerations the demands of sensor industries for small size and highly efficient sensors which show promise of better sensitivity and selectivity, we designed a specific aim of fabricating hybrid sensors that incorporate the synergistic benefits of one dimensional nanostructures as the main building block functionalized with CPs that can be used in gas sensing and biosensing applications.

1.6 Objective of the work:

Based on the aforementioned discussion on the importance of one dimensional nanostructures and the scope of carbon nanotube based hybrid sensors in a wide range of potential applications, the objective of the dissertation is three fold based on three specific goals.

-To design and fabricate low cost and highly sensitive CNT based hybrid sensors.

Although one-dimensional nanostructure like nanowires, nanotubes, nanobelts have been fabricated for sensing applications; most studies to date have been carried out on individual nanowires/nanotubes being wired up with appropriate contacts for measuring transport measurements. However using a versatile technique like electrochemistry enables simple and efficient way of modifying one dimensional nanostructures with conducting polymers and metal nanoparticles that leads to the fabrication of hybrid devices exhibiting superior properties over pristine one dimensional structures. In addition, one needs to consider sophisticated engineering strategies for producing large number of individual transducer elements that can be regionally modified and individually read which is accomplished using a method like electropolymerisation. Thus the goal of the research work is to develop a novel cost-effective, simple fabrication technique which can modify the nanostructures with desired sensing material in order for creation of a powerful device that can detect minute quantities of environmentally sensitive substance against a intricate and changing environment.

-Study of the morphology and electrical characteristics of these devices prior to their application in sensing.

Characterization studies in terms of I-V, C-V, SEM and AFM on the hybrid devices fabricated by the method of electropolymerization were performed to obtain a clear understanding of the morphology and electrical properties of the devices.

-Application of the CNT based hybrid devices in fields of gas sensing and other bioanalytical applications

Sensing performance was systematically optimized by varying several parameters that affect the physical and electrical properties of these devices. Gas sensing and biosensing properties of these devices was then investigated using different modes of sensor configurations wherein the sensor devices were exposed to various concentrations of the analyte of interest and sensitivity of the devices was measured .

1.7 Organization of the thesis:

Chapter 2 discusses the synthesis, fabrication and characterization of Poly (3, 4-ethylenedioxythiophene) poly (styrenesulfonate) (PEDOT: PSS) coated SWNT sensors and their application in the field of sensing VOCs of interest.

Chapter 3 describes the synthesis, fabrication and characterization of Polyaniline boronic acid (PABA)-SWNT hybrid sensors for the purpose of saccharide detection.

Chapter 4 illustrates the concept of molecular imprinting of saccharide on carbon nanotube based sensors and its application in detecting sugars with enhanced sensitivity.

Chapter 5 describes amperometric glucose detection using an enzyme-free MWNTs based hybrid sensor.

Chapter 6 gives the summary of the work done and conclusion.

Appendix # 1 elaborates the use of SWNTs-based chemiresistor aptasensors for highly sensitive and selective detection of weakly or uncharged molecules of ATP. The detection of ATP, a small weakly charged molecule, is demonstrated by displacement of the ssDNA anti-ATP aptamer hybridized to a small capture oligonucleotide covalently attached on SWNTs, with picomolar sensitivity and selectivity over GTP.

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Figure

A) 1-D Nanowire FET
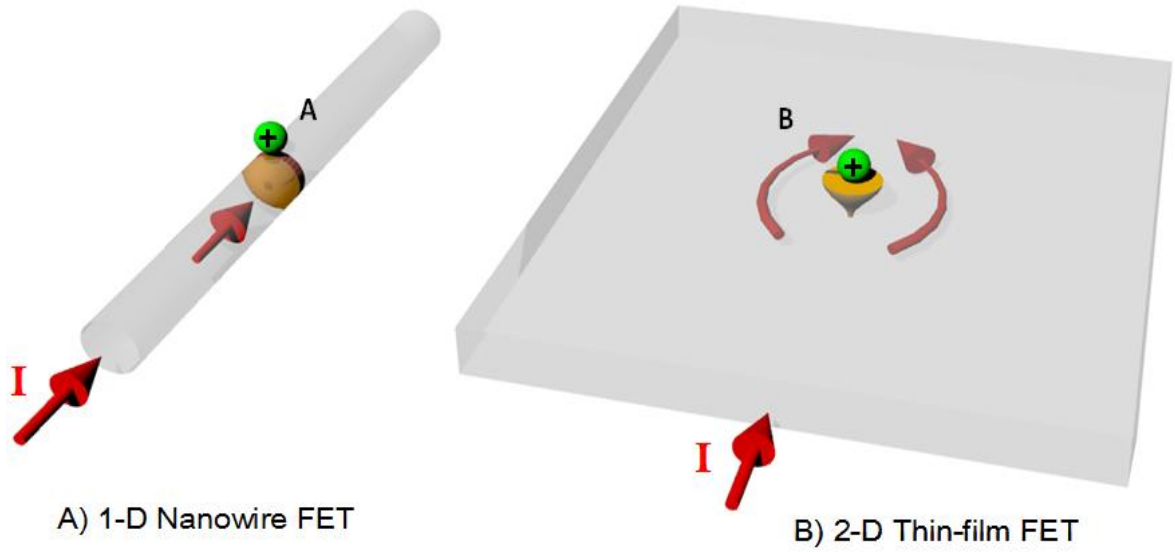
B) 2-D Thin-film FET

Fig. 1.1 Schematic showing the advantage of (A) 1 D nanowire FET over the (B) 2-D thin film FET.

Chapter 2: Conducting polymer coated single-walled carbon nanotube gas sensors for the detection of volatile organic compounds

Abstract

The current work involves fabrication, characterization and subsequent evaluation of PEDOT: PSS coated SWNT sensors for detecting analytes of interest in industrial manufacturing. By varying the sensor's synthesis conditions in terms of charge controlled electropolymerization of the monomer EDOT in presence of the dopant PSS, the sensing performance was systematically optimized. Electrical characterization in terms of change in resistance, cyclic voltammetry and field-effect transistor measurements were performed to confirm the presence of PEDOT: PSS coating on SWNTs. The optimized sensors showed sensing properties over a wide dynamic range of concentrations of saturated vapors of volatile organic compounds (VOCs) such as methanol, ethanol and methyl ethyl ketone at room temperature. In terms of performance, when compared with bare SWNTs, these hybrid sensors exhibited better sensitivity. The underlying mechanism of sensing was also investigated by using them as chemFET mode of sensor configuration.

2.1 Introduction

Ever since the discovery of carbon nanotubes (CNTs) (Iijima 1991), they have been put into a myriad of electronic applications such as room temperature field effect transistors

(Martel *et al.*, 1998; Tans *et al.*, 1998), interconnects (Yao *et al.*, 1999) and actuators (Baughman *et al.*, 1999). Very high electrical (Hwang *et al.*, 2009) and thermal conductivities, extraordinary mechanical strength together with their ultra-small size and low power consumption make them perfect candidate for use as an electronic material. Sensors form a basic division in which the CNTs are being increasingly used as active material for sensing gases and vapors (Kauffman and Star, 2008; Li *et al.*, 2003) . Their high aspect ratio enables them to have a high surface area which consists of all surface atoms. This renders them the property of exhibiting high sensitivity and rapid response times towards any change in the chemical environment. Current analytical techniques being used in the field of gas sensing mainly involve gas and liquid chromatography. They offer sensitive and reliable estimation of gas concentrations but are time consuming, expensive and require high temperature operation and sophisticated handling by trained technicians (Sherma 1993; Yao *et al.*, 1991). These limit their applications on site and *in situ* and call for a paradigm shift in the sensor technology for more sensitive recognition layers, increasingly complex architectures and reduced size.

The earliest attempts at using CNTs as gas sensors was made by Kong *et al.*, in 2000 where they demonstrated bare carbon nanotubes to respond to gases like ammonia and NO_2 at room temperature (Kong *et al.*, 2000). Since then studies have shown that CNTs can be used to sense a large number of other gases and VOCs (Li *et al.*, 2003; Nguyen *et al.*, 2006; Nguyen and Huh, 2006; Ueda *et al.*, 2008; Ueda *et al.*, 2006). However, using pristine CNTs has disadvantages. Gases which have low absorption capacity on carbon are difficult to be detected using single-walled carbon nanotubes (SWNTs) (Kong *et al.*,

2000). To overcome this difficulty several techniques have been incorporated which involve modifying the surface of SWNTs using materials like conducting polymers (Huyen and Chien, 2008; Srivastava *et al.*, 2009), metals (Kauffman *et al.*, 2010; Mubeen *et al.*, 2010; Mubeen *et al.*, 2007; Star *et al.*, 2006) and metal oxides (Wongwiriyapan *et al.*, 2009) that have shown better sensitivity to gases and VOCs. Thus the concept of a hybrid sensor arises which would have SWNTs as the charge conduit material along with a modifying material as the sensing element bringing about an increase in the overall sensor performance.

Conducting polymers (CPs) and their derivatives have been long used as chemical sensors. However their wide application is limited due to their inability to be used in a broad pH range (Nikolou and Malliaras, 2008). Poly (3,4-ethylenedioxythiophene) doped with poly(styrene sulfonic acid) (PEDOT:PSS) is a promising CP which is being used widely in chemical sensors owing to its properties like being electrochemically active, environmentally stable and maintaining its activity over a wide pH range . The use of poly(styrene sulfonic acid) (PSS) (Jonas *et al.*, 1995) as the counter ion renders enhanced conductivity and facilitates easier processibility. Reports have been made governing the use of PEDOT nanowires and thin films towards sensing gases and alcohols (Dan *et al.*, 2009; Dan *et al.*, 2007; Lin *et al.*, 2009; Myung *et al.*, 2011).

In this work, a facile fabrication technique of coating the SWNTs with PEDOT: PSS using the method of electropolymerization is reported and subsequent evaluation of the real time response of these SWNT coated PEDOT: PSS hybrid chemFET sensors towards

sensing three VOCs namely methanol, ethanol and methyl ethyl ketone is performed. Using electropolymerization offers a great deal of flexibility in terms of controlling the thickness of the CP film on the surface of the SWNTs by altering parameters like charge, electrolyte composition and potential (Mubeen *et al.*, 2007). In addition to it being a cost effective method of enhancing a sensor's response, it offers the creation of a high density nanosensor arrays by site specific electropolymerization approach in a sensor array consisting of multiple individually addressable devices.

2.2 Experimental Details

2.2.1 Sensor design and fabrication

Microfabricated gold electrodes were fabricated on highly doped p-type silicon substrate using the cleanroom facilities available in University of California, Riverside. First, a 300 nm SiO_2 thick film was deposited on a (100) oriented highly doped p-type Si substrate by thermal CVD deposition to insulate the substrate. It was followed by defining the drain and source electrode areas by photolithography using the positive photoresist 5214. The thickness of the chromium adhesion layer was maintained at 20 nm and that of gold above it was 180 nm. The width and gap of the electrodes were fixed at 200 μm and 3 μm, respectively. The chip configuration thus obtained contained 16 addressable electrode pairs.

2.2.2 SWNTs solubilization and alignment

Carboxylated-SWNTs (SWNT-COOH 80-90% purity) procured commercially from Carbon Solution, Inc. Riverside, CA were dispersed (1 μg/mL) in dimethyl formamide

obtained commercially from Sigma Aldrich, MO. Though carbon nanotubes are known to have poor solubility in most solvents, the amide group of dimethyl formamide (DMF) can attach to the surface of the nanotubes making it a suitable solvent for obtaining uniformly suspended SWNTs in DMF (Li *et al.*, 2003). The suspension of SWNTs in DMF solution was prepared in steps which involved first sonicating the dispersed carboxylated SWNTs followed by centrifugation at a speed of 10,000 rpm to remove soluble fraction and aggregates.

The suspended SWNTs were aligned in the 3 μm spaced microfabricated gold electrodes by ac dielectrophoresis (DEP) (Dan *et al.*, 2007; Duchamp *et al.*, 2010; Li *et al.*, 2004). The procedure involved addition of a 0.1 μL drop of SWNTs suspended in dimethyl formamide and subsequent application of an AC voltage of the order of 3 V peak to peak amplitude at a frequency of 4 MHz across the electrodes. The aligned SWNTs were then annealed at 300 ^{0} C for 1 hour in an atmosphere of 5% hydrogen and 95% nitrogen gas. This was done in order to improve the contact between the electrodes and the SWNTs and to remove DMF residues accumulated during the process of alignment.

2.2.3 Electropolymerization

Electrochemical functionalization of SWNTs with PEDOT:PSS was conducted at ambient temperature with a three electrode configuration where the SWNTs network with the gold electrodes, a Pt wire, and chlorinated silver wire (Ag/AgCl wire) were employed as working, counter, and reference electrodes, respectively. A 0.1 μL drop of 5 mM solution of the electrolyte EDOT (monomer) and 5 mM PSS (dopant) in water was placed

on top of the SWNT networks followed by potentiostatic electropolymerization at 0.9 V vs. Ag/AgCl wire reference. The electrodes were placed in contact with the electrolyte to constitute an electrochemical cell. Charge controlled electropolymerization was performed at three different charges namely 1, 2.5 and 5 µC. After the functionalization, the sensors were rinsed with deionized water followed by blow drying lightly with nitrogen gas.

2.2.4 Device characterization and sensing

Sensors were characterized in terms of their current–voltage (I–V) response measured using a potentiostat (Model 1202A, CH Instruments, Inc., TX, USA) before and after electropolymerization. The voltage was swept from -1 V to +1 V and the current was recorded. The device resistance was measured as the slope of I–V near zero voltage in the linear range of +/- 100 mV. Transport measurements were performed using a dual channel Keithley source meter (Keithley- Model 2636A, CA) wherein the gold electrodes acted as the source and drain while polysilicon behaved as the back gate. A drain to source bias of -1 V was applied while the gate voltage was varied in the range of +/- 20 V at a scan rate of 0.1 V/s. Source–drain current (I_{SD}) as a function of the gate voltage (V_{GS}) was measured. Cyclic voltammetry was conducted in an aqueous solution of 0.1 M NaCl at a scan rate of 50 mV/s using a potentiostat (Model 1202A, CH Instruments, Inc., TX, USA).

2.2.5 Gas sensing setup

The 16 electrodes pair chip consisting of 16 individual addressable sensor devices, each electropolymerized with PEDOT: PSS were wirebonded and packaged to a 40 pin ceramic inline package, which was then mounted on to the breadboard of the sensing system set up. The sensors were connected in series with a load resistance of equal resistance value and were subject to a fixed voltage of 1 V DC. Real time measurements were carried out using a custom made sensing set up that was controlled by LabView program.

A 3.6 cm^3 air tight sealed glass chamber with gas inlet and outlet ports for gas flow-through was positioned over the sensor chip. For sensing of volatile organic compounds, saturated vapors of the VOCs were produced by bubbling dry air through the bubbler column containing the VOC of interest. The carrier gas in this set up was dry air. Various concentrations of the vapors were introduced to the gas chamber by regulated flow of the vapors with the help of mass flow controllers purchased from the Alicat Scientific Incorporated, Tucson, AZ. Prior to all the sensing experiments, the sensors were first exposed to dry air (purity: 99.998%) to attain a steady baseline resistance following which they were exposed to different concentrations of the saturated vapors of the VOC mixed in dry air for 15 minutes with an interval of 20 min recovery in air between two successive vapor exposures. This constituted one complete cycle. This cycle was repeated for n number of times based on the range of concentrations being sensed. For real time gas sensing, the sensors thus fabricated were operated as chemiresistive sensors wherein the change in resistance upon exposure to an analyte formed the basis for

measuring the sensitivity of the sensor. All sensors with an initial resistance in the range of 3 kΩ - 9kΩ were used for sensing for better reliability and consistency in gas sensing results.

2.3 Results and discussions

Several techniques have been used over the past few years for fabricating carbon nanotube based semiconducting devices. They involved manipulating CNTs onto pre-patterned electrodes by an atomic force microscope (Roschier *et al*., 2002) random dispersion of suspended CNTs onto pre-patterned electrodes, (Bezryadin *et al*., 1998; Tan *et al*., 1998) and lithographically patterning catalyst (Franklin *et al*., 2002; Guillorn *et al*., 2002) as CNT nucleation sites on electrode and drop casting to obtain CNT network between the electrodes. However these techniques yielded low throughput and their complexity and limited controllability rendered them unsuitable for applications which require high density sensor arrays that can be mass producible. DEP technique eliminates such issues by offering a simple, cost-effective and controllable alternative over such methods. In this method of alignment, the dielectrophoretic force field changes upon nanotube deposition and thereby self-limits the directed assembly to a single nanotube or nanotube bundle at predefined locations in the gap between the electrodes. Hence this technique offers versatility in terms of controlling the number of SWNTs bridging the electrode gap thereby making it possible to obtain nanotube based sensor devices with a desired resistance range. It is compatible with SWNTs from any source, which are

suitably dispersed in an aqueous surfactant solution and can be used to align nanowires as well.

CPs can be incorporated onto the surface of CNTs either by possessing functional groups that are reactive toward CNTs (Liu *et al.*, 2008; Liu and Chen, 2007; Liu *et al.*, 2005) or by in situ polymerization (Lee *et al.*, 2006). The former approach of functionalization limits its application pool by incorporating one kind of polymer or sometimes one sort of polymers on to the surface of CNTs. In situ polymerization overcomes this issue as it enables the polymerization of a wide range of polymers on SWNTs based on doping type molecular interactions. Electropolymerization of EDOT: PSS was carried out on the surface of SWNTs to obtain a coating of the conducting polymer on the surface of SWNTs. Electropolymerization apart from being a simple, cost effective method of surface modification holds several advantages over other functionalization methods. It offers site specific electrodeposition and can be used to deposit a wide variety of nanomaterials like metals, metal oxides and semiconductors under ambient operating conditions. The thickness, grain size and the orientation of the electrodeposited material can be varied depending upon electrodeposition parameters (Fan *et al.*, 2005) such as electrolyte composition, deposition time and applied potential thus making it a very versatile technique of surface modification. Charge controlled electropolymerization was performed at several different charge conditions with an attempt to understand the effect of the electrodeposition parameter and to find a suitable charge which would result in better sensing behavior of the PEDOT: PSS coated sensors. It was seen that for the same applied potential of 0.9 V, sensors which were coated with PEDOT:PSS at 2.5 μC

charge exhibited better dynamic sensing response than sensors coated at charges lower and higher than it (Fig. 2.5). The observed trend can be attributed to the fact that at lower charge controlled electropolymerization, the PEDOT: PSS coating is too thin to enhance the performance of the sensor while at higher charges, the PEDOT: PSS coating is too thick to allow SWNTs contribute to the sensing behavior. Hence it was inferred that coating the sensors at 2.5 μC charge with PEDOT: PSS will result in an optimum thickness of the conducting polymer that will enable a synergistic contribution of both the coating and the SWNTs underneath to contribute to the superior performance in sensing of analytes.

Electrical characterization was performed on the bare SWNTs and the PEDOT: PSS coated SWNT sensors as a part of the confirmation studies for verifying the presence of the conducting polymer coating on the SWNTs. These techniques involved resistance measurement; cyclic voltammetry and field-effect transistor (transfer characteristics) before and after electropolymerization. As can be seen in Fig. 2.2, the hybrid sensors exhibited a drop in resistance as compared to the bare SWNT sensors upon electropolymerization. PEDOT is a stable polymer, which exhibits relatively high electrical conductivity (Pei *et al.*, 1994). Furthermore, a well-processable form of this polymer is obtained by oxidative polymerization in the presence of PSS. Charge transfer takes place between the polymer and the SWNTs upon polymerization causing an external doping that impacts the electronic structure of both the polymer and SWNTs thereby leading to a change in conductance (Kalbac *et al.*, 2009; Kalbac *et al.*, 2007). As an additional confirmation of the successful electropolymerization of PEDOT:PSS on the

SWNTs surface, cyclic voltammograms on both bare and coated devices were performed (Fig. 2.3) which revealed that electropolymerization results in an increase in the current density of the PEDOT:PSS coated sensor. FET characteristics studies performed both on the bare SWNTs and the PEDOT: PSS coated SWNTs (Fig. 2.4) infers that the devices retain their p-type semiconducting behavior after electropolymerization with an increase in the source -drain current for all values of gate voltages applied.

Figures 2.6, 2.7 and 2.8 show the calibration curve along with the dynamic response of the hybrid sensor for various VOCs. The normalized response $\Delta R/R_O$ is given by $\{(R - R_0)/R_0\}$, where R and R_0 are the resistances in analyte gas and air, respectively. As shown in the figures, exposure to the VOCs of interest resulted in an increase in the resistance of the sensors. The hybrid sensors responded linearly to a wide range of saturated vapors of methanol i.e., from 2.5% till 75% concentrations with a limit of detection of 1.3% considering a signal-to-noise ratio (SNR) of 3. While the bare SWNT devices didn't respond to ethanol and MEK, the hybrid devices responded to both the analytes. The limit of detection was calculated to be 5.95% and 3% for ethanol and MEK vapors respectively with SNR of 3. Thus, when compared with the performance of bare SWNTS, the hybrid sensors show enhanced sensing response towards a wide dynamic range of saturated vapor concentrations of these VOCs at room temperature.

To gain an understanding underlying mechanism governing the interaction of the PEDOT: PSS coated SWNT sensors with the analyte, the sensors were configured in the chemFET mode of operation with polysilicon as the back gate. Transfer characteristics

(Fig. 2.9) reveal that with increasing concentration of the analyte (methanol in this case), there occurs a change in the slope of the transfer characteristics curve along with a shift in the threshold voltage towards more negative voltage values of the gate voltage. This observation can be attributed to the charge transfer phenomenon wherein adsorption of the analyte induces additional negative charge in the SWNT, thus n-doping the SWNT and shifting the I-V_g curve toward more negative gate voltages. Similar trend was observed also in the case of ethanol and ethyl methyl ketone. In addition, PEDOT: PSS is soluble in water miscible solvents and in this case, high polar solvents as well. PSS being a large polymeric counter ion tends to increase the spacing between conjugated chains thereby also resulting in an increase in the overall conformational disorder of the polymer. As a result, when PEDOT: PSS gets in contact with the vapors of the VOC, rapid interactions take place between the relatively disordered and open structure of the PEDOT:PSS coating and the vapors (Mabrook *et al.*, 2005). Exposure to solvent vapors results in the swelling of the polymer which in turn increases the hopping distance for charge carriers (Bai and Shi, 2007; Cao *et al.*, 2008) and hence the lowering of conductivity occurs. A detailed study relating to the mechanism of interaction is required at this point.

2.4 Conclusion

Nano gas sensors based on AC dielectrophoresis assembly of SWNT networks followed by electropolymerization of PEDOT: PSS on SWNTs surface were developed. These hybrid sensors showed response over a wide dynamic range, enhanced sensitivity over bare SWNT sensors and a lower limit of detection for saturated vapors of methanol,

ethanol and MEK at room temperature. Further, incorporating different dopants and/or solvents into the PEDOT matrix can be investigated in terms of their sensing performance towards various analytes. Electropolymerization of such conducting polymers on the surface of SWNTs could endow the SWNTs with multiple tailor made materials and can become an effective platform for the development of new kinds of nanostructured electrochemical devices with superior properties for multi component analysis.

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Figures
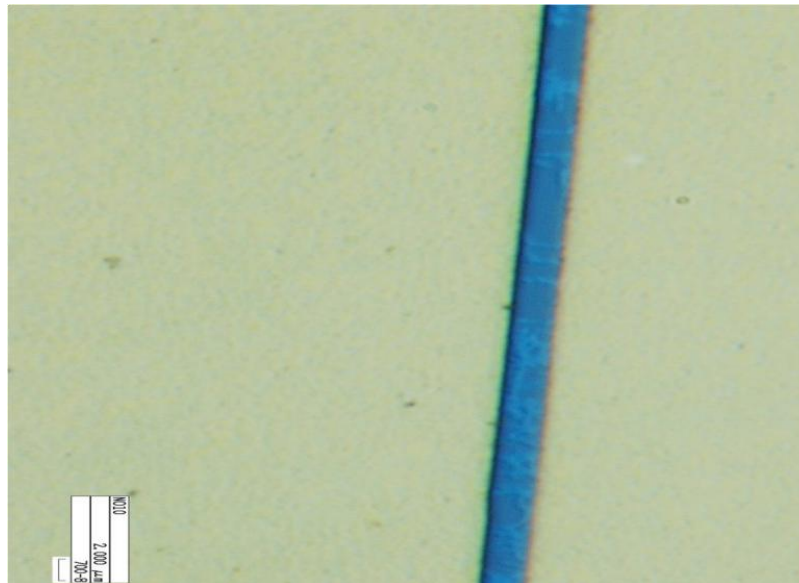
Fig. 2.1 High resolution optical image of aligned SWNTs coated with PEDOT:PSS at 2.5 μC charge at 0.9 V.
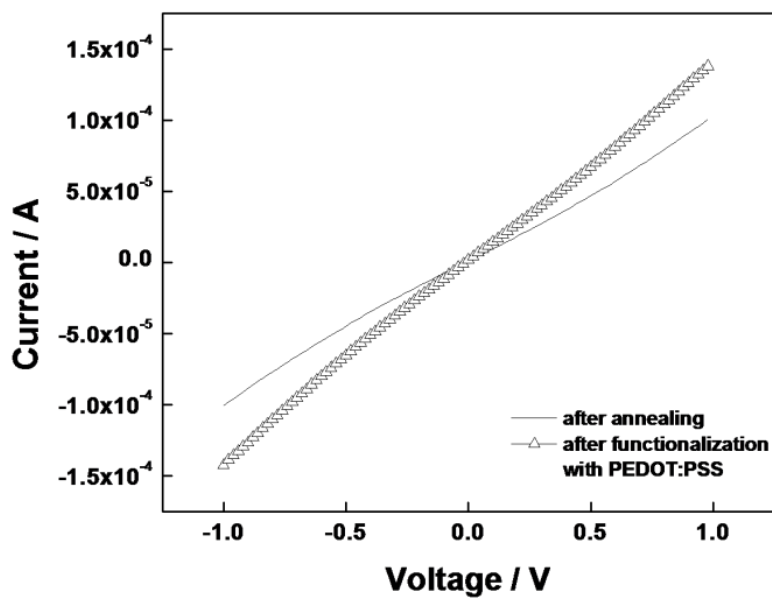
Fig. 2.2 I-V curve of bare and PEDOT:PSS coated SWNTs.
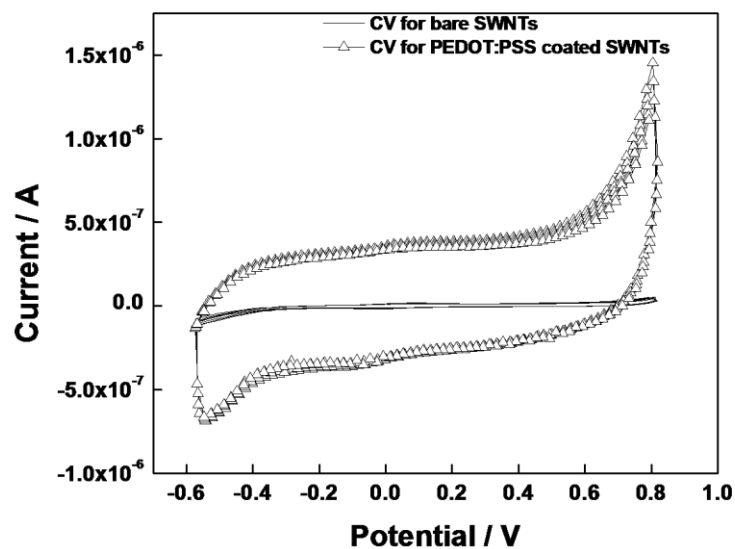
Fig. 2.3 Cyclic voltammograms of bare SWNTs and PEDOT:PSS coated SWNTs; scan rate of 50m V/sec.
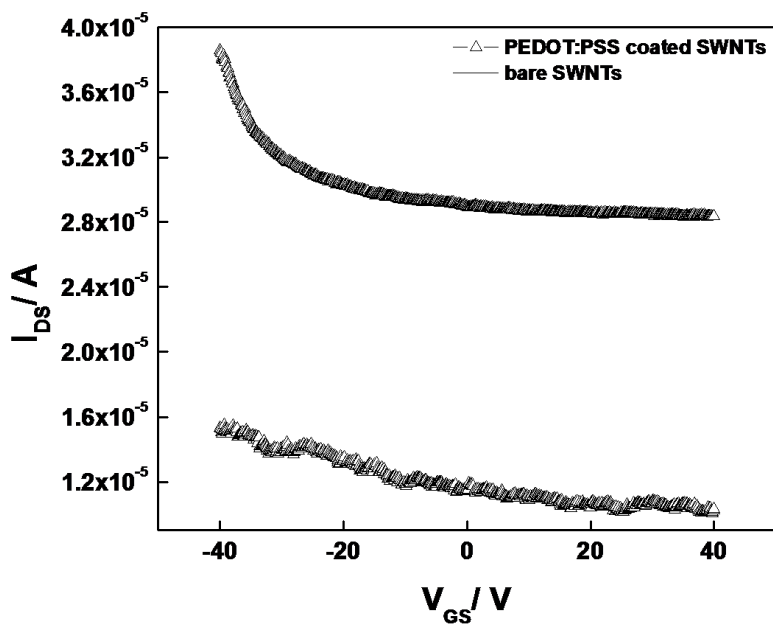
Fig. 2.4 Transfer characteristics curve for bare and PEDOT:PSS coated SWNTs at V_{DS} = -1 V.
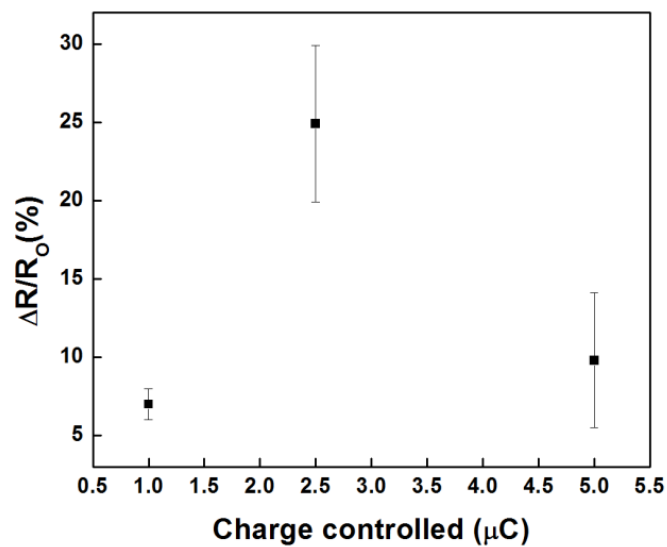
Fig 2.5 Effect of PEDOT:PSS electropolymerization charge on the hybrid sensor sensitivity for 50% saturated vapors of methanol.
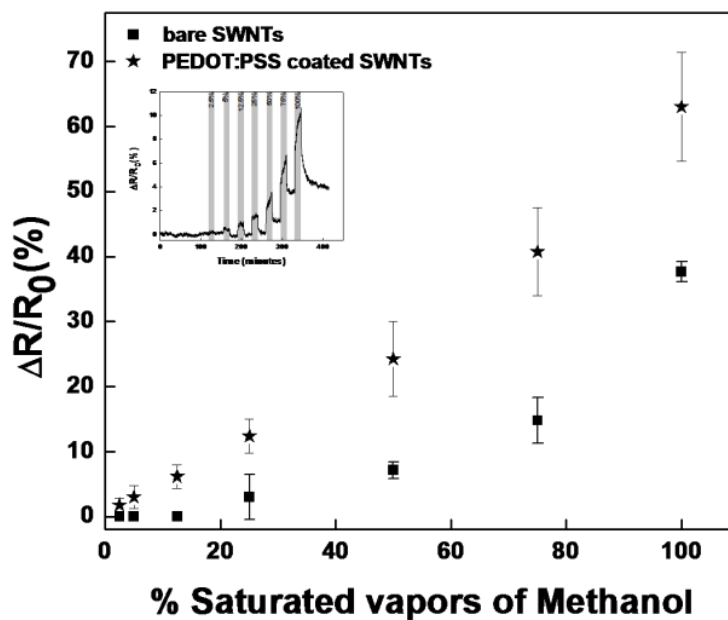
Fig. 2.6 Calibration curves for bare and PEDOT:PSS coated SWNT for methanol vapors and dynamic response of the PEDOT:PSS coated SWNTs sensor (inset).
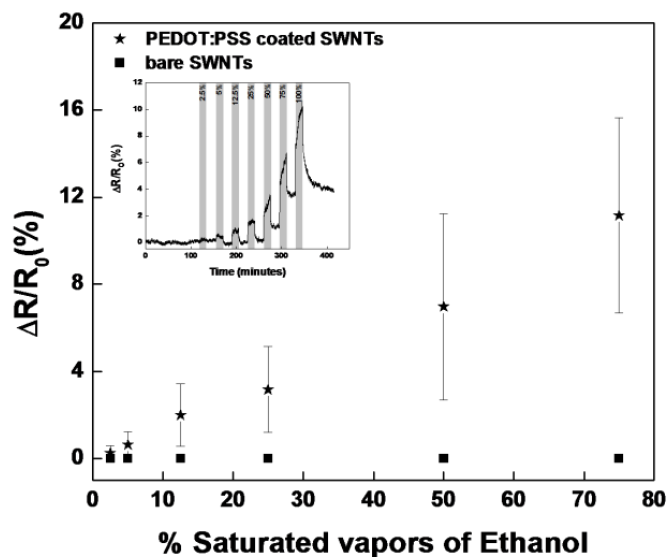
Fig. 2.7 Calibration curves for bare and PEDOT:PSS coated SWNT for ethanol vapors and dynamic response of the PEDOT:PSS coated SWNTs sensor (inset).
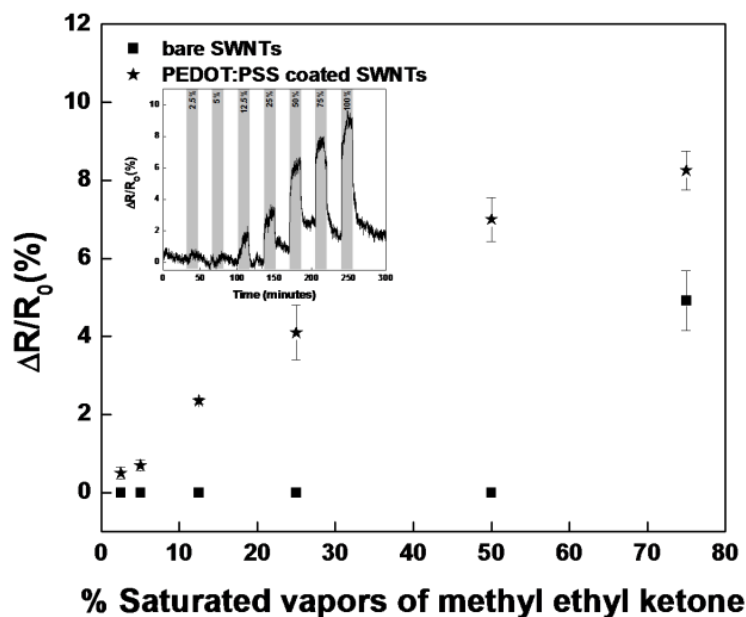
Fig. 2.8 Calibration curves for bare and PEDOT:PSS coated SWNT for methyl ethyl ketone vapors and dynamic response of the PEDOT:PSS coated SWNTs sensor (inset).
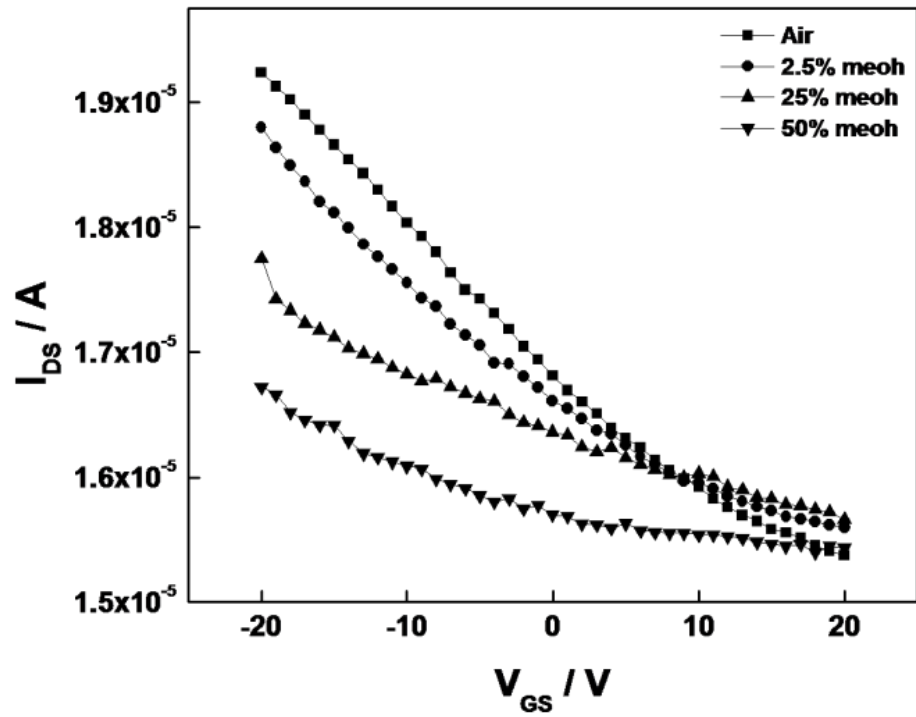
Fig. 2.9 Transfer characteristics curves of PEDOT:PSS coated SWNT sensors when exposed to air and different concentrations of methanol vapors performed at $V_{DS} = -1$ V.

Chapter 3: Poly (3-amino phenyl boronicacid)-functionalized carbon nanotubes-based sensors for detection of sugars

Abstract

Polyaniline boronic acid (PABA)-single walled carbon nanotube based non enzymatic sensor was developed and used for detection of saccharides. The work involved coating of SWNTs with PABA by electrochemical polymerization of 3-amino phenyl boronic acid (APBA) in presence of fluoride and their subsequent evaluation as chemiresistive sensors towards detection of D-fructose and D-glucose. By varying the sensor's synthesis conditions by charge controlled electropolymerization of the monomer 3-APBA, the sensing performance was systematically optimized. Electrical characterization in terms of change in resistance, cyclic voltammetry and structural characterization using AFM were performed to confirm the presence of PABA coating on SWNTs. The optimized sensors showed sensing response over a wide dynamic range of concentrations and a limit of detection of 2.92 mM for D-fructose and 3.46 mM for D-glucose. The hybrid sensors could be regenerated on the basis of the reversible nature of the binding between PABA and 1, 2 or 1, 3-diols at lower values of pH.

3.1 Introduction

Detection of saccharides is of prime importance in biomedical diagnostics and quality control in food industries. The conventional approach mostly employs techniques that use enzymatic assays (Rauf *et al.*, 2006; Siegel *et al.*, 2000) to detect and quantify

saccharides. However, the gradual degradation of their enzymatic activity calls for timely replenishment of the enzyme thereby limiting the lifetime and stability of these sensors. Furthermore, their need for frequent calibration, temperature and oxygen dependence (Mano *et al.*, 2003; Moussy *et al.*, 1993) limits their potential application pool and renders them unsuitable for easier and continuous monitoring of glucose concentrations.

Polyaniline is a popular conducting polymer which possesses attractive properties like stability, easy processibility and high conductivity. The ability to tune its electrical properties by reversible doping and undoping of the polymer backbone via chemical manipulation along with its well-behaved electrochemistry makes it an ideal sensing material. Its low cost and facile nature of preparation (Skotheim and Reynolds, 2007) makes it popular in the field of molecular electronics. Numerous accounts in literature have reported the synthesis of functionalized polyaniline (Liu and Freund, 1996; Zheng *et al.*, 1994). Boronic acid substituted polyaniline synthesis route (Nicolas *et al.*, 2000; Wolfbeis *et al.*, 2001) proves to be of great interest in the detection of saccharides (Cao and Heagy, 2004; James and Shinkai, 2002; Shoji and Freund, 2001, 2002; Striegler 2003). Complexation of saccharides (as well as alkyl and aromatic diols) with aromatic boronic acids produces a stable boronate anion (Springsteen and Wang, 2002) and a proton in the pH range 6-10 thus opening up possibilities of numerous electrochemical approaches to detect sugars based on saccharide- boronic acid functionality interactions.

In this work, we have developed and demonstrated an enzyme-free PABA (poly 3-amino phenyl boronic acid) coated SWNT based nanosensor towards detection of saccharides in

solution. Over the years, SWNT-conducting polymer hybrid structure have provided an ideal platform for building reliable and highly sensitive sensor for an wide array of sensing applications (Dai *et al*., 2002). Dai and coworkers synthesized conducting polymer-carbon nanotube (CP-NT) coaxial nanowires and demonstrated amperometric glucose detection using the same (Gao *et al*., 2000). Apart from providing mechanical stability (de Heer *et al*., 1999) and enhanced electrical conductivity in terms of efficient transduction (de Heer *et al*., 1998) to and from the conducting polymer layer, the large surface area of the SWNTs leads to enhanced sensitivity towards detecting the analyte. Our key strategy involves electropolymerization of PABA on the surface of SWNTs in a simplistic, reproducible and controllable manner at room temperature. By varying the electrodeposition time, the thickness of the PABA film could be controlled. The boronic acid-saccharide complexation brings about a change in the net electrical charge of the system thereby resulting in a change of the overall conductance which in turn is detected by the chemiresitive method of sensor configuration. Unlike the enzymatic assays which consume the analyte in course of detection, this approach utilizes the pH dependant reversible nature of boronic acid-saccharide complexation wherein the sugar in released back to the solution at lower values of pH.

3.2 Experimental

3.2.1 Materials

Carboxylated single-walled nanotubes (SWNT-COOH, 80–90% purity and 1.5 to 3 atomic %–COOH content) were procured commercially from Carbon Solution Inc

(Riverside, CA, USA). 3-Aminophenylboronic acid hydrochloride salt 98% (3-APBA) was purchased from Sigma Aldrich (St Louis, Mo, USA).D-Fructose, D-Glucose were purchased from Alfa Aesar. Uric acid, Ascorbic acid and citric acid were purchased from Fisher Scientific. All buffer solutions were prepared in deionized water obtained by purifying distilled water through a Milli-Q plus (Millipore Inc) ultrapure water system.

3.2.2 Sensor design and fabrication

Microelectrodes Fabrication: An array of 16 source-drain gold electrodes pairs with 3 μm channel length was defined on SiO_2/Si substrate using standard photolithography technique as reported previously (Deshusses *et al.*, 2007). In brief, each source-drain electrode patterns are predefined on a SiO_2 (300 nm)/Si substrate. Each pair consists of two 200-μm-wide fingers pointed head to head at a distance of 3 μm.

3.2.3 DEP Deposition of Single walled carbon nanotubes (SWNTs)

The SWNTs as described in Chapter 2 were suspended in DMF solution by brief sonication process. A 0.1 μL drop of SWNTs suspension was placed between the electrodes using micropipette followed by applying an ac electric field of 3V p-p (0.36V_{RMS}) at 4 MHz frequency across the electrodes for few seconds as reported earlier (Myung *et al.*, 2010). The duration of the application of the dielectrophoretic force was optimized over time to obtain carbon nanotube aligned devices that had an initial resistance in the range of 0.2 MΩ to 1 MΩ for consistency. The aligned SWNTs were then annealed at 300 ^{0} C for 1 hour in an atmosphere of 5% hydrogen and 95% nitrogen

gas. This improved the contact resistance between the electrodes and the SWNTs and helped to remove DMF residues accumulated during the process of alignment.

3.2.4 Electropolymerization of PABA

Poly 3-amino phenyl boronic acid (PABA) was deposited electrochemically onto the aligned SWNTs electrodes. A three electrode configuration where the aligned SWNTs network with the gold electrodes, a Pt wire, and chlorinated silver wire (Ag/AgCl wire) were employed as working, counter, and reference electrodes, respectively was constituted. The monomer solution containing 40 mM 3-APBA and 300 mm NaF was prepared in the undiluted PBS stock solution (10X PBS) and under conditions where the pH was reduced to 5.0 by addition of 0.5 M HCl. A 0.1 μL drop of the electrolyte was placed on top of the SWNT networks followed by potentiostatic electropolymerization at 0.7 V (vs. Ag/AgCl). After electrodeposition, the sensors were rinsed with deionized water followed with phosphate buffer saline (PBS) at pH 7.4 and then kept in stirred PBS solution overnight to allow the electrochemical potential to stabilize.

3.2.5 Apparatus for device characterization and sensing

Electrical characterization was performed using a potentiostat (Model # 1202A, CHInstruments, Inc., TX, USA) in terms of the resistance of the sensors by measuring the current versus voltage response of the sensors. The initial or baseline resistance of the sensor was recorded by incubating the SWNT coated PABA device with a 20 ml of PBS buffer and sweeping the voltage from -1 V to +1 V. For the purpose of better precision of measurements, the slope of the I-V was measured in a region near to the zero voltage

preferably +/- 100 mV. Upon exposure to different concentrations of D-glucose and D-fructose solutions made in PBS buffer, change in resistance was measured after incubating the sensor for 30 mins followed by washing with PB buffer twice.

3.3 Results and Discussions

Functionalization of SWNTs by aromatic boronic acid can be performed either by covalent attachment of APBA or non-covalent attachment routes (Balasubramanian and Burghard, 2008). In our work, we have focused on the non covalent approach by electropolymerization of APBA in the presence of fluoride. The complexation of fluoride with boronic acid leads to the formation of a negatively charged species (Cooper *et al.*, 1998; Westmark *et al.*, 1994). As discussed in literature (Nicolas *et al.*, 2000) fluoride catalyzed reaction results in poly(aminophenylboronic acid) to have a self-doped structure under acidic conditions. Fig. 3.1(a) shows a cyclic voltammogram obtained for 3-aminophenylboronic acid in the presence of 40 mM fluoride and 300 mM NaF in 10X PBS adjusted to pH 5.0. It has been reported earlier that increasing the concentration of sodium fluoride results in significant negative shifts in the oxidation potential, thereby enhancing polymerization rates with the polymer film thus formed exhibiting better stability and adhesion properties(Shoji and Freund, 2002).

This high concentration of fluoride resulted in sustained polymerization and significant and continuous polymer growth (fig. 3.1(b)). Thus, a self-doped polymer was produced along with the formation of formation of a tetrahedral anionic boronate species (Deore and Freund, 2003).

Electrical characterization in terms of I-V characteristics was performed after electropolymerization of PABA on the SWNT surface. As shown in fig. 3.2, the PABA coated devices exhibited higher resistance as compared to bare SWNT devices. This can be attributed to the fact that aligned SWNTs between gold contact electrodes behave as p-type semiconductors. Upon electropolymerization of 3-APBA, the amino functional groups which are protonated and therefore positively charged, reduce the overall hole concentration in SWNTs in a similar manner as applying a positive potential to the gate reduces the conductance in a p-type semiconductor channel as confirmed from literature (Balasubramanian *et al.*, 2003). As an additional confirmation of successful electropolymerization, CV was performed on the coated SWNT devices in the monomer solution as shown in fig. 3.3 which showed peaks corresponding to PABA.

Inorder to obtain consistent sensing results, devices which had resistance in the range of 20 KΩ to 30 kΩ after annealing were selected and electropolymerized. The purpose of electropolymerization was to develop a synergic platform where both SWNTs and PABA coating contribute their maximum towards the sensing performance of the device. Hence, charge controlled electropolymerization of PABA was carried out and the sensing behavior towards one definite concentration (in this case 10 mM) of D-fructose was recorded as shown in fig. 3.4. Optimal charge for electropolymerization was determined to be around 25 μC i.e., devices electropolymerized at this charge yielded better sensitivity towards D-fructose than the ones electropolymerized at charges lower and higher than it. A suitable explanation to this phenomenon could be the difference in the thickness of the PABA coatings on the SWNTs as the charge was varied. Charge

controlled electropolymerization at lower charges resulted in a thinner coating of PABA with lesser number of BA receptors which weren't adequate enough to bind with all the cis-diol groups present in the analyte. On the other hand, higher charges resulted in thicker coatings thereby offering some hindrance in the efficient charge transfer from the polymerized coating onto the SWNTs when the BA receptors attached with the cis-diol groups of the saccharide to form tetrahedral anionic cyclic esters. The presence of fluoride enhances the complexation of saccharides with the BA receptors under these conditions by disrupting any B-N interactions and facilitates the formation of the anionic ester (Westmark *et al.*, 1994). The formation of the ester leads to an increase in relative negative charge at the surface of the nanotube resulting in an increase in the resistance of the sensor which can be detected electrically. Thus the extent of binding event is detected and quantified by the chemiresistive sensor.

Fig. 3.5 and fig. 3.6 show the nanosensor calibration plot for different concentrations of D-fructose and d-glucose respectively. The response of the sensor is measured in terms of its relative change in resistance, expressed in percentage, when exposed to a particular concentration of the saccharide. The sensor showed a linear range of detection from 1 to 10 mM with a sensitivity (measured as the slope in the linear region) of 3.34×10^{-2} mg^{-1} l for D-fructose and 1 to 10 mM with a sensitivity of 3.1×10^{-2} mg^{-1} l for D-glucose respectively. The estimated limit of detection given by LOD = 3 SD/ m where m is the slope of the linear part of the calibration curve and SD is standard deviation of the blank measurement was found out to be 2.92 mM and 3.46 mM for D-fructose and D-glucose respectively. The degree of complexation depends on the the binding constants (k)

between 3-APBA and the monosaccharides. It has been found that fructose shows higher affinity to 3-APBA for all pH values owing to its higher binding constant (D-fructose > D-glucose > R-methyl-D-glucoside) (Boyaci *et al.*, 2009). This explains the higher sensitivity of the sensors towards D-fructose as compared to D-glucose.

Owing to the reversible nature of the binding between the BA receptors and the sugar media (Cao and Heagy, 2004; James and Shinkai, 2002; Striegler 2003), the sensors could be regenerated by incubating them in buffer of pH 5 for 10 min as shown in fig. 3.7. Lowering the pH resulted in the disruption of the binding between the BA moieties and the sugar thus releasing the sugar back to the medium (Balasubramanian *et al.*, 2010). Following the regeneration, for every subsequent use in detecting sugar at physiological pH, the sensor was washed twice and incubated for 10 min in PBS buffer of pH 7.4.

Several redox-active species such as Ascorbic acid (AA), Uric acid (UA) and Citric acid (CA) commonly coexist in food samples and beverages. To investigate the effects of interference arising from them, physiological concentration levels of these samples were tested. As seen in fig. 3.8, while a certain higher concentration of ascorbic acid showed a higher response, the effects of other samples were found to be negligible. Thus, the sensors can be used to selectively detect a monosaccharide like glucose or fructose while providing high immunity against other common interferences.

3.4 Conclusion

In summary, a simple, cost effective and enzyme-free approach of detection of saccharides in solution using PABA coated SWNT sensor was developed. These hybrid sensors exhibited a linear range of glucose detection from A to B mM with a sensitivity of C. Negligible interference from analytes like uric acid and citric acid and relatively small influence of ascorbic acid were observed while investigating the target specificity of the sensors during glucose detection. The reversible nature of the reaction between 3 amino phenyl boronic acid with 1, 2 or 1, 3 diols enables the release of sugar back to the medium at lower values of pH, thus providing a simpler, faster and regenerative way for detecting saccharides in solution. Due to the site-specific functionalization strategy of electropolymerization, it is foreseeable that a synthetic molecular receptor sensor array system can be constituted with each individual entity designed for specific analyte detection. This could lead to the development of cost effective and highly efficient lab-on-a-chip configurations.

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Graphics

Change of resistance upon formation of tetrahedral anionic boronate ester.

Poly (3-aminophenyl boronic acid)

Anionic boronate ester

1,2 or 1,3-diol

Silicon SiO$_2$ SWNT Source;Drain
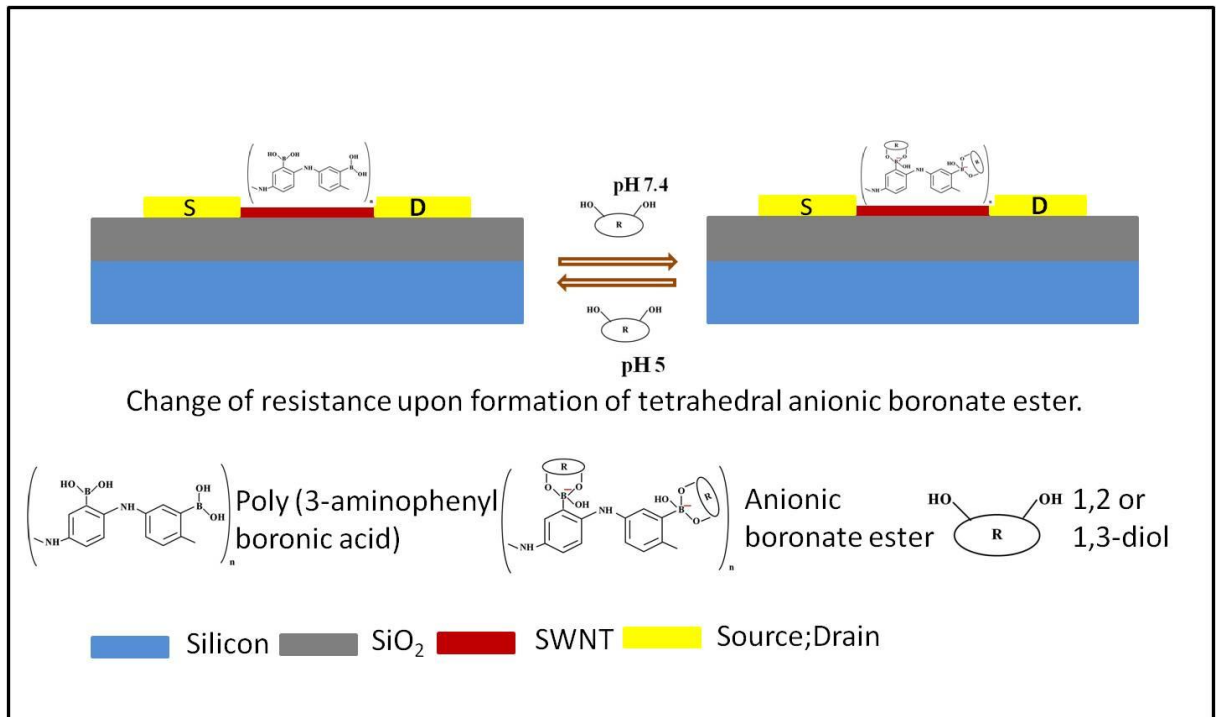
Figures
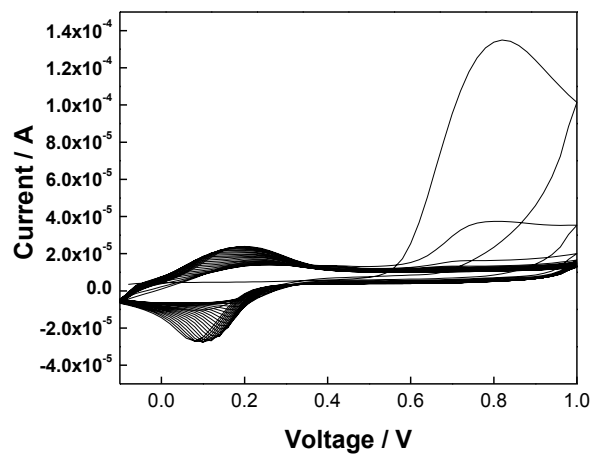
Fig. 3.1(a) Cyclic voltammogram of 40 mM 3-aminophenylboronic acid in 10X PBS plus 300 mM NaF; pH 7.4. Scan rate: 100 mV /s.
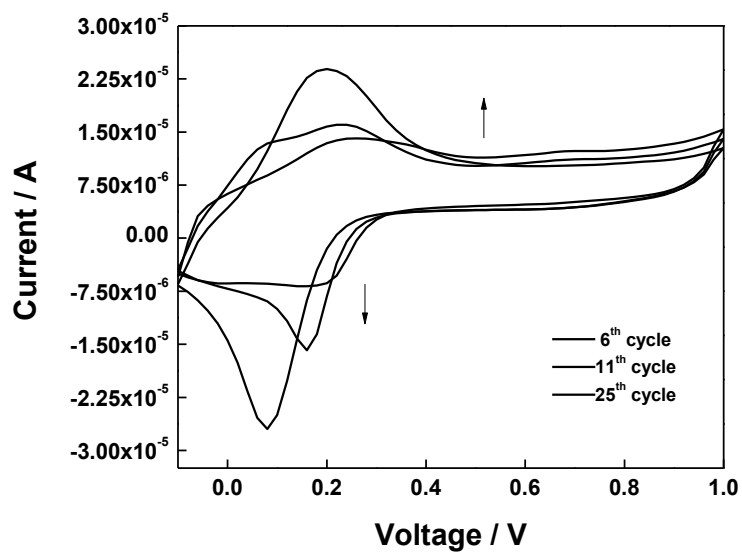
Fig. 3.1(b) CV under conditions of 1(a) showing continuous polymer growth; Scan rate: 100 mV s^{-1} .
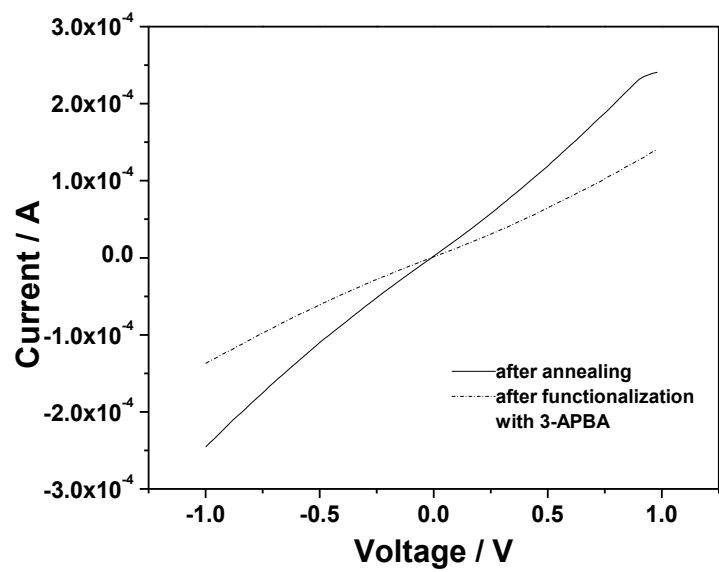
Fig. 3.2 I_{DS} vs. V_{DS} of AC dielectrophoretically aligned SWNTs network before and after electropolymerization of 3-APBA.
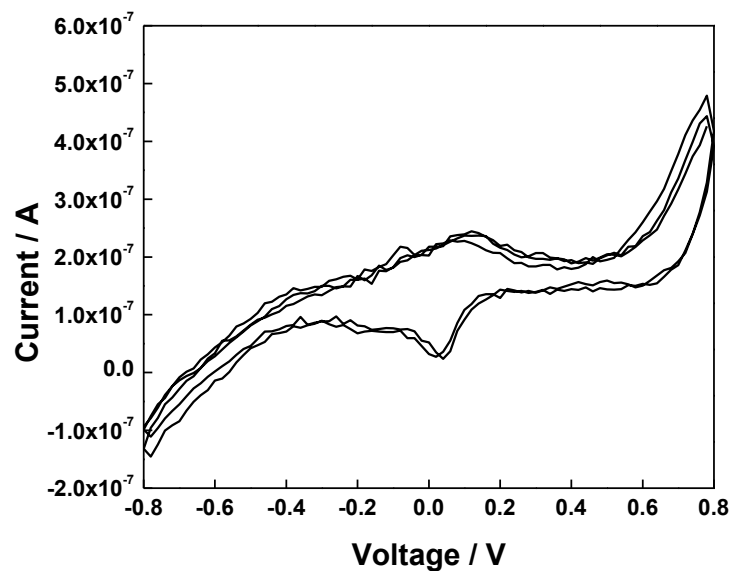
Fig. 3. 3 CV of PABA coated SWNT device in 10X PBS plus 300 mM NaF; pH 5.0. Scan rate: 100 mV s^{-1}
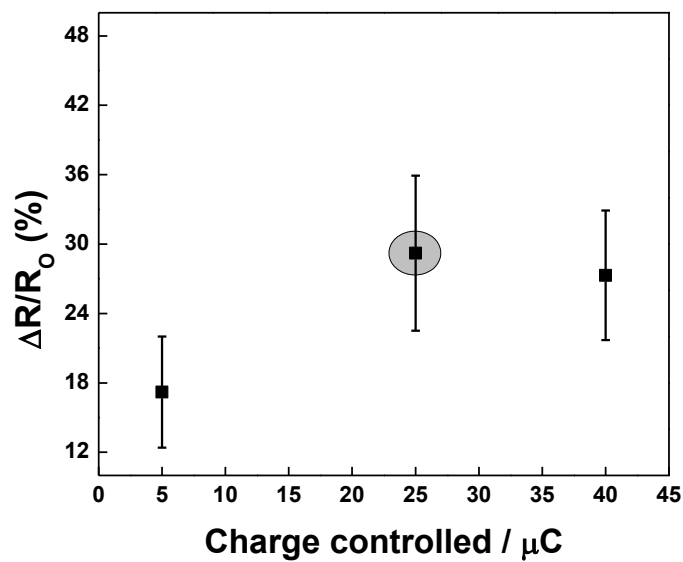
Fig. 3.4 Sensing response of PABA coated SWNT sensors electropolymerized at 5, 25 and 40 μC charge towards 10 mM D-fructose.
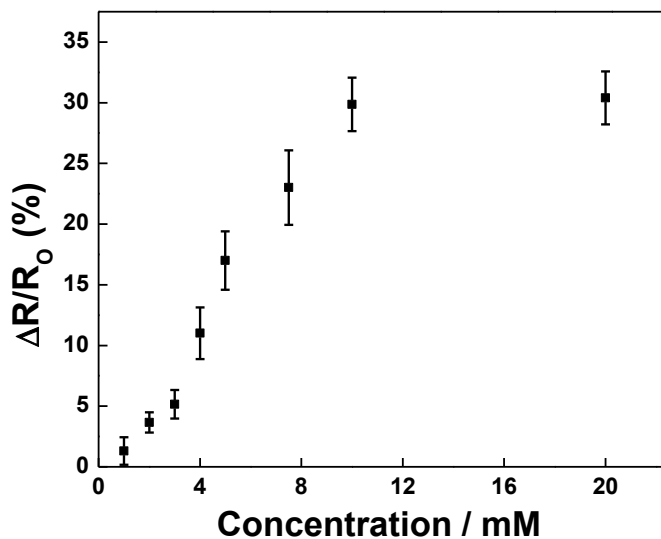
Fig. 3. 5 Calibration curve showing the response of the sensors towards D-fructose in phosphate buffer.
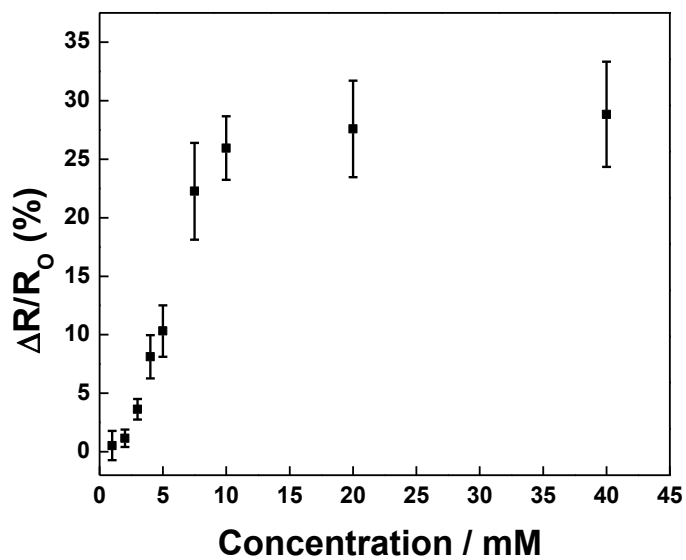
Fig. 3.6 Calibration curve showing the response of the sensors towards D-glucose in phosphate buffer.
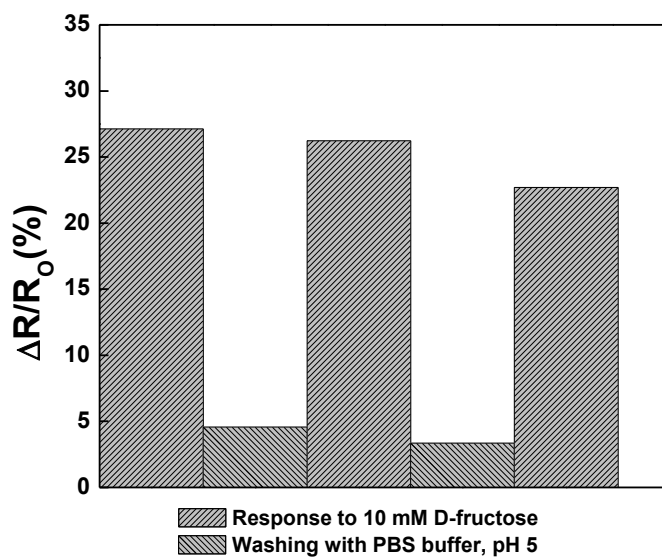
Fig. 3. 7 Regeneration of the sensor in buffer, pH 5.
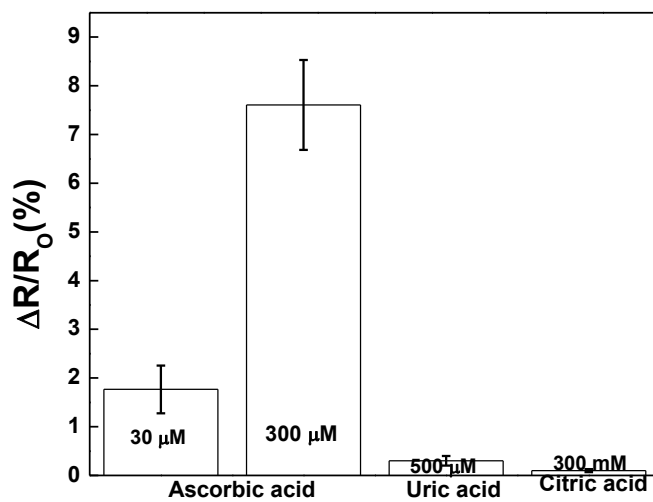
Fig. 3.8 Sensing response of PABA coated SWNT sensors towards AA, UA and CA.

Chapter 4: Molecular imprinted polymer functionalized single-walled carbon nanotube sensors for detection of saccharides

Abstract

In this work, we have demonstrated the synthesis and fabrication of a sensor based on saccharide imprinted polymer on the surface of single walled carbon nanotubes (SWNTs). Electropolymerization of a mixture of 3-aminophenylboronic acid (3-APBA) and 10 M D-fructose at neutral pH conditions in presence of fluoride resulted in the formation of a self-doped, molecularly imprinted conducting polymer (MICP) on aligned SWNTs surface. The templated devices were then used for sensing monosaccharides such as D-fructose and D-glucose using chemiresistive mode of sensor configuration. The imprinted devices yielded better sensitivity towards D-fructose. This is due to the fact that imprinting imparts higher selectivity towards D-fructose by creating recognition sites which are formed by template directed formation of imprinted cavities that are of same chemical nature in terms of shape, size and functionality as D-fructose.

4.1 Introduction

Molecular recognition forms the basis of developing highly selective tailor-made recognition systems that find widespread usage in medical, analytical and biological applications. Molecularly imprinted polymers (MIPs) proves to be an attractive technique in this regard which has been successfully demonstrated towards detecting biological entities such as receptors, enzymes, and antibodies (Sellergren 2001; Shea 1994; Vlatakis

et al., 1993; Wulff 2002). It is based on the complexation between the target molecule and functional monomer(s) of the polymer that exhibits a high recognition affinity only towards the target molecule. The technique involves co-polymerization of functional monomers and crosslinkers around template molecules (Haupt and Mosbach, 2000) resulting in the formation of highly cross-linked polymers with chains in a fixed arrangement. Removal of the template thereafter renders the polymer matrix with well-defined binding sites that are complementary to the analyte both in shape and in positioning of functional groups (Teasdale and Wallace, 1993) thus resulting in selective recognition of the target molecule.

Conducting polymers (CPs) are a class of polymers which exhibit superior electronic and mechanical properties along with processing advantages of polymers (Heeger 2001; MacDiarmid 2001; McQuade *et al.*, 2000).Their high electrical conductivity, tunable charge transport properties and good electrochemical reversibility i.e., the ability to directly convert a binding event into an electrical signal has made   them ideal components   for use as tranducing elements in developing efficient electrochemical sensors.(Bartlett and Astier, 2000; Chaubey *et al.*, 2002; Wallace and Kane-Maguire, 2002).They have also   been suitably modified chemically with appropriate functional groups for specific recognition and detection of different biological or chemical target molecules (Garnier 1989).

However their associated sensing ability has so far been confined to detection of large bioactive molecules such as DNA (Williams *et al.*, 2011) and peptides (Aguilar *et al.*, 2005). Detection of small molecular weight molecules still remains a challenge that

plagues most of the biosensors systems developed so far owing to the poor transduction mechanism that results from conversion of the binding event into a measurable signal in particular at a low concentration of the analyte. In addition, elimination of non-specific interactions also becomes a critical issue to address when detection of small molecules is concerned.

Molecular imprinting of conducting polymers (MICPs) is an approach which combines the enhanced selectivity arising from highly specific binding sites of molecular imprinting together with the properties of CPs thus creating highly sensitive and selective platforms for analyte detection. Over the past few years, synthesis of MICPs and their applications for detecting a wide range of molecules have been reported. Some of them include detection of glutamic acid using overoxidized polypyrrole-based films (Deore *et al.*, 1999, 2000) electrochemical synthesis of conjugated MICP, poly(3,4-ethylenedioxythiophene-co-thiophene-acetic acid) for the detection of small pesticide target molecule, atrazine (Ramita *et al.*, 2009), detection of bovine leukemia virus glycoproteins using polypyrrole based MICP (Ramanavicius and Ramanaviciene, 2004) and saccharide-imprinted poly(aniline boronic acid) for the detection of D-fructose (Deore and Freund, 2003).

In this work, we report the electropolymerization of D-Fructose imprinted Polyaniline boronic acid (PABA) on the surface of SWNTs. Carbon nanotubes (CNTs) have proven to be excellent transducer active elements in sensing applications due to their small size and superior electronic and electrochemical properties. They possess large surface area which leads to enhanced sensitivity towards detecting an analyte. Electropolymerization

of D-fructose and PABA in presence of fluoride results in the formation of a self-doped molecularly imprinted polyaniline which is selective towards detection of D-fructose. This approach takes into account the fact that polyaniline boronic acid–saccharide imprint can be formed under neutral pH conditions in presence of fluoride ion as catalyst and can be used for the detection of saccharides based on the selectivity complexation reactions involving boronic acids. The relative response of D-fructose and D-glucose to the imprinted film brings about a change in the net electrical charge of the SWNT based device based on predetermined selective molecular recognition and efficient electrical conductivity of the SWNTs thereby resulting in a change of the overall conductance which in turn is detected by the chemiresitive method of sensor configuration.

4.2 Experimental

4.2.1 Materials

Carboxylated single-walled nanotubes (SWNT-COOH, 80–90% purity and 1.5 to 3 atomic %–COOH content) were procured commercially from Carbon Solution Inc (Riverside, CA, USA). 3-Aminophenylboronic acid hydrochloride salt 98% (3-APBA) was purchased from Sigma Aldrich (St Louis, Mo, USA). D-Fructose, D-Glucose were purchased from Alfa Aesar. All buffer solutions were prepared in deionized water obtained by purifying distilled water through a Milli-Q plus (Millipore Inc) ultrapure water system.

4.2.2 Instrumentation

Electrical characterization was performed using a potentiostat (Model # 1202A, CHInstruments, Inc., TX, USA) in terms of the resistance of the sensors by measuring the current versus voltage response of the sensors. The initial or baseline resistance of the sensor was recorded by incubating the SWNT coated D-fructose imprinted PABA device with PBS buffer overnight and sweeping the voltage from -1 V to +1 V. For the purpose of better precision of measurements, the slope of the I-V was measured in a region near to the zero voltage preferably +/- 100 mV. Upon exposure to different concentrations of D-glucose and D-fructose solutions made in PBS buffer, change in resistance was measured after incubating the sensor for 30 mins followed by washing with PBS buffer twice.

4.2.3 Sensor design and fabrication

Microelectrodes Fabrication: An array of 16 source-drain gold electrodes pairs with 3 μm channel length was defined on SiO_2/Si substrate using standard photolithography technique as reported described in chapter 2 and 3. In brief, each source-drain electrode patterns are predefined on a SiO_2 (300 nm)/Si substrate. Each pair consists of two 200-μm-wide fingers pointed head to head at a distance of 3 μm.

4.2.4 DEP Deposition of Single walled carbon nanotubes (SWNTs)

The SWNTs as described in Chapter 2 were suspended in DMF solution by brief sonication process. A 0.1 μL drop of SWNTs suspension was placed between the

electrodes using micropipette followed by applying an ac electric field of 3V p-p ($0.36V_{RMS}$) at 4 MHz frequency across the electrodes for few seconds as reported earlier (Myung *et al.*, 2010). The duration of the application of the dielectrophoretic force was optimized over time to obtain carbon nanotube aligned devices that had an initial resistance in the range of 0.2 MΩ to 1 MΩ for consistency. The aligned SWNTs were then annealed at 300 ^{0} C for 1 hour in an atmosphere of 5% hydrogen and 95% nitrogen gas. This improved the contact resistance between the electrodes and the SWNTs and helped to remove DMF residues accumulated during the process of alignment.

4.2.5 Electropolymerization of molecularly imprinted PABA

Electropolymerization of D-fructose imprinted PABA was performed on the aligned SWNTs electrodes. A three electrode configuration where the aligned SWNTs network with the gold electrodes, a Pt wire, and chlorinated silver wire (Ag/AgCl wire) were employed as working, counter, and reference electrodes, respectively was constituted. The monomer solution containing 40 mM 3-APBA and 40 mM NaF along with 10 M D-fructose was prepared in the undiluted PBS stock solution (10X PBS) and under conditions where the pH was reduced to 5.0 by addition of 0.5 M HCl. A 0.1 μL drop of the electrolyte was placed on top of the SWNT networks followed by potentiostatic electropolymerization at 0.7 V (vs. Ag/AgCl). After electrodeposition, the sensors were rinsed with deionized water followed with PBS at pH 7.4 and then kept in stirred PBS solution overnight to remove D-fructose and fluoride leaving behind molecularly imprinted PABA on surface of the aligned SWNTs.

4.3 Results and discussions

The complexation of saccharides with aromatic boronic acids produces a stable intermediate where the binding constant is known to be dependent on the pH, electrolyte concentration and pKa of the aromatic boronic acid (Wiskur *et al.*, 2004). For the complexation between PABA and saccharides, pH values above 8 are desired (Westmark *et al.*, 1994). However, because of the conflicting pH requirements for the electrochemical synthesis of polyaniline (which is typically carried out near a pH value of 0), efforts were being to form a saccharide complex with PABA at neutral pH conditions. Studies showed that the equilibrium reaction of boronic acid with fluoride is known to produce a tetrahedral anionic complex as described in literature (James *et al.* 1998; Westmark *et al.*, 1994). This fluoride catalyzed reaction results in the self-doped structure of PABA under acidic conditions (Nicolas *et al.*, 2000). As has been discussed in chapter 3, electropolymerization of PABA in the presence of 40 mM fluoride and 300 mM NaF in 10X PBS adjusted to pH 5.0 resulted in sustained polymerization and formation of a self doped polymer. Fig. 4.1(a) shows the cyclic voltammogram of 40 mM 3-aminophenylboronic acid in 10X PBS along with 10 M D-fructose in presence of 40 mM NaF at pH 7.4 at a scan rate of 100 mV/sec. Complexation of saccharides (as well as alkyl and aromatic diols) with aromatic boronic acids produces a stable boronate anion. In this case, D-fructose reacts with boronic acid moieties to form a fluoride D-fructose boronate complex. Significant and sustained polymerization of the saccharide complex with 3-aminophenylboronic acid in the presence of one molar equivalent of fluoride at

neutral pH was observed as in fig. 4.1(b). Both fluoride and D-fructose were involved in the process that resulted in the formation of a self doped MICP as confirmed from literature (Deore and Freund, 2003).

Electrical characterization in terms of I-V characteristics was measured after electropolymerization of molecularly imprinted, self-doped PABA on the SWNT surface. As shown in fig. 4.2, the devices exhibited higher resistance after electropolymerization as compared to bare aligned SWNT devices. Incubation of the imprinted SWNT based devices in buffer overnight resulted in the removal of fluoride and D-fructose moieties thus forming D-fructose imprinted PABA on the surface of SWNTS. The imprinted polymer consists of binding sites in a definite spatial arrangement that have a shape to match that of the removed template (in this case D-fructose). The imprinted polymer coated devices were then used for detection of D-fructose and D-glucose. The sensing results obtained are shown in the calibration plot (fig. 4.3). Changes in electronic properties accompanying molecular interactions between the sugar and the imprinted polymer matrix are monitored using the chemiresistive mode of sensor configuration. It can be observed that the imprinted devices show an enhanced response towards D-fructose as compared with D-glucose. This clearly arises from the fact that imprinting results in selective binding of D-fructose which possess the same functional groups of fixed structure and arrangement at the complementary binding sites thus resulting in subsequent template molecule recognition. Thus imprinting imparts selectivity by enabling the identification and classification of saccharides at the binding sites based on

the complexation reaction between saccharides and boronic acid moieties prior to removal of template molecules formed in the MICP backbone.

4.4 Conclusion

Single walled carbon nanotube based MICP devices were demonstrated towards detecting monosaccharides. This was achieved via electropolymerization that resulted in a self-doped polymer at neutral pH conditions involving the formation of a stable anionic boronic ester complex between PABA and D-fructose. These sensors exhibited selectivity in detecting D-fructose over D-glucose since the binding sites on the polymer matrix left after template removal are complementary to D-fructose both in structure i.e. shape, size and positioning of functional groups. Using carbon nanotubes along with MICPs resulted in the fabrication of efficient electrochemical sensor by enhancing analyte recognition and signal generation. These sensors can be regenerated and used multiple times unlike conventional affinity based biosensors which suffer from physical and chemical stability. Thus, the versatile molecular recognition capabilities of MICPs coupled with the efficient transducing properties of SWNTs and CPs provide a strong platform for the detection of wide range of analytes such as biomolecules and drugs used in analytical technologies.

4.5 References

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Figures
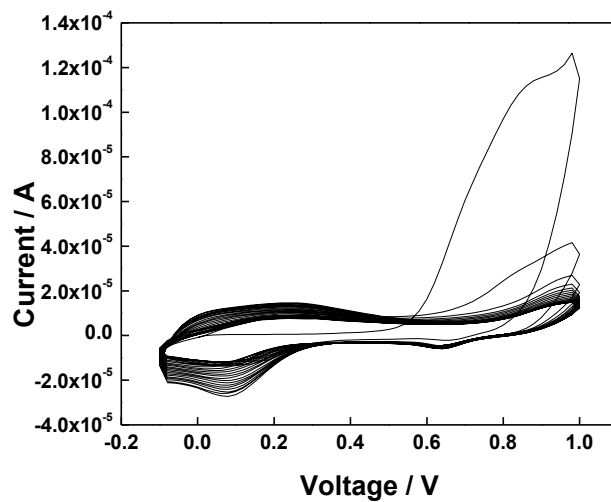
Fig. 4.1(a) Cyclic voltammogram of 40 mM 3-aminophenylboronic acid and 10 M D-fructose in 10X PBS plus 40 mM NaF; pH 7.4. Scan rate: 100 mV /s.
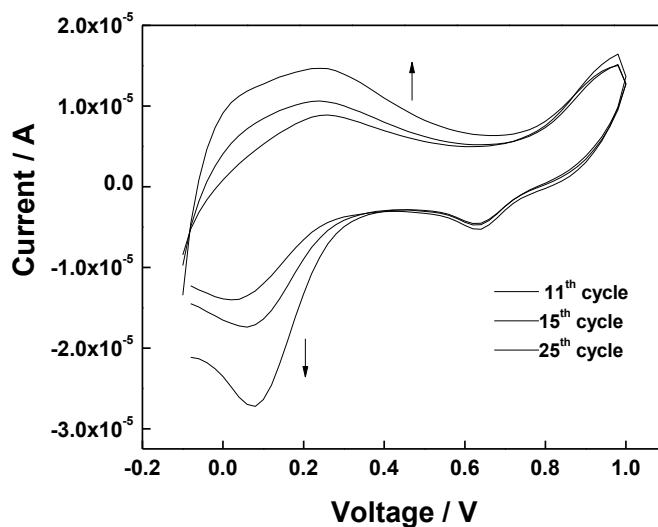
Fig. 4.1(b) CV under conditions of 1(a) showing continuous and sustained electropolymerization of molecularly imprinted PABA; Scan rate: 100 mV s^{-1}.
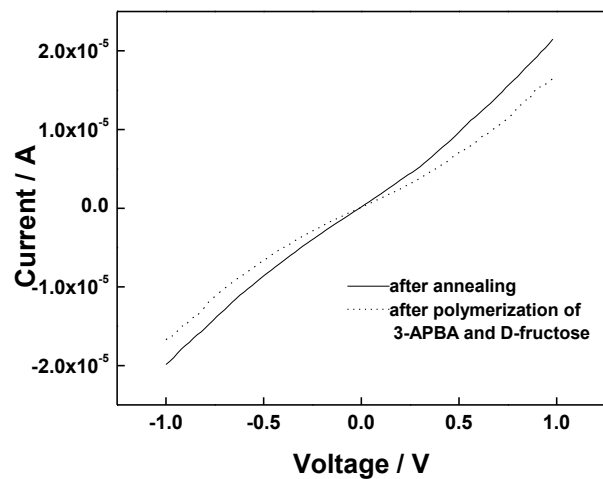
Fig. 4.2 I_{DS} vs. V_{DS} of AC dielectrophoretically aligned SWNTs network before and after electropolymerization of molecularly imprinted PABA.
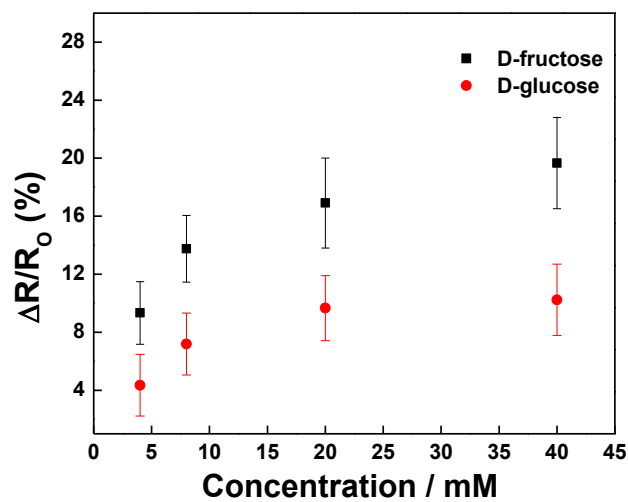
Fig. 4.3 Calibration curve showing the response of the D-fructose imprinted PABA sensors towards D-fructose and D-glucose in phosphate buffer.

Chapter 5: Nonenzymatic glucose sensor based on Platinum nanoflowers on multi-walled carbon nanotube-graphene hybrid

Abstract

In this work, we demonstrate the electrodeposition of platinum nanoflowers on multi walled carbon nanotube (MWNT)/ graphene hybrid which is synthesized by one step chemical vapor deposition process via in situ vapor–liquid–solid and surface-catalyzed mechanisms. Structural characterization revealed that the roots of MWNTs were directly connected to the graphene floor. Electrodeposition of platinum with optimized parameters was performed at room temperature to obtain high density flower like nanostructures of platinum uniformly distributed over the hybrid membrane. This arrangement of Pt-nanoflowers/ MWNT/ graphene was used for amperometric detection of glucose in the physiological range at neutral pH. Direct oxidation of glucose takes place due to the electrocatalytic property of the Pt-nanoflowers resulting in the non-enzymatic detection of glucose. The developed sensor responded linearly to glucose over the range of 1-7 mM (R^2 = 0.978) with a sensitivity of 11.06 μA mM^{-1} cm^{-2}.

5.1 Introduction

Monitoring blood glucose levels is of prime importance in medical diagnostics and clinical applications. Over the past few decades, enzymatic glucose sensors have been developed and widely used for continuous blood glucose detection. However, the activity

of enzymes is easily affected by temperature, pH value, humidity, and presence of toxic chemicals (Wilson and Turner, 1992). Further, the gradual degradation of enzyme over time, their high oxygen dependency and inability to offer anti-interference from other electroactive components present in blood glucose are certain issues that render them unsuitable for real time and reliable usage (Huot *et al.*, 2009; Wilkins *et al.*, 1995) for blood glucose monitoring.

Thus, the interest for enzyme-free glucose sensor that would directly oxidize glucose in solution has been keen. Among the nonenzymatic glucose sensors reported so far, platinum (Pt) has been the most popular material due to its high catalytic activity toward glucose oxidation (Aoun *et al.*, 2003; Chung *et al.*, 2003; Jin and Chen, 2007; Sheu *et al.*, 2007; Xia *et al.*, 2005).

Direct electrochemical oxidation of glucose on bulk platinum has been reported (Vassilyev *et al.*, 1985). Ever since, different kinds of platinum based electrode materials like macroporous platinum (Chung *et al.*, 2003) and (Xia *et al.*, 2005) and platinum-nanotubule arrays (Yuan *et al.*, 2005) electrodes with high electrode surface roughness have been developed to enhance the amperometric response of glucose oxidation and effectively lower the interference arising from other co-existing electroactive species. However, surface poisoning by adsorbed intermediates (Ernst *et al.*, 1979) and chloride ion, low sensitivity and poor selectivity are some drawbacks that still plague these electrodes. It has been reported that many metal nanoparticles and carbon nanotubes electrode show reproducible sensitivity in the presence of high concentration of chloride ion (Xu *et al.*, 2004). (Xia *et al.*, 2007) reported a nonenzymatic glucose sensor by using

highly dispersed Pt nanoparticles supported on carbon nanotubes as sensing interface that provided better screening towards interfering analytes when detection of glucose is performed at an appropriate potential. Nano-structured Pt possesses a very large surface activation area, thereby favoring kinetically controlled reactions (i.e., the electrocatalytic oxidation of glucose) more than diffusion controlled reactions (i.e., the common electroactive species) thus offering higher sensitivity for glucose detection along with better selectivity towards interfering analytes.

There are fewer reports which exploit the unique combined properties of both carbon nanomaterials and Pt nanoparticles for enzyme free glucose detection via direct glucose electrocatalysis. Some examples include amperometric glucose detection using Pt nanoparticles in different carbon matrices such as Pt-activated carbon, Pt-Carbon nanofibers, Pt-MWNTs (Dempsey *et al.*, 2010), Pt-nanoflowers on SWNT membrane (Lei *et al.*, 2010) , Pt nanoparticles supported onto mesoporous carbon (Su *et al.*, 2010) and Pt nanoparticles supported on multi-walled carbon nanotubes (Xia *et al.*, 2007). Nonenzymatic glucose detection using multi-walled carbon nanotube electrodes has been reported (Xu *et al.*, 2004). In this report, Xu and co-workers suggested that electrocatalytic oxidation of glucose in alkaline medium takes place directly at well-aligned MWNT with possible minor contributions from the Co catalysts present on the Ta substrate.

Herein we report the synthesis of Pt- nanoflower like structures as the catalyst supported on MWNT/graphene hybrid and demonstrate its application as an enzyme free glucose sensor over the physiological range at neutral pH. Electrodeposition of Pt nanoparticles

provides for a simple, cost effective and controlled approach of synthesizing nanoparticles of desired shape, size, distribution, and crystallinity by varying deposition parameters and substrate properties. It results in high purity nanomaterials at room temperature thus overcoming the short comings of other techniques that require elevated temperatures, extensive template removal procedures and relatively high loadings of Pt precursor for nanoparticles synthesis. Large area MWNT/graphene hybrid, on the other hand, synthesized by one step chemical vapour deposition technique (CVD) with its high surface to volume ratio and superior chemical, electrical, and mechanical properties constitutes an excellent catalyst supporting membrane. Thus the electrodeposition of uniformly spread, large surface area Pt-nanoflowers on MWNT/graphene hybrid provides a synergistic platform for the detection of glucose which results in better sensitivity and the ability to efficiently discriminate against other electroactive interferents.

5.2 Experimental

5.2.1 Chemicals and Reagents

Uric acid, Ascorbic acid and D-Glucose were procured commercially from Fisher Scientific and were used as received. Hydrogen hexachloroplatinate (IV) hexahydrate ($H_2PtCl_6 \cdot 6H_2O$) was purchased from ACROS. All buffer solutions used as supporting electrolytes were prepared in deionized water obtained by purifying distilled water through a Milli-Q plus (Millipore Inc) ultrapure water system.

5.2.2 Instrumentation

The structure and surface composition of the MWNT/graphene hybrid and later Pt-nanoflowers/ MWNT/graphene were characterized by a scanning electron microscope SEM (Leo, 1550) with a field emission source. Cyclic voltammetric and amperometic measurements were performed on a CHI electrochemical workstation (CHI Instruments, Inc., Austin, TX) at room temperature. A three electrode cell (5 ml) was used which consisted of the modified GC electrode (2.5 mm in diameter) as the working electrode, an Ag/AgCl electrode as the reference electrode and a large area Pt mesh as the counter electrode.

5.2.3 Synthesis of MWNT/ graphene hybrid

CVD synthesis of MWNT/graphene hybrid nanostructure was performed by a combination of in situ vapor–liquid–solid and surface-catalyzed mechanisms from a nearly similar procedure adapted from literature (Ozkan *et al.*, 2010) . In brief, 1 nm Fe nanoparticles were deposited on the surface of copper film by electron beam evaporation (Temescal, BJD-1800). C_2H_2 (50 sccm) was used as a carbon source in an atmosphere of flowing Ar (100 sccm) and H_2 (50 sccm) ; the flow rates being precisely controlled by using mass-flow controllers (MFC) to synthesize a large area, approx 1 inch sq. in dimension MWNT/graphene hybrid structure at 750^0 C for 10 minutes time. Growths of graphene and carbon nanotube take place simultaneously on copper foil and iron catalyst particles respectively. The mechanism of growth involved the synthesis of graphene film on copper substrate (Colombo *et al.*, 2009) by vapor–liquid–solid mechanism technique

and simultaneous in-situ growth of MWNTs through surface catalyzed expansion of Fe particles during the diffusion of carbon atoms. The Cu foil with the MWNT/graphene hybrid on top of it was then transferred into aqueous $FeCl_3$ solution (1M) and kept overnight wherein the copper was etched away leaving behind the hybrid structure on the surface of the etchant. The hybrid was then transferred onto aqueous HCl (5%) and DI water solution for cleaning residues, if any. No noticeable bulk defects were observed during the etching and cleaning processes, which confirmed the flexibility of the synthesized hybrid structure that consisted of high density MWNTs on top of monolithic graphene film.

For the purpose of electrochemical sensing, the MWNT/graphene hybrid was then transferred onto a freshly polished and cleaned glassy carbon (GC) electrode, diameter 2.5 mm by simple contact lifting from the surface of DI water. To ensure better adhesion of the hybrid onto GC, the electrode was kept in the oven maintained at 50^0C for 1 hour. Prior to the transfer of the hybrid graphene onto the GC electrode, the electrode was polished successively with 1 µm, 0.3 µm and 0.05 µm α-alumina powder and rinsed thoroughly with distilled water between each polishing step. The GC was ultrasonicated thereafter in acetone and distilled water for 5 mins each.

5.2.4 Electrodeposition of Pt-nanoflowers

The electrodeposition of Pt-nanoflowers was carried out on the surface of the MWNT/ graphene /GC electrode from 5mM chloroplatinic acid hexahydrate (H_2PtCl_6) solution in presence of 0.1M HCl at ambient temperature. A three-electrode system was set up

consisting of MWNT/ graphene/ GC as the working electrode, a platinum mesh and an Ag/AgCl (saturated with KCl) as the counter and reference electrode respectively. Pl-nanoflowers were synthesized on the surface of MWNT/graphene hybrid via cyclic voltammetry performed in the metallic precursor based electrolyte for 25 cycles at a scan rate of 50 mV/s between -0.7 and 0.3 V (vs. Ag/AgCl 3M KCl) at room temperature.

5.3 Results and discussions

5.3.1 Characterization

Structural characterization in terms of SEM was performed on the synthesized MWNT/graphene hybrid as shown in fig. 5.1.The as grown hybrid revealed the roots of MWNTs to be directly connected to the graphene floor. Highly dense MWNTs with uniform and regular morphologies were spread over the large area graphene. This makes for an excellent conductive substrate for electrodeposition with high flexibility and stability. SEM micrographs were also recorded to study the morphology and distribution of the electrodeposited Pt nanoparticles on the surface of graphene/ MWNT hybrid. As can be seen in fig. 5.2, high density flower like Pt nanostructures were found uniformly deposited throughout the cross section of the graphene/ MWNT hybrid. Apart from having a uniform distribution, these nanoflowers like structures have a very high surface area.

5.3.2 Electro oxidation of glucose

In order to determine the accurate potential range for the electrooxidation of glucose, CVs of the electrodeposited Pt-nanoflowers on MWNT /graphene surface (Pt-

nanoflower/ MWNT/ graphene) were performed before and after addition of glucose into phosphate buffer solution (pH 7.4). Injection of glucose enhances the glucose oxidation current. As seen clearly in fig. 5.3, pronounced oxidation current peaks were observed at a low positive potential window of 0.4 to 0.7 V. Hydrodynamic voltammetry performed at three different potentials revealed that the sensor exhibits improved signal-to-noise ratio and enhanced sensitivity towards glucose at an applied potential of 0.4 V as compared to 0.3 V and 0.5 V (data not shown). Lowering the working potential would improve the selectivity of the sensor further; however, it would also affect the sensitivity towards detecting glucose. Hence, in order to achieve a glucose sensor which exhibits better sensitivity and considerable selectivity in terms of its response towards interfering analytes at the same time, a trade off in applied potential is necessary. Thus, 0.4 V vs. Ag/ AgCl was chosen to the working potential for glucose detection.

5.3.3 Amperometric detection of glucose

Amperometric measurements of the Pt-nanoflowers/ MWNT/ graphene electrode to the sequential addition of glucose were carried out in a standard three electrode electrochemical cell configuration at +0.4 V in PB solution (pH 7.4, 5ml) under constant gently stirring conditions. The initial current response obtained in the buffer was considered as the saturated background current of the sensor. With every subsequent addition of glucose into the solution, rapid and steady state current signals were obtained as shown in fig. 5.4. This was due to the direct electro-oxidation of glucose which involved the steps of adsorption, electron transfer and subsequent chemical

rearrangements limited within the electro deposited Pt surface. In brief, the mechanism (Chung *et al.*, 2006) of glucose detection involves the glucose molecules to undergo electrosorption on the Pt-nanoflower electrode surface to form a layer of glucose intermediates, which can be easily oxidized. These adsorbed intermediates are further oxidized at more positive potentials to form products such as gluconolactone or gluconic acid in neutral media. Fig. 5.5 shows the calibration plot for the successive increments of glucose concentrations from 1 mM upto 10 mM range obtained from 3 electrodes. The calibration curve yields a linear chronoamperometric response range between 1 mM to 7 mM of glucose concentrations with a sensitivity of 11.06 μA mM^{-1} cm^{-2} (R^2 = 0.978) calculated as the slope of the linear region of the calibration curve divided by geometric surface area of the GC electrode. The limit of detection of this Pt-nanoflowers/ MWNT/ graphene hybrid electrode was found out to be 0.387 mM based on the three times of signal-to noise ratio. To confirm that the direct oxidation of glucose is caused only due to the electrocatalytic property of the Pt-nanoflowers, a control experiment was performed wherein the as transferred MWNT/graphene hybrid was used as the working electrode and amperometric responses were recorded for subsequent additions of glucose (fig. 5.6). No change in current response was observed thus confirming the fact that response comes from the direct glucose oxidation at the active sites of the catalyst.

5.3.4 Interference studies

The interferences arising from electroactive compounds like Ascorbic acid (AA) and Uric acid (UA) that co-exist along with glucose in physiological samples of blood was investigated. The range of concentration of these reducing agents in normal blood ranges

between 0.02 and 0.08 mM (AA) and 0.18 to 0.42 mM (UA). Selectivity studies were performed using amperometric I (t) curves at +0.4 V that recorded the response signals of physiological levels of AA and UA during the detection of glucose. Fig. 5.7 shows the amperometric current responses to 5 mM glucose, 0.08 mM AA and 0.3 mM UA in PB buffer, pH 7.4 at +0.4 V operational potential. The current responses for the interfering analytes obtained by normalizing to the response for glucose i.e. 61.55 μA /cm^2 were found to be 16.5 % and 15.8 % for AA and UA respectively. In case of higher concentrations of interferants, surface modification of the Pt-nanoflowers/MWNT/graphene electrode can be done possibly by coating it with Nafion that has a considerable influence on the selectivity towards glucose by providing good anti-interference towards co-existing interferants (Tang *et al.*, 2009; Xia *et al.*, 2007).

Most of the electrochemical glucose sensors based on metals (Vassilyev *et al.*, 1985) tend to lose their electroactivity due to the poisoning of chloride ions. The effect of chloride ions on the electrocatalytic ability of Pt-nanoflowers towards glucose oxidation was examined by recording amperometric response in supporting electrolyte with 0.15 mM NaCl (data not shown). It remained unchanged, thus, implying that the electrode retains its electroactivity in presence of chloride ion.

Results obtained from this work were compared with most recently reported Pt-nanoflowers on SWNT membrane for glucose detection (Lei *et al.*, 2010). The demonstrated sensor in our case exhibits a higher sensitivity because of the synergistic benefits of high surface-to-volume ratio of the catalyst supporting structure along with

high density, large surface area Pt-nanoflowers thus providing more active sites for the direct electrocatalysis of glucose. The quick response time (i.e. the time taken to reach 90% of the signal) of this sensor notably 12 seconds together with the ability to detect glucose with negligible interference from co-existant electroactive components makes it an ideal device for the detection of blood glucose level in medical diagnostics and clinical applications.

5.4 Conclusion

A highly sensitive, low-potential and fast amperometric sensor based on Pt-nanoflowers electrodeposited on MWNT/graphene hybrid for the detection of blood glucose over the physiological range was developed and demonstrated. This enzyme free sensor exhibited a good linear dependence on the physiological glucose concentration range from 1 to 7 mM with a sensitivity of 11.06 μA mM^{-1} cm^{-2}. These results can be attributed to the enhanced surface-to-volume ratio of the catalyst supporting membrane which in turn facilitates uniform and good area coverage of the electrodeposited Pt-nanoflowers that act as active sites for direct glucose oxidation with high utilization efficiency. The developed sensor offers good anti-interference to electroactive interferences such as ascorbates and urates that are commonplace in real blood samples. This novel platform of MWNT/ graphene hybrid with its high electrical conductivity, mechanical strength and large specific surface area can be used as a superior catalyst supporting matrix in a wide array of electrochemical applications such as biosensors and renewable, sustainable direct methanol fuel cells.

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Figures

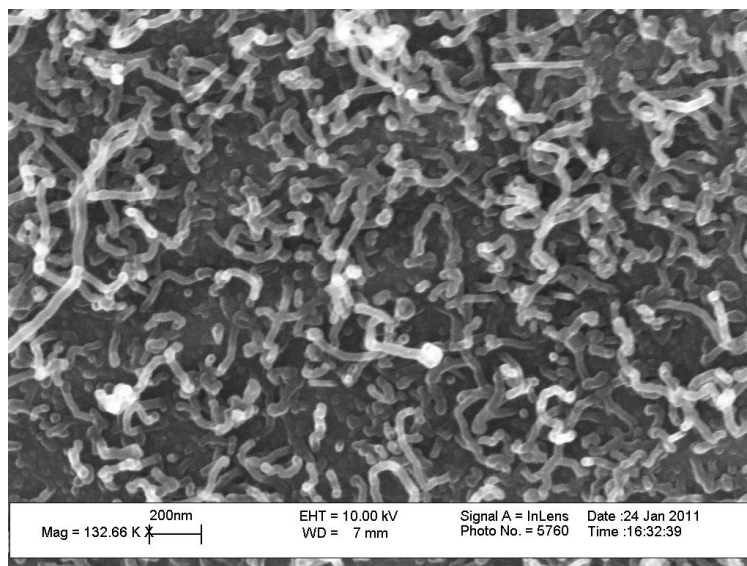Fig. 5.1 FESEM images of MWNT/graphene membrane.
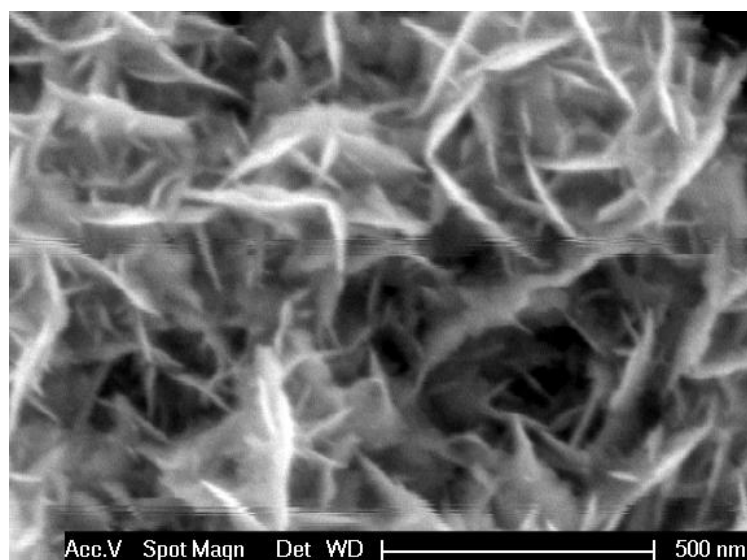
Fig. 5.2 SEM image of Pt nanoflowers electrodeposited from 0.1 M HCl containing 5 mM H_2PtCl_6 for 25 cycles at a scan rate of 50 mV/s between -0.7 and 0.3 V (vs. Ag/AgCl 3M KCl) at room temperature.
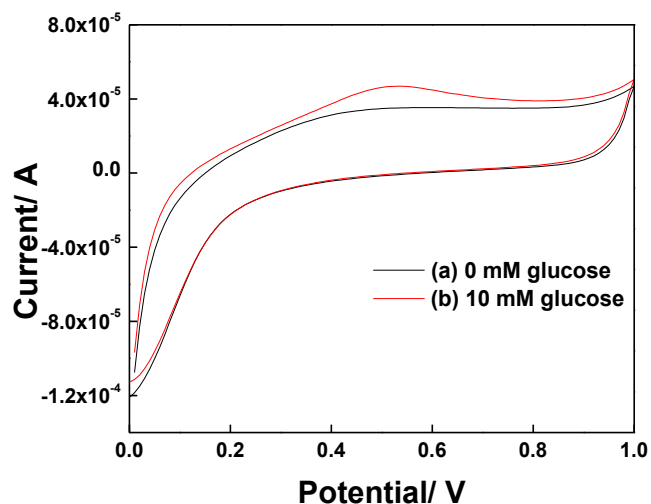
Fig. 5.3 Response of Pt-nanoflower/ MWNT/ graphene to glucose electro-oxidation from 0.4 to 0.7 V vs. Ag/AgCl for (a) 0mM glucose, (b) 10 mM glucose at scan rate of 50 mV/s in 0.1M PB; pH 7.4.
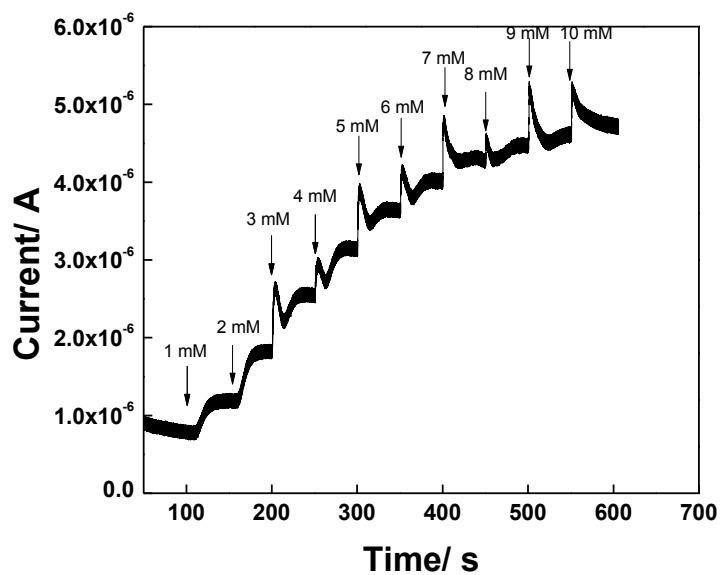
Fig. 5.4 Real-time amperometric response of the Pt nanoflower/ MWNT/ graphene working electrode towards successive addition of glucose at 0.4 V vs. Ag/AgCl in 0.1M PB; pH 7.4.

Fig. 5.5 Calibration curve showing the response of electrodes (n=3) towards glucose.

Fig. 5.6 Real-time amperometric response of the MWNT/ graphene working electrode towards successive addition of glucose at 0.4 V vs. Ag/AgCl in 0.1M PB; pH 7.4.

Fig. 5.7 Real-time amperometric response of the Pt nanoflowers/MWNT/ graphene working electrode towards 5 mM glucose, 0.08 mM AA and 0.3 mM UA at 0.4 V vs. Ag/AgCl in 0.1M PB; pH 7.4.
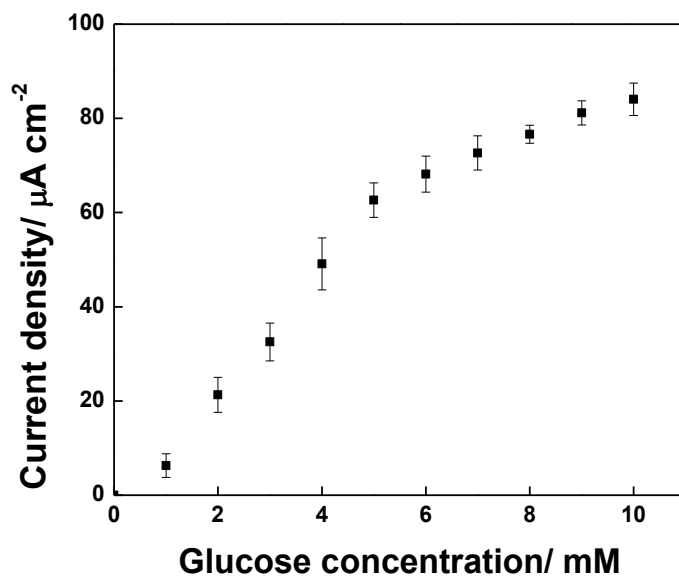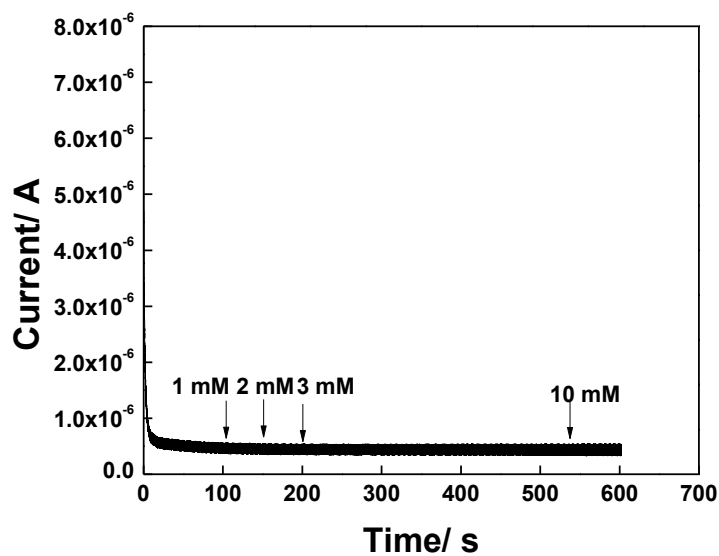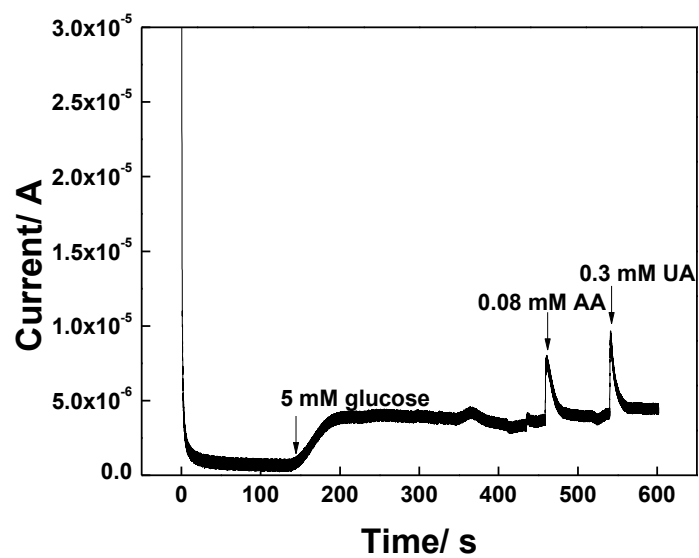
Chapter 6: Summary and conclusion

One-dimensional nanostructures have shown great promise over thin film structures for sensing applications. Their small sizes allow modification in the electrical properties across its entire cross-section and surface chemistry to play a role as compared to in bulk state. Carbon nanotubes (CNTs) display excellent chemical stability, good mechanical strength and a range of electrical conductivity. When compared with other materials like metals, metal oxide semiconductors; single walled carbon nanotubes (SWNTs) offer advantages in terms of being less sensitive to variations in temperature (compared to silicon piezoresistors), higher sensitivity, smaller sizes that facilitates fabrication of miniaturized sensors and massive nanosensor arrays for detection of gases, chemicals or biological molecules. To improve the sensitivity of bare SWNTs and to widen their applications, surface modification with metals, metal oxides and conducting polymers (CPs) etc has been done over the years. CPs possess excellent electrical, optical and mechanical properties along with high chemical sensitivity, room temperature operation and tunable charge transport properties that has made them ideal for use as tranducing materials in chemical sensors. In this dissertation, several applications of carbon nanotube based hybrid devices have been demonstrated. These included conducting polymer-carbon nanotube and graphene-carbon nanotube-metal nanoparticles based sensors for bioanalytical applications. These hybrid devices, as they were also named as, combined the synergistic benefits of CNTs as an excellent transducing element along

with their respective material properties thus enabling the development of highly sensitive and superior sensing platforms.

Detection and quantification of volatile organic compounds (VOCs) is of prime importance in a lot of industrial applications where Permissible Exposure Limit (PEL) regulations are required to be met. Conventional methods to detect gases and VOCs such as Gas chromatography, Mass Spectrometry, Fourier Transform Infrared Spectroscopy (FTIR) etc. are often large, expensive and not suitable for in situ use. Hence nanomaterial based gas sensors are a better alternative that provide high sensitivity, fast response along with being low cost, facilitate high volume production and deliver high reliability performance on site and in situ. Applications of conducting polymer based nano structures in gas sensing applications have been widely demonstrated. PEDOT: PSS coated SWNT gas sensors have been fabricated and demonstrated towards detecting volatile organic compounds at room temperature as discussed in chapter 2. These hybrid sensors showed response over a wide dynamic range, enhanced sensitivity over bare SWNT sensors and a lower limit of detection for saturated vapors of methanol, ethanol and MEK at room temperature. Incorporating dopants onto CPs results in change in their conductivity levels depending upon the dopant type and its concentration. Thus by varying the dopant, studies can be explored to evaluate the response of the CP towards a wide range of analytes.

Chapter 3 and 4 describe Polyaniline boronic acid-single walled carbon nanotube based nonenzymatic sensors for detection of saccharides using two different approaches. While

chapter 3 deals with electropolymerization of PABA on SWNTs enabling the detection of monosaccharides on the basis of the reversible nature of binding between PABA and 1, 2 or 1, 3-diols, chapter 4 explores the concept of saccharide imprinted PABA on SWNTs that imparts selectivity towards one particular type of saccharide over the other. Molecularly imprinted polymer exhibits excellent operational stability and their recognition properties are unaffected by acid, base or heat thus making them highly suitable for sensing applications. Both the strategies are based functionalization using electropolymerization, which can be used to create a synthetic molecular receptor sensor array system with each individual entity designed for specific analyte detection. This could lead to the development of cost effective and highly efficient lab-on-a-chip configurations. Even though these initial demonstrations indicate potential of molecular imprinting for detection purposes, their scope is not yet fully explored. MIP represents a simple, ingenious procedure to prepare specific molecular recognition sites in polymer films. However, it still remains a critical technique where issues such as long response-times of the sensors, poor electrical communication between remote binding sites and the electrodes need to be addressed. Overcoming these limitations would certainly mean reliable and detection of various compounds of medical, environmental and industrial applications with accuracy and high specificity.

In chapter 5, a non-enzymatic glucose sensor based on direct electrocatalysis of glucose on platinum nanoflowers was discussed. The developed sensor apart from exhibiting a wide linear range of detection that finds utility in measuring blood glucose levels at neutral pH offers good anti-interference to electroactive interferences such as ascorbates

and urates that are commonplace in real blood samples. This novel platform of MWNT/ graphene hybrid with its high electrical conductivity, mechanical strength and large specific surface area can be envisioned as a novel electrode material. It can be used as a superior catalyst supporting matrix over conventional electrode materials like Au, GC in a wide array of electrochemical applications such as biosensors and renewable, sustainable direct methanol fuel cells.

Nanomaterials such as carbon nanotubes have proven to be ideal building blocks in sensing applications. Conducting polymers due to their easy, scalable and cost effective synthesis routes have a lot of potential in sensing applications. Detection of a wide range of analytes such as gases, proteins, viruses, biomarkers, cancer markers are still some fields where their scope is to be fully explored. Variations in fabrication conditions of metal nanoparticles and conducting polymers can provide an easy access to dictate their unique properties to a large extent based on the type of application. As sensor technology is rapidly advancing beyond clinical and industrial applications towards fields such as food safety, space explorations and environmental pollution control etc, there has been a paradigm shift in the requirements of the sensor industry towards new materials that can deliver more sensitive recognition layers, increasingly complex architectures, low cost, reduced size and low power applications. Most sensors based on a single sensing element often suffer from lack of sensitivity, narrow dynamic range, and poor stability. Hybrid devices which couple the added advantages of two or more materials in terms of their chemical, mechanical and electrical properties thus seem to be an attractive alternative to address issues governing sensing. These devices when integrated with modern electronic

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fabrication technologies could lead to the development of energy efficient nanosensor arrays which can be used for multi component analysis with high sensitivity and reliability.

Appendix # 1

Single-walled carbon nanotubes chemiresistor aptasensor for small molecules: Picomolar level detection of adenosine triphopshate

Here we report single walled-carbon nanotubes (SWNTs)-based chemiresistor aptasensors for highly sensitive and selective detection of weakly or uncharged molecules using the displacement format. As a proof-of-concept we demonstrate the detection of ATP, a small weakly charged molecule, by displacement of the ssDNA anti-ATP aptamer hybridized to a small capture oligonucleotide covalently attached on SWNTs, with picomolar sensitivity and selectivity over GTP.

Aptamers are short synthetic nucleic acids, either single stranded DNA (ssDNA) or RNA, that can bind a variety of targets. Since the first reports in 1990 that short RNA, and subsequently ssDNA, with high binding affinity can be selected from a large randomized library through *in vitro* selection, "aptamers" has captivated the interest of researchers in the fields of therapeutics and analytical methodologies (Ellington and Szostak, 1990; Tuerk and Gold, 1990). The growing interest in the latter field stems from the many benefits such as ease of producing mass quantity *in vitro* by PCR without the need of an animal host or elaborate and expensive cell culturing facilities, simple isolation and purification, reproducibility of synthesis and better stability, over the traditional bio-recognition/capture agent, antibodies (Lee *et al*., 2003). Using the Systematic Evolution

of Ligands by EXponential enrichment (SELEX) technique, aptamers for a variety of targets ranging from metal ions, small organic molecules (adenosine triphosphate (ATP), caffeine and cocaine) and biomolecules to entire organisms have been isolated and applied as probes in analytical methodologies (Ellington *et al.*, 2004; Mascini *et al.*, 2005).

Nano-sensors based on one-dimensional (1-D) nanostructure (nanowire, nanotube and nanobelt) chemiresistor/field-effect transistor (FET) transducers are becoming very promising candidates for the development of label-free affinity/immuno-sensors. Besides label-free detection, 1-D chemiresistor/FET biosensor has advantages of extremely high sensitivity, ease of miniaturization, low power requirement and development of high density arrays. Single-walled carbon nanotubes (SWNTs) have been extensively studied as the transducer element of biosensors as they meet the important requirements of an efficient biosensor: excellent electrical, chemical and mechanical properties and a large surface area to volume ratio results in surface phenomena predominating over the chemistry and physics that happen in the bulk (Li *et al.*, 2002; Wei *et al.*, 2001). The resistance/conductance of these devices is extremely sensitive to any surface adsorption/perturbation and is a function of the analyte charge. SWNTs-based chemiresistor/FET transducers have been modified with antibodies, enzymes, and aptamers, for highly sensitive and selective detection of macromolecules (IgE, thrombin, PA toxin, bacteria, and virus) with distinct charge properties (Ikebukuro *et al.*, 2004; Kim *et al.*, 2005; Lee *et al.*, 2005; Plaxco *et al.*, 2006; Plaxco *et al.*, 2007). The objective of this communication was to investigate the sensing of a target that is small in size

displaying minimal charge using a SWNTs-based aptasensor. Adenosine triphosphate (ATP), which is important for controlling the cellular mechanism and many biochemical pathways in a living organism, was used as a model system. An anti-ATP ssDNA aptamer (5′-ACC TGG GGG AGT ATT GCG GAG GAA GGT GTC ACA-3′) reported by Li and Ho (Ho and Li, 2008) was employed as the bioreceptor.

We initially investigated ATP sensing using the traditional 1-D nanostructure chemiresistor affinity-sensor architecture in which the modulation of the resistance of the bioreceptor (ssDNA anti-ATP aptamer) modified gate was monitored.

1. Aptasensor Fabrication:

Device fabrication protocol followed in this work was adapted from procedure described previously.1 A uniformly dispersed and separated SWNTs suspension was prepared by ultrasonication (power level 9) and centrifugation (10,000 rpm) a 25 ìg SWNTs (high carboxylated functionality, sold under the trade name of P3-SWNT, were purchased from Carbon Solutions, Inc. Riverside, CA, USA) in 1 mL DMF for three different times (90, 60, 30 min for each cycle). A 0.1 μL drop of the dispersed SWNTs was dispensed between the gap (3 μm) of a pair of microfabricated gold electrodes and aligned by AC dielectrophoresis (DEP) by applying a 4 MHz (amplitude 0.366V p-p) AC field across the electrodes for a few seconds using a function generator (Wavetek, Alpharetta, GA, USA) and then annealed at 300° C for an hour under a continuous flow of 5% H_2 plus 95% nitrogen gas to evaporate residual DMF and reduce the contact resistance between the carbon nanotubes and the gold electrodes. The SWNTs interconnects/channel of the chemiresistor was then incubated with 6 mM 1-pyrenebutanoic acid succinimidyl ester

(PBASE) in DMF for 1 h followed by thorough washing with DMF to remove residual esters. The capture oligonucleotides were covalently attached to the PBASE-modified SWNTs by incubating overnight at 4°C 200 nM oligo (5'-/5AmMC6/TGT GAC ACC TTC CC-3') or aptamer (5'-ACC TGG GGG AGT ATT GCG GAG GAA GGT GTC ACA-3' for the traditional format) in 10 mM pH 7.2 phosphate buffer (PB) through the amide bond between the amine at its 5' end and N-hydrosuccinimide ester of PBASE washed three times with PB to remove excess oligos followed by treatment with 0.1 mM ethanolamine for 30 min at room temperature to block excessive reactive groups and finally by incubation with 0.1% Tween 20 to prevent nonspecific binding. The capture oligos were subsequently hybridized to aptamers by incubating with a 200 nM aptamer solution in PB heated at 65^{0}C for 5 min, then for 2 h at room temperature and washed with PB 3 times to remove excess aptamers.

Upon the addition of different concentrations (1 pM to 10 nM) of ATP to the biosensor its response (normalized resistance change) for each of the concentrations over the investigated range averaged to a meager $1.72 \pm 0.7\%$ and had no relationship to the concentration (data not shown). The very weak response, not much different from that for blank, is not completely unexpected considering that the response of 1-D nanostructure-based chemiresistor/FET biosensors is a function of the analyte charge; which for ATP is small in comparison to the targets that have been successfully detected by 1-D nanostructure-based chemiresistor/FET aptasensors and affinity/immuno-sensors (Mulchandani *et al*., 2010a; Mulchandani *et al*., 2010b; Tang *et al*., 2008). In order to sense/detect ATP using 1-D nanostructures-based chemiresistor/FET transducers, we

report a modified aptasensor architecture, depicted in fig.1. In this new format, a network of SWNTs forming the conduction channel between the source and drain electrodes of the nano-chemiresistor was first modified with a short capture oligonucleotide through the 5′ amine. Subsequently, the ssDNA anti-ATP aptamer was allowed to hybridize to the capture oligonucleotide to fabricate the aptasensor. The addition of ATP, the target analyte, to the sensor caused the release of the hybridized aptamer through the aptamer structural shift producing a large change, several folds higher than the noise, in the chemiresistor resistance/conductance from the removal of the large negatively charged DNA molecule. Using the displacement principle, we were able to detect as low as 1 pM ATP with very good discrimination against guanidine triphosphate (GTP). Fig.2 shows the current *vs.* voltage recordings of the fabrication steps, non-covalent modification of SWNTs with 1-pyrenebutanoic acid succinimidyl ester (PBASE), covalent attachment of the capture oligonucleotide (5′-/5AmMC6/TGT GAC ACC TTC CC-3′) through the amide bond between the *N*-hydrosuccinimidyl ester (NHS) of PBASE and amine at the 5′ end of the capture oligo, neutralization of the unbound NHS with ethanolamine and blocking of unfunctionalized SWNTs with Tween 20 and hybridization of the ssDNA anti-ATP aptamer, and sensing process. 2. Sensing measurements

The sensing protocol consisted of monitoring the initial resistance (R_0) of the aptasensor fabricated above by measuring the source-drain current (I) as a function of source-drain voltage (V) from -0.5 V to +0.5 V using a HP 4155A (Agilent, Santa Clara, CA, USA) semiconductor parameter analyzer and taking the inverse of the slope of the I-V curve from -0.1 V to +0.1 V followed by incubation for 10 min at room temperature with

different concentrations of ATP in 10 μl PB, washing three times with PB, and recording the new resistance under wet conditions in presence of PB. Figures S1(A) and S1(B) show the I-V curves for SWNTs-based aptasensor at various stages of fabrication and after incubation with different ATP concentrations, respectively.

As shown, the current at the same voltage for the SWNTs after each modification step decreased. These current decreases, *i.e.* resistance increases, were in accordance with the literature and a result of electron donation from these molecules to the nanotubes resulting in charge carrier reduction in the p-type SWNTs and/or scattering potential generated by the immobilization of the molecules and thereby decreasing the hole mobility (Gruner 2006). Upon incubation of the final aptasensor device with 1 nM ATP for 5 min at room temperature, the source–drain current of the device increased, *i.e.* the resistance decreased back to the value of the capture oligo functionalized SWNTs.

Negative controls, *i.e.*, SWNTs devices functionalized with only the capture oligo and blocked with ethanolamine and Tween 20, *i.e.* without the aptamer, showed no response to ATP. These results confirmed the effectiveness of the proposed sensing modality for a small charge and/or size molecule by a nanostructure-based chemiresistor/FET aptasensor.

Fig. 3 shows the calibration plot, relationship between the SWNTs based chemiresistive aptasensor response $[(R - R_{apt})/R_{apt}$, where R is the resistance after exposure to ATP molecules and R_{apt} is the resistance after exposure to the aptamer] and ATP concentration. The resistance was calculated as the inverse of the slope of the $I–V$ plot between −0.1 and + 0.1 V (linear range). As shown in the figure the sensor had a

broad dynamic range spanning over three orders of magnitude from 1 pM to 1 nM and attained a plateau at higher concentrations. The response was linear from 1 pM to 100 pM and 1.3 nM^{-1} sensitivity. The 1 pM limit of the detection is the best observed so far using this aptamer with different sensing modalities (Mirkin *et al.*, 2009), including the ones similar to that used in this work, and a variety of transduction principles. The high sensitivity is attributed to the extremely high sensitivity of the chemiresistive/FET transduction combined with the displacement principle. Furthermore, in contrast to assays and sensors reported in the literature, the reported nano-aptasensor is a truly label-free system, requiring the aid of no labels attached to the aptamer or the capture oligo or the intercalating   dye.
The selectivity/specificity is a critical parameter in the acceptance and utility of a sensor. The aptasensor had excellent selectivity as evidenced by $2 \pm 1\%$ response to 1 nM GTP when compared to $24.3 \pm 1.1\%$ for the same ATP concentration. This result is in agreement with the literature. We also investigated the feasibility of reusing the sensor platform multiple times. Incubation of the aptasensor with the ssDNA anti-ATP aptamer after each use restored its functionality for up to three repeated measurements (data not shown).

In conclusion, we have developed a SWNTs-based chemiresistor aptasensor for detection of small molecules which otherwise are difficult to detect by the chemiresistor/FET transduction principle by adapting the displacement mode of biosensing with the detection limit in the picomolar range without compromising the selectivity. While the displacement detection principle was demonstrated for ATP, it can

also be extended to other weakly or uncharged molecules. A further amplification of the biosensor sensitivity can be achieved by augmenting the charge of the displacing aptamer, introducing mismatches between the capture oligo and aptamer sequence and using a shorter oligo.

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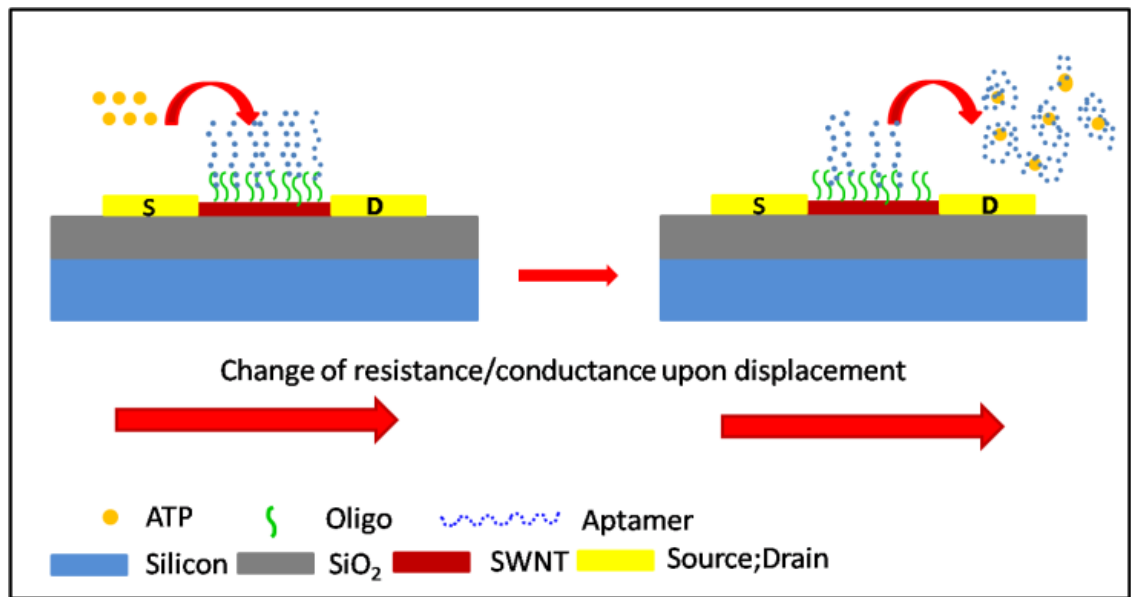
Figures :

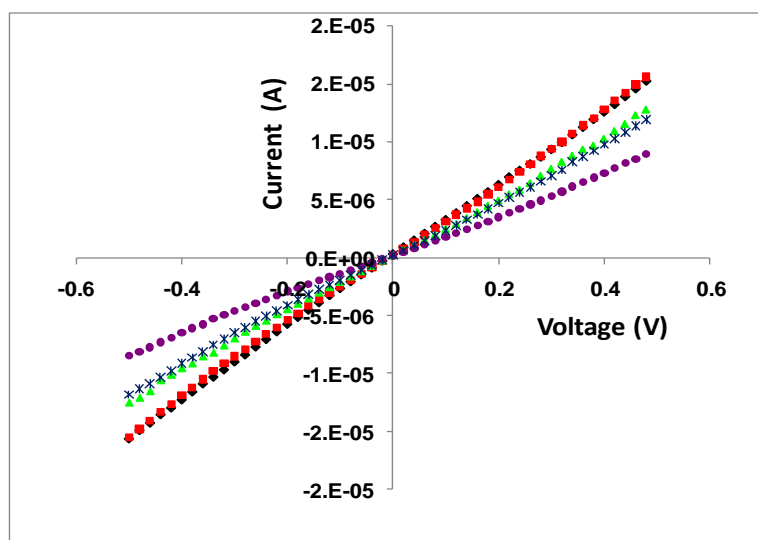Fig. A.1 Schematic of the displacement-based chemiresistive biosensor.

Fig. A.2 I–V characteristics of the biosensor at various stages of fabrication and upon addition of ATP. (◆ PBASE; (■) capture oligo; (▲) ethanolamine + Tween 20; (●) aptamer; (*) 1 nM ATP.
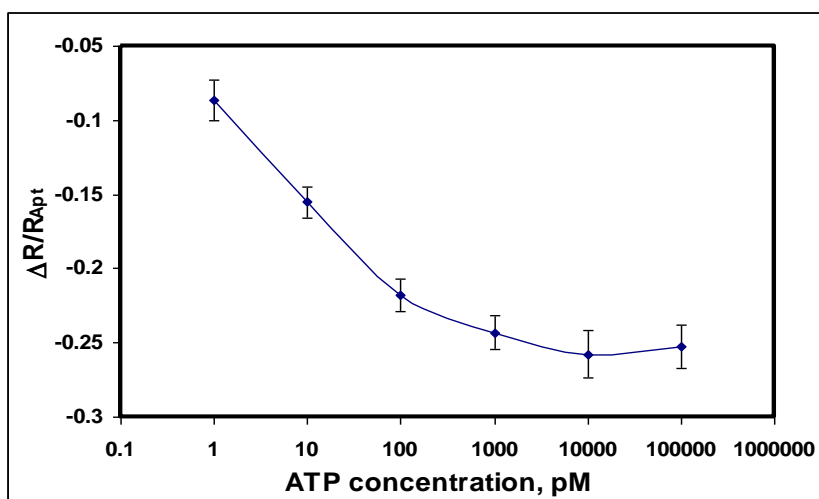

Fig. A.3 Aptasensor calibration for ATP. Each data point is an average of measurements from 10 sensors prepared in three batches and error bars represent ±1 S.D. The standard deviation of the biosensor response to zero ATP concentration, i.e. buffer, was ±1.1%.
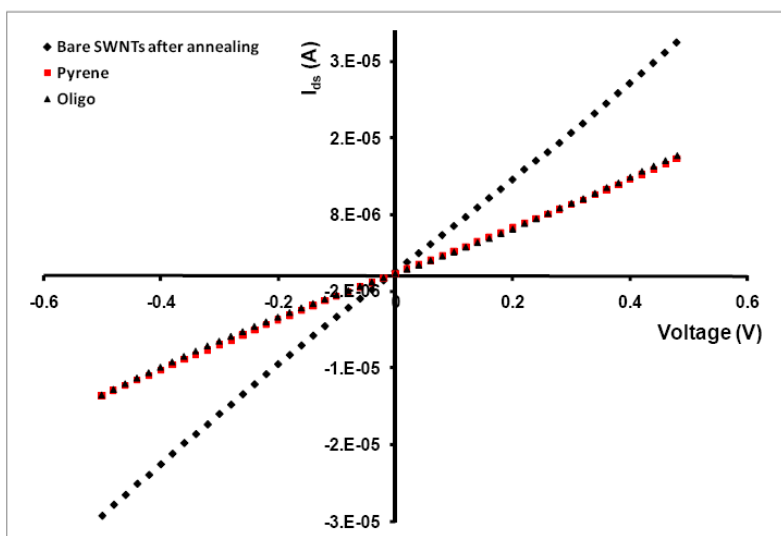
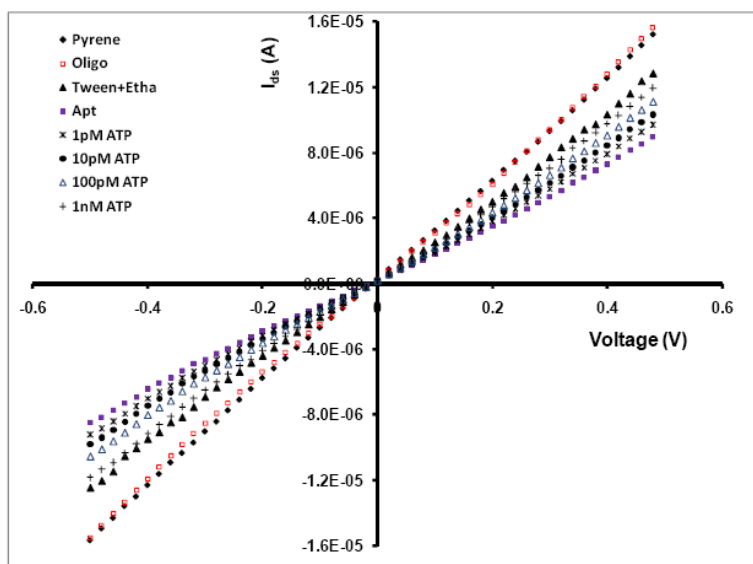Figure S1(A). I-V curves for SWNTs after annealing, after PBASE and after oligo functionalization.

Figure S1(B). I-V curves of aptasensor to 1 pM, 10 pM, 100 pM and 1 nM ATP.