Carbon nanotube based (Bio) electronic devices

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**NANYANG
TECHNOLOGICAL
UNIVERSITY**

**CARBON NANOTUBE BASED
(BIO)ELECTRONIC DEVICES**

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**SCHOOL OF ELECTRICAL AND ELECTRONIC
ENGINEERING**

2008

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Carbon Nanotube Based (Bio)electronic Devices

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School of Electrical and Electronic Engineering

**A thesis submitted to the Nanyang Technological University
in fulfilment of the requirement for the degree of
Master of Engineering**

2008

Statement of Originality

I hereby certify that the work embodied in this thesis is the result of original research and has not been submitted for a higher degree to any other University or Institution.

Date

Liu Ningyi

Acknowledgment

I would like to express my sincere gratitude towards my supervisor, Professor Zhang Qing for giving me the opportunity to work on this project and for his guidance, valuable time encouragement, constructive feedback and financial support along the way. The knowledge I have learnt from him is not only about the project itself, but also about how to be a scientific researcher.

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Summary

Novel single-walled carbon nanotube (SWNT) based biosensors and chemical sensors for real-time detection of organophosphate and nitrylphenol compounds, respectively, have been developed. Horizontally aligned SWNTs are assembled to desirable electrodes using AC dielectrophoresis technique. For SWNT based organophosphate sensors, organophosphorus hydrolase (OPH) immobilized on the SWNTs by non-specific binding triggers enzymatic hydrolysis of organophosphates (OPs), such as paraoxon, consequently causing a detectable change in the conductance of the SWNTs. The conductance change is found to be correlated to the concentration of organophosphate. For nitrylphenol compounds detection, as-prepared CNTFETs were used. The response of the SWNT conductance was also found to be directly proportional to the concentration of nitrylphenol compound in the solution. Our results suggest that the novel biosensors and chemical sensors have great potentials to serve as a simple and reusable platform of sensing organophosphate and nitrophenol on a real-time basis. Fabrication details and detection mechanisms of these SWNT based electronic sensors are also discussed in the report. In addition, we analyzed the current fluctuation for these SWNT devices and found that $1/f$ noise at low frequency region plays a key role of affecting the CNT channel current.

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Chapter 1 Introduction

1.1 Motivations

Biosensors are used for monitoring the environment and gathering data for diverse purpose, including detecting environmental and food contaminations, biowarfare agents, and screening molecular interactions for drug discovery and diagnosis, etc. Biosensors provide specific quantitative and semi-quantitative analytical information using a biological recognition element which is in direct spatial contact with a transduction element. Methods used to transduce specific bio-recognition events include optical, acoustic, and electronic techniques. Similarly, chemical sensors are also widely used for multiple purposes, such as toxic species monitoring. After the discovery of carbon nanotubes (CNTs), the CNT based electronic and electrochemical biosensors and chemical sensors are being explored intensively because this kind of nanoscale material has advantages of lower cost, real-time and/or label-free detection, the possibility of integrating the recognition elements into microelectronic system for multiplexed detection and etc. Such advantages make CNT based sensor a promising candidate to detect toxic compounds which may require convenient in situ test.

However, nowadays the sensor devices based on CNT are also facing some problems such as accompanied noise in detection. The resulting low signal-to-noise ratio can degrade the sensitivity of sensors. As a result, the noise analysis in CNT based device should be implemented in order to improve the performance and realize further commercial applications.

In summary, the motivations of this project are to use SWNTs as a key sensing element in carbon nanotube field-effect transistor (CNTFET) for real-time and label-free chemical and biochemical detecting applications. The noise analysis of the detected current is also studied.

1.2 Objectives

The main objectives of my M. Eng project are:

- 1) To study the influences of organophosphate and nitrylphenol molecules on the electronic properties of CNTs.
- 2) To utilize CNTFET as a platform for the application of CNT biosensors and chemical sensors.
- 3) To study the mechanisms of these chemical and biological detections.
- 4) To analyze the noises of the detected currents from CNT based devices.

1.3 Major contributions of this dissertation

I have fabricated and characterized CNTFET devices and investigated the possible applications of such devices for organophosphate and nitrophenol compounds detections. In addition, I have also studied the noise properties of CNTFETs. The major contributions of this M. Eng. project are listed as following:

1. Fabricated organophosphorus-hydrolase (OPH)-functionalized-CNTFET based biosensors for one of organophosphate compounds, i.e. paraoxon. Concentration-correlated response and reusability of such biosensors have been studied.
2. Studied the effect of hydrolysis products of paraoxon on the CNTFET in order to investigate the sensing mechanism of OPH functionalized CNTFET to paraoxon.
3. Utilized CNTFET as sensor platform to detect nitrophenol compounds in solution, such as 2-nitrophenol. The selectivity of this chemical sensor to buffer solution and chemicals with similar structure, e.g. phenol, has been confirmed. The possible mechanism of CNTFET detection for nitrophenol compounds has also been discussed comprehensively.
4. Analyzed the noise characterization for CNTFET devices, including SWNT-FET and DWNT-FET with back-gate or top-gate layout and found the $1/f$ noise is a dominant component in low-frequency region. The properties of $1/f$ noise, such as noise amplitude, have been calculated and analyzed.
5. Made a comprehensive review for recently developed CNT based electrochemical and electronic biosensors. Their device setup, fabrication methodology and device performance parameters have been integrated in the review article.

1.4 Organization of the report

Chapter 2 reviews the fundamental properties of CNTs and CNT based field-effect transistors, as well as various fabrication methods and applications for CNT based

biosensors, including electrochemical biosensors and electronic biosensors. The noise characterization in CNT based devices is also discussed. Chapter 3 introduces our fabrication technique for back-gated and top-gated CNTFETs. Chapter 4 presents the experimental results obtained in the project so far. The paraoxon and nitrylphenol compounds sensor based on CNTFET devices and its correlated noise property are studied and discussed. Finally, Chapter 5 concludes the entire project, lists the future direction and gives recommendations for future work.

Chapter 2 Literature Review

2.1 Overview of carbon nanotubes

Carbon nanotubes (CNTs) are hollow cylinders composed of one or more concentric layers of carbon atoms in a honeycomb lattice arrangement. Accordingly, CNTs includes single-walled nanotubes (SWNTs) and multiwalled nanotubes (MWNTs). MWNTs were firstly observed in 1976 [1] and studied in transmission electron microscopy (TEM) [2], while single-walled nanotubes (SWNTs) were produced independently in 1993 [3]. SWNTs typically have a diameter of 1-2nm and a length from several micrometers to tens of micrometers. The large aspect ratio makes the nanotubes nearly ideal one-dimensional (1-D) objects.

The electronic structure and electrical properties of SWNTs are usually discussed in terms of the electronic structure of a graphene sheet (a layer of graphite) [4]. The circumference of the nanotubes is expressed by the so-called chiral vector, $\mathbf{C}$, connecting two crystallographically equivalent sites of the two-dimensional (2-D) graphene sheet (see Figure 2-1). $\mathbf{C}$ is expressed as $n\mathbf{a}_1 + m\mathbf{a}_2$, where $\mathbf{a}_1$ and $\mathbf{a}_2$ are the unit vectors of the hexagonal honeycomb lattice. The pair of integers (n, m) defines SWNTs' chiral vector, that is, the chirality. As shown in Figure 2-1a, the chiral vector describes a (4,4) SWNT. The translation vector $\mathbf{T}$ is defined as $t_1\mathbf{a}_1 + t_2\mathbf{a}_2$, where t_1 and t_2 are integers. They are related to (n,m) by $t_1 = (2m+n)/d_R$ and $t_2 = -(2n+m)/d_R$, respectively, where d_R is the greatest common divisor of (2m+n) and (2n+m). Figure

2-1b shows the atomic structures of a (10,10) and a (20,0) SWNT. Depending on their chiralities, which decide the detail arrangement of carbon atoms in SWNTs, SWNTs can be either metallic (m-SWNTs) or semiconducting (s-SWNTs).

Figure 2-1 (a) The chirality vector $\mathbf{C}$ of a (4,4) SWNT. (b) Atomic structure of a (10,10) SWNT (top) and a (20,0) SWNT (bottom).

The electrical properties of CNTs are due in a large part to the peculiar electronic structure of the graphene. Examples for the band structure and hexagonal first Brillouin zone of SWNTs are shown in Figure 2-2. The energy surfaces shown in Figure 2-2a are the band structure of a graphene sheet. The valence (π) and conduction (π^*) states touch at six points (Fermi points) lying at the Fermi level. The dimensionality of the system (2-D) results in a vanishing density of states when integrating over the Fermi surface. Because of this special situation, graphene is metallic in some directions and semiconducting in the others; it is therefore called a zero-gap semiconductor. In the case of a SWNT, the confinement of the electrons in the circumferential direction in the tube introduces an additional quantization. This requires that the circumferential component of the wave vector k_C can only take the values fulfilling the condition $k_C C = 2\pi j$, where j is an integer. As a result, each band of graphene splits into a number of 1-D sub-bands labeled by j . Figure 2-2b shows the states of a (3,3) SWNT, which is metallic. The allowed energy states of the tube are

cuts of the graphene band structure. When these cuts pass through a Fermi point, the tube is metallic [4]. In cases where no cut passes through a K point, as shown in Figure 2-2c for (4,2) SWNT, the SWNTs are semiconducting [5]. Mathematically, an (n,m) SWNT is metallic when $n=m$. It is small-gap semiconducting (semi-metallic) [6] when $n-m=3i$, where i is a non-zero integer, while SWNTs with $n-m \neq 3i$ are truly semiconducting. For semi-metallic and semiconducting SWNTs, the bandgaps depend on specific (n,m) indices. Generally speaking, the bandgap of semi-metallic SWNTs are in the range of 2-50 meV and that of the semiconducting SWNTs are in the range of 50 meV to 2 eV.

Figure 2-2 (a) Band structure of a graphene sheet (top) and the first Brillouin zone (bottom). (b) Band structure of a metallic (3,3) SWNT. (c) Band structure of a (4,2) semiconducting SWNT [7].

With a general view of the structure of SWNT, we can see some of advantages of SWNT over the silicon technologies as follows [7]:

1. Carrier transport is one-dimensional (1-D). This reduces phase space for scattering of the carriers and opens up the possibility of ballistic transport.
2. All chemical bonds of the C atoms are satisfied and there is no need for chemical passivation of dangling bonds as in silicon. This implies that SWNT electronics would not be bound to use SiO_2 as gate oxide.

3. The strong covalent bonding gives the SWNTs high mechanical (Young's modulus about ten times higher than that of steel) and thermal stability and immunity to electromigration. Current densities as high as 10^9 A/cm^2 can be sustained.
4. Their key dimension, their diameter, is easily controlled by chemistry.
5. In principle, both transistors and interconnects can be made out of semiconducting (s-) and metallic (m-) SWNTs, respectively.

The electrical properties of MWNTs have attracted less attention because of their complex structure, Whereas SWNTs have great potential to be used as nanoscale electronic devices such as field-effect transistors [6], field emitters [8] and chemical sensors [9].

2.2 Single wall carbon nanotube based CNTFET

Making use of the unique electronic properties, high performance CNT based field-effect transistors can be fabricated. S-SWNTs with their appealing electrical properties are natural candidates for the fabrication of terminal nano-devices. Indeed, already in 1998 it was demonstrated that SWNTs could be used as channels of field-effect transistors (FETs) [5]. In these devices a SWNT is used to bridge two noble metal electrodes prefabricated using e-beam lithography on top of a SiO_2 film grown on a silicon wafer in Figure 2-3.

Figure 2-3 (Top) AFM image of one of early CNTFETs. (Bottom) Schematic of the CNTFETs

The SWNT plays the role of the “channel”, while the two metal electrodes functioned as the “source” and “drain” electrodes. The heavily doped silicon wafer itself is used as the “gate” (back-gate). These CNTFETs behaved as p-type FETs and had an I_{ON}/I_{OFF} current ratio of $\approx 10^5$. While functional, the devices had a high parasitic contact resistance ($\geq 1\text{M}\Omega$), low drive currents (a few nanoamperes), low transconductance $g_m=1\text{nS}$, and high inverse subthreshold slopes $S\approx 1\text{-}2\text{V/decade}$. To a large extent the unsatisfactory characteristics were due to bad contacts. The CNT was simply laid on the gold electrodes and was held by weak van der Waals forces. To improve the contacts we adapted a different fabrication scheme where the semiconducting SWNTs were dispersed on an oxidized Si wafer, and the source and drain electrodes, now made of metals, such as Ti and Co, that are compatible with silicon technology, were fabricated on top of them. Thermal annealing of the contacts, which in the case of Ti electrodes led to the formation of TiC, produced a stronger coupling between the metal and the nanotube and a reduction of the contact resistance [7].

Fig 2-4 shows the output characteristics of such a CNTFET with Co electrode. The I_D - V_{DS} curve shows the transistor is p-type and has a high on-off current ratio of 10^6 .

Figure 2-4 Output of CNTFETs with cobalt contacts. The inset shows schematically the structure of the devices.

This new CNTFET configuration has a significantly reduced contact resistance, $\sim 300\text{k}\Omega$, a much higher current in the μA range, and a transconductance $g_m = 0.34\mu\text{S}$, ~ 200 times higher than that of van der Waals-bonded CNTFETs.

A next generation of CNTFETs is top-gated CNTFETs. Fig 2-5 shows a schematic of a top-gated CNTFET with Ti electrodes and a 15nm SiO_2 gate insulator film. Such a CNTFET can also be switched by the bottom gate (wafer) and the resulting characteristics can be compared with those of the device under top-gate operation. This device has a superior performance; the threshold voltage of the top-gated CNTFET is significantly lower, -0.5V , than under bottom-gated operation, -12V . Similarly, the drive current is much higher under top gating, and the transconductance is similarly high, $g_m = 3.3\mu\text{S}$ per nanotube [7].

Figure 2-5 Schematic of the top-gated CNTFET with Ti source, drain and gate electrodes. A 15nm SiO₂ film was used as the gate oxide

Although CNTFETs are still far from being optimized, they are already very competitive with the corresponding Si devices. Table 2-1 shows the comparison of the characteristics of the CNTFET with two recent high-performance Si p-channel devices: a 15-nm-gate length MOSFET built on bulk silicon and 50-nm-gate length device built using SOI technology [7].

Table 2-1 Comparison of Key Performance Parameters for a 260-nm-long top gate p-CNTFET, a 15-nm-bulk Si p-MOSFET, and a 50-nm SOI p-MOSFET.

	p-type CNTFET	Ref a	Ref. b
Gate Length (nm)	260	15	50
Gate oxide thickness (nm)	15	1.4	1.5
V _t (V)	-0.5	~0.1	~0.2
I _{ON} (μA/μm) (V _{DS} = V _{GS} - V _t ~ -1 V)	2,100	265	650
I _{OFF} (nA/μm)	-150	<-500	-9
Subthreshold slope (mV/dec)	130	~100	70
Transconductance (μS/μm)	2,321	975	650

a) B. Yu et al. IEDM Tech. Dig. 2001, p. 934; b) R. Chau et al. IEDM Tech. Dig. 2001, p. 621

2.3 Schottky barrier CNTFET

The working principle of the CNTFETs is different from that of Si MOSFETs. Heinze and co-worker proposed the Schottky barrier model [10], in which the transistor action occurs primarily by modulation of the contact resistance rather than the channel conductance. For ordinary field-effect transistors, the contacts are Ohmic contacts for

the purpose of effective switching. However, there is a substantial Schottky barrier (SB) at the contacts between CNTs and metal electrodes. The gate voltage control electrostatic potential at the SB contact. Hence, the SB barrier height for both electrons and holes could be modulated by gate voltage. Figure 2-7a shows the simulated electrostatic potential in a top gate CNTFET at 2V gate voltage. Figure 2-7b shows the conductance for different SB heights. When the metal Fermi level is situated in the middle of the CNTs' band gap, the conductance at zero drain voltage shows a symmetric dependence on the gate voltage. The switch mechanism for the CNTFET is illustrated in Figure 2-7c.

Figure 2-6 Conductances for realistic FET geometries [10]. (a) Electrostatic potential (contour lines) for a top gate CNTFET with gate voltage of 2V. (b) Corresponding conductance versus gate voltage at room temperature, for different SBs. (c) CNT conduction band energy near the contact, for gate voltages of 4V and 10V.

The current is calculated by the Landauer formula,

$$I(V) = \frac{4e}{h} \int [F(E) - F(E + eV_D)] P(E) dE \quad (1)$$

where V_D is the drain voltage ($V_S=0$) and F is the Fermi function. The energy dependent transmission probability $P(E)$ is calculated within the WKB approximation using the idealized band structure. $P(E)$ is given by the following formula,

$$\ln P(E) = -\frac{4}{3bV_p} \int_{Z_i}^{Z_f} (\Delta^2 - [E + f(Z)]^2)^{1/2} dz \quad (2)$$

where $b=0.144\text{nm}$ is C-C bond length, $\Delta=0.3\text{eV}$ is half the CNT bandgap. $V_p=2.5\text{eV}$ is the tight-binding parameter, and $\Phi(Z)$ is the electrostatic potential along the CNTs. Increasing the voltage difference between source and gate electrodes leads to a large electric field at the contact, reducing the width of the SB and allowing the thermally assisted tunneling. Asymmetric conductance shown in Figure 2-7b is caused by different SB height for electrons and holes. The metal Fermi level does not fall in the center of the CNT bandgap, resulting in the different SB heights for electrons and holes. Figure 2-7 shows that the device geometry plays an important role in switch operation. In addition, adsorbed gases affect the work functions of the metal electrode, and hence influence the switching behavior. Figure 2-8 is the experimentally measured effect of oxygen absorption. The as-prepared p-CNTFET changes to n-type after annealing in vacuum. In Figure 2-8, the annealed (n-type) CNFET has been exposed to oxygen for 2 minutes at $P=0$, 10^{-4} , 5×10^{-4} , 5×10^{-3} , 10^{-1} Torr and in ambient from left to right, respectively. Eventually, the n-CNTFET changes back to p-CNTFET.

Figure 2-7 experimental results for the effect of the oxygen on the current of the top gate CNTFET [10].

2.4 CNTs based electrochemical and electronic biosensing applications

Biosensors, a subtype of sensor devices, are designed to characterize biological subjects by monitoring relevant physical and chemical signals. Biosensors, typically, consist of sensing elements and signal transducers. The sensing elements selectively detect the analytes of interest, while the transducers convert chemical and biological variations into appropriate physical signals, such as electrical and optical signals, whose change corresponds to the analyte concentration. Often the sensing elements of a biosensor are functionalized with biological materials, such as single-strand DNA (ssDNA), proteins (enzymes, antibodies, etc), cells and etc for specific biological recognition. Various biosensors have been developed and applied to detect the presence of biological substances or to track complex biological processes ([11] and references therein).

Carbon nanotube (CNT) is a type of macromolecular systems whose structure can be thought as rolling up a graphene sheet along certain directions. The unique properties of CNT have drawn a lot of research attention in various biosensor applications. For example, taking advantage of its high surface/volume ratio, CNT has been used to coat electrochemical electrodes to increase their effective surface area. Moreover, CNTs exhibit outstanding chemical and mechanical stability that assures reliable and reproducible performance. It has also been found that the CNT can enhance electrocatalytic activity and promote electron-transfer reactions for a wide range of electroactive species. CNT-modified electrodes can alleviate surface-fouling. On the other hand, CNTs can be easily functionalized with biorecognition layers which

selectively react with bio-analytes of interest. Due to its one-dimensional structure, CNT enables efficient charge transfer between the surface-anchored biomolecules and CNT. In addition, the conductivity of CNTs, especially semiconducting single wall nanotubes (SWNT), is found to be remarkably sensitive to the surface adsorbates. These properties make CNT an appealing material for electrical biosensors, including electrochemical biosensor and electronic biosensor ([12, 13] and references therein).

The aim of this review is to summarize the recent development of integrating CNTs into electrical biosensing systems. This chapter is organized as follows. Various design principles of CNT based biosensors are described in the first sub-section. In the second sub-section, a collection of CNT-based electrochemical biosensors are presented. Finally, the CNTFET based electronic biosensors are discussed.

2.4.1 Design principles of CNT-based biosensors

Biological species could be detected by a variety of classical methodologies, such as fluorescence spectrometry with high sensitivity and selectivity. However, these techniques usually require complicated equipments and are difficult to be miniaturized. These drawbacks could be overcome by electrical biosensing techniques. In the last decade, CNTs have been increasingly utilized as electrodes or transducers to perform electrical biosensing. In the following discussion, we classify CNT-based biosensors into several categories according to different architectures.

2.4.1.1 CNTs as modifiers of electrode surfaces

The commonly used electrodes for electrochemical biosensing include carbon electrodes (e.g., glassy carbon, graphite, and activated carbon), metallic electrodes (e.g., Au, Pt), conducting polymer electrodes, metal oxides electrodes, composite electrodes, etc. Some of these electrodes are of poor sensitivity and stability, long response time and high overpotential for electron transfer reactions. Some of them are expensive such as noble metal electrodes. These problems could be overcome by modifying the traditional electrodes with CNTs because of their fast electron transfer and anti-surface fouling properties.

2.4.1.1.1 Non-oriented modification

Non-oriented modification means that CNTs on the electrode surface are randomly distributed. Casting a CNT suspension onto the support electrodes is the simplest and mostly used method. Because CNTs are insoluble in most solvents, the first step of processing CNTs into a thin film on electrodes is to get a homogeneous CNT suspension, for example, by dissolving CNTs in a solution of concentrated sulfuric acid [14] or Nafion [6, 15-19]. Nafion, a perfluorosulfonated and negatively charged polymer, brings additional benefits like improved anti-interference ability and enhanced mechanical strength due to its good cation exchange, discriminative and biocompatibility properties. With the aid of surfactants, such as dihexadecylphosphate (DHP) [6, 20] and sodium dodecylbenzenesulfonate (SDBS) [6], CNTs can be easily dispersed into aqueous solution. Oxidized CNTs after long-time acid treatment could be stabilized in aqueous solution [21, 22] because of the electrostatic repulsion induced by the negatively charged chemical groups on MWNTs [22]. In addition to aqueous media, other solvents such as N,N-dimethylformamide (DMF) [6, 23-26],

chloroform [6] and acetone [6, 27] have also been used to prepare CNT suspension. Ultrasonication is usually used to assist effective dispersion of CNTs. Finally, a small volume of CNT suspension can be drop-casted on the polished glassy carbon electrode (GCE) or metallic electrodes.

Chemical vapor deposition (CVD) can also be applied to modify an electrode with non-oriented CNTs [28]. Another simple preparation method involves gently rubbing the electrode surfaces on filter papers coated with purified MWNTs [29].

2.4.1.1.2 Oriented modification

Assembling oriented CNTs on electrodes is another way to fabricate CNT-modified electrodes for electrochemical detections. Most of these modifications were originated from the CNT growth process, which not only improves the electrical contact between CNTs and the conducting electrodes, but also makes CNTs free of impurities caused by surfactants or binders.

Direct growth of vertically aligned CNT arrays on graphite or gold substrate could be immediately utilized for electrical biosensing [30, 31]. In some applications of biological detection, such electrodes were functionalized with various biomaterials [32, 33]. Nanoelectrode array (NEA) based on low-density aligned CNTs were developed for detecting glucose [34] and DNA [35-37] with high signal-to-noise ratio and low detection limit. The CNTs were firstly grown on the substrate with controlled spacing and density (Figure 2-9). Then CNT-NEAs were insulated from each other with spin-coated Epon epoxy resin or deposited SiO₂. Subsequently the protruding

parts of CNT-NEA were removed by polishing process. The exposed tips of CNT-NEA were functionalized and covalently immobilized with glucose oxidase (GOx) or probe ssDNA. The aligned CNT NEA exhibited high electrocatalytic activity and fast electron transfer rate (ETR) [38].

Figure 2-8 SEM images of CNT nanoelectrode array: a 3×3 electrode array; b array of CNT bundles on one of the electrode pads; c and d array of CNTs at UV-lithography and e-beam patterned Ni spots, respectively. The scale bars are 200, 50, 2 and 5 μm , respectively. Reprinted from [35] with permission.

Post-synthesis transfer of the CNT array has also been applied to fabricate oriented-CNT modified electrodes [39-41]. Briefly speaking, a thin layer of metal (such as Au) was deposited on the top surface of as-synthesized aligned CNT array and then the substrate which supported the CNT to grow was etched away.

Another way to prepare vertically aligned CNT array was the self-assembly technique [6, 42]. The carboxylized CNTs generated from oxidative scission were covalently and perpendicularly immobilized on cysteamine monolayer coated gold electrodes via amide bonds.

2.4.1.2 CNT-based composite electrodes

Carbon paste and composite electrodes, fabricated by mixing carbon powder with mineral oil or other binders, have been used in electrochemical detection for years. CNT-based composite electrodes could be prepared in a similar manner by mixing CNTs powder with a number of binders, e.g. mineral oil, bromoform, Teflon, polymers like Polypyrrole (PPy) and chitosan (CHIT) and so on. Then the resulted composite can be casted on the top of a support substrate electrode (Figure 2-10a) [6], or packed into a glass capillary or a Teflon tube (Figure 2-10b) [43-45].

Figure 2-9 Schematic drawing of two types of CNT composite electrodes: (a) Composite of CNTs and binder was casted on the top of a support electrode. (b) Composite was packed into the electrode cavity of a glass capillary or a Teflon tube.

The first electrode of this kind used bromoform as the binder and the CNT composite was packed into a glass tube [46]. CNTs are usually mixed with mineral oil at a certain ratio of weight percentage to form CNT-based composite electrodes [45, 47-49]. CNT/Teflon composite was prepared in dry state by hand-mixing CNTs and Teflon, and the resulted composite was then packed firmly into the cavity of a glass sleeve [43]. A composite electrode using poly-pyrrole (PPy) as the binder was made by electropolymerization process in the mixed solution of pyrrole and MWNTs [50].

CHIT was also used as a binder [6] as MWNTs can be solubilized in the matrix of this hydrophilic ion-conducting biopolymer. In some biosensing applications, CNT composite was further mixed with biological molecules (enzymes for example) to obtain bio-functionalized CNT composite electrodes [43, 45, 47, 48].

Layer-by-layer (LBL) deposition is another method to fabricate CNT-based composite electrode. It was reported that alternate drop-casting of carboxylized MWNT suspension and electropolymerized neutral red (NR) assembled five layers of homogeneous and stable MWNTs and poly(neutral red) (PNR) film on a GCE [51].

2.4.1.3 Nanoparticles decorated CNT-based electrodes

Due to their unique size and shape, nanoparticles (NPs) frequently exhibit unusual physical and chemical properties, such as large surface-to-volume-ratio and promotion of electron transfer. Some nanoparticles, such as Pt nanoparticles, are the bio-compatible allowing the preservation of the biological activity of attached molecules. Nanoparticles made by transition metals, especially noble metals, display high catalytic activities for many chemical reactions. Therefore, metallic nanoparticles have been successfully used for chemical/biochemical sensing. Incorporating nanoparticles with CNTs, which also have a large surface-to-volume ratio, a high electron transfer rate and electrocatalytic activity, often leads to biosensors of higher sensitivity.

The main techniques for immobilizing metallic nanoparticles on CNT-modified electrodes include: direct adsorption of preformed nanoparticles [6, 44, 45, 52, 53], chemical deposition from metal salt solutions [54], or electrodeposition from metal

salt solutions [6, 28]. Among them, electrodeposition method is much more efficient as it is able to control the density and size of metallic nanoparticles through adjusting applied potential [28, 55].

In direct adsorption method, Pt nanoparticles, which rapidly oxidize H_2O_2 produced from enzymatic reaction, are prepared beforehand. Subsequently they can be dissolved in a Nafion solution [53] or a silicate sol [44], followed by the mixing with CNTs. Chemical deposition and electrodeposition of Pt nanoparticles are usually done via the reduction of H_2PtCl_6 : after immersing the CNTs or CNT-modified electrodes in H_2PtCl_6 solution, a reductive chemical $\text{Na}_2\text{S}_2\text{O}_4$ [54] or certain electrical potential [6, 28] is applied.

Cu nanoparticles prepared through the reduction of copper dodecyl sulfate ($\text{Cu}(\text{DS})_2$) were embedded in Nafion and SWNTs composite on the surface of a GCE or a Cu electrode as shown in Figure 2-11 [52]. A composite electrode for glucose detection was prepared by mixing enzyme, Cu or Ir nanoparticles and MWNTs in the presence of mineral oil [45].

Figure 2-10 TEM image of SWNT decorated with Cu nanoparticles, prepared by reduction of $\text{Cu}(\text{DS})_2$. (Inset) TEM image of Cu nanoparticles in the presence of Nafion. Reprinted from [52] with permission.

A MWNT modified Au electrode with Au-colloids adsorption was prepared by dispersing MWNTs in a homogeneous colloid-Au/DHP solution at first, then coating such solution on the gold electrode for the determination of cytochrome c[6].

2.4.1.4 CNTs as key sensing elements

So far, we have discussed using CNTs as the microelectrode modifier for electrochemical detection purpose. In these devices, CNTs mainly work as a role of transducer. On the other hand, CNTs, especially single-wall carbon nanotubes (SWNTs), can also function as key sensing elements in biosensors.

CNT based field effect transistors (CNTFET) is an emerging class of electronic biosensor. Comparing to traditional MOSFETs which have embedded silicon conducting channel, CNTFETs use SWNTs as the conducting channel which is open to the environment. Therefore, CNTFETs are highly sensitive to the variations of local environmental conditions. To construct a CNTFET, SWNTs have to be assembled across the source and the drain. It can be realized through direct growth using CVD technique or AC dielectrophoresis (ACDEP) technique [56, 57]. Individual semiconducting nanotube or bundles [58-60] or networks [59, 61] have been used in CNTFETs. While SWNTs serves as the sensing element exposing to target species, and often also with a back gate voltage (silicon or gold) [58, 62] or a liquid gate voltage [63, 64] applied, the change of source-drain conductance of devices is monitored as the device responses to detection species.

In order to achieve higher sensitivity and specificity, SWNTs in most of CNTFETs were functionalized with biological molecules, such as antibodies for specific recognition of antigens, ssDNA probes for detection of DNA hybridization and enzymes for the study of enzymatic reactions, etc. As shown in Figure 2-12a, these biological molecules can be non-covalently adsorbed onto SWNTs [59, 61, 62, 64-67] via weak interactions such as hydrophobic interaction between the nanotubes and hydrophobic domains of biological molecules [68]. The immobilization of biological molecules could also be implemented through a linking layer, such as carbodiimide-activated Tween 20 (CDI-Tween) [63, 69], polyethyleneimine/polyethyleneglycol (PEI/PEG) [58, 70], 1-pyrenebutanoic acid succinimidyl ester [60, 71]. These linking molecules can be coated on the nanotubes prior to the functionalization (Figure 2-12b). One end of these molecules binds to SWNTs through van der Waals interactions, while the other end couples to the biological molecules through amide bond formation.

Figure 2-11 (a) AFM images of the SWNT channel of CNTFET before (left) and after (right) the direct adsorption of α -PSA. Reprinted from [62] with permission. (b) Schematic of the CNTFET with a polymeric linking layer. A molecular receptor was used to functionalize such polymer for the recognition of a biomolecule. Reprinted from [58] with permission. (c) Chemical modification scheme at the gold back gate region of CNTFET for the conjugation with biomolecules. Reprinted from [72] with permission.

It has been reported that the CNTFET could also be functionalized at the back gate region instead on SWNTs [72, 73], and it might affect the effective potential around SWNTs (Figure 2-12c).

2.4.1.5 CNT-based biosensors with immobilized biological molecules

In order to improve the detection sensitivity and selectivity of CNT-based biosensors, a broad spectrum of biological molecules, including DNAs and proteins (enzymes and

antibodies, etc.), were immobilized on these biosensors. These biosensors can be grouped into two main categories: electrochemical biosensors and CNTFET-based electronic biosensors. In the former, CNT mainly serves as transducer which converts the signals from the active biological molecules to the electrode substrate through electrochemical reactions. While in the latter as described in the previous part, CNT plays a key role in sensing, usually with the aid of attached functional biomolecules. Covalent binding and noncovalent attachment including direct adsorption and entrapment can be used to immobilize the functional biomolecules. In the following, a brief overview of various immobilization techniques is given.

2.4.1.5.1 Direct adsorption

Noncovalent functionalization of CNTs could be realized through weak interactions, e.g. hydrogen bonding, π - π stacking, electrostatic forces, van der Waals forces and hydrophobic interactions, which help to directly adsorb biological molecules on CNTs ([74] and references therein).

Casting the mixture of CNTs and biomolecules onto an electrochemical electrode is a simple way to deliver biological molecules on the electrode surface via adsorption. A glucose biosensor was demonstrated by using a mixture of MWNTs, Nafion and GOx as the GCE modifier [19]. CNT-composite electrodes could be made by similar processes [47, 48]. For example, MWNT, Teflon and GOx were hand-mixed together in the dry state and the prepared composite electrode was used for glucose detection [43].

Biomolecules can alternatively be immobilized after CNT-modification, by incubating the CNT-modified electrode in the solution of relevant biomolecules [6, 28, 39, 41], or by drop-casting a small volume of the solution on the CNT-modified electrode [17, 53, 75, 76]. GOx/PtNP/CNT/graphite electrode for glucose detection was prepared by incubating the PtNP/CNT/graphite electrode in the enzyme GOx solution for 12 h, and then washing carefully with double-distilled water followed by drying process [28]. As another example, a MWNT-modified electrode for detecting organophosphorus compound was prepared by drop-casting with 10 μ L AChE solution [75].

In order to improve performance of electrodes through customizing the thickness, structural morphology, and biocatalyst loading of the functional layer, the LBL technique is often used. Alternate layers of GOx adsorbed MWNTs could be simply prepared by repeatedly immersing the electrode to MWNT solution and then GOx solution [77]. Alternate layers of differently charged components can also be deposited via electrostatic adsorption. For example, MWNTs wrapped by positively charged poly(diallyldimethylammonium chloride) (PDDA) were assembled layer-by-layer with negatively charged GOx on a chemically functionalized Au electrode [78] (Figure 2-13). Similar structures were presented in the references [6, 79].

Figure 2-12 (a) Schematic of the multilayer membranes prepared by LBL technique; (b) AFM image of GOx-PDDA·MWNT (LBL)/PSS/PDDA/MPS membranes on gold electrode. Reprinted from [78] with permission.

Noncovalent adsorption of biological molecules could also be enhanced via cross-linking the adsorbed molecules. After dropping the enzyme solution on Pt nanoparticle decorated SWNT/GCE, glutaraldehyde was applied on the resulting electrode to crosslink the enzymes [53]. Similarly, GOx was immobilized onto PNR/MWNT multilayers modified GCE by glutaraldehyde crosslinking [51]. Prevention of the loss of adsorbed biological molecules from the electrode surface could alternatively be achieved by covering a protective thin film (e.g., Nafion) [28].

Biological molecules were found to directly adsorb on the SWNTs in CNTFET sensors even without a molecular linking layer [59, 61, 62, 64-67].

2.4.1.5.2 Entrapment

Molecule entrapment is another method to noncovalently immobilize biological molecules on the electrode surface, including encapsulation and electropolymerization.

In encapsulation methodology, biological molecules are immobilized within hydrogels or sol-gel materials while their native bioactivity is retained. Hydrogel and

sol-gel have excellent properties to enhance the sensor response, such as high binding capacity with electrodes, large surface area, and easy electron exchange between electrodes and biological molecules, etc. Encapsulation can be realized by incorporating the mixture of biological molecules and CNTs into the hydrogel or the sol-gel matrix at first and subsequently casts the composite onto the support electrode (Figure 2-14a) [80]. Two glucose biosensors were made this way by encapsulating the mixture of GOx and CNTs into a sol-gel matrix [44, 81]. Alternatively, biological molecules embedded in hydrogel or sol-gel matrix could be brought onto CNT-modified electrodes (Figure 2-14b), as being adopted for a glucose biosensor [82] and cholesterol biosensor [54].

Figure 2-13 Schematic of biomolecules encapsulation with CNT: (a) CNTs were first incubated with an enzyme solution, and then the hydrogel or sol-gel was introduced to form a matrix, which is later brought on a substrate. (b) A film of CNTs was casted onto a support electrode at first. Subsequently, a hydrogel or sol-gel composite containing enzyme is casted on such a CNT-coated electrode. Reprinted from [80] with permission.

Biological molecules can be embedded into a polymer matrix simply by mixing them with the monomer solution. The mixture is then electropolymerized on the support electrode. The intimate contact between the biocomponent and polymer enables efficient signal transduction. A highly sensitive glucose sensor was constructed on a

MWNT modified electrode based on the entrapment of GOx within electropolymerized poly-*o*-aminophenol (POAP) matrix [83]. PPy is another polymer that can be electropolymerized at neutral pH and allow the entrapment of a wide range of biocatalysts. The pyrrole electropolymerization aided GOx immobilization was used on non-oriented CNT-modified electrode [84] and aligned CNT arrays [40] via mixing pyrrole, GOx and oxidized MWNTs. Figure 2-15 shows the SEM images of a PPy-coated CNT array.

Figure 2-14 SEM images of: (a) pristine CNT array; (b) aligned PPy-CNT coaxial nanowires; (c) PPy only deposited on the top surface of CNTs due to the high density of tube array; (d) polymer formed on both walls and top surface of the CNT array. Reprinted from [40] with permission.

2.4.1.5.3 Covalent attachment

Typically, the biological molecules are randomly distributed on the electrode surface if noncovalent immobilization method is utilized. And the direct adsorption relies on weak interactions so that some of the absorbed biological molecules may walk away over time. In contrast, covalent attachment method produces more stable

immobilization of biological molecules. And the distribution of biological molecules could be somewhat controlled by covalently attached to CNT framework. For instance, enzyme GOx was covalently attach to the broken tips of vertically aligned MWNTs via amide linkages between amine residues on GOx and carboxylic groups on the MWNT tips in the presence of coupling agents 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) [34]. It has been confirmed that flavin adenine dinucleotide (FAD) covalently bound to the tips of self-assembled MWNT arrays through amide linkage, and then apo-GOx was reconstituted on the FAD units. This structure enhances direct electron transfer between electrode and redox active center of GOx [6, 42]. Figure 2-16 illustrates the fabrication scheme and the AFM images of such an electrode.

Figure 2-15 (a) Schematic of self-assembled SWNT array and then covalent binding with GOx. (b) AFM image of self-assembled SWNT array through covalently linking to a cystamine/2-thioethanol monolayer functionalized Au electrode after 90 mins of coupling. (c) AFM image of the GOx reconstituted on the FAD-functionalized CNTs array. Reprinted from [42] with permission.

In comparison, it is not ideal to immobilize biological molecules directly on SWNTs through covalent bonds in CNTFET-based electronic biosensors. Because it is

believed that oxidation of SWNTs broke up the aromaticity of benzene units of SWNTs and imparted carboxyl and ether substituents on sidewall of SWNTs, and it may affect the intrinsic electronic property of SWNT. Instead, biological molecules were covalently attached to the SWNTs via linking molecules, of which the other end bound to SWNTs through van der Waals interactions or π - π stacking [58, 60, 63, 69, 71-73, 85].

2.4.2 Electrochemical Detection of Biomolecules

Electrochemical techniques of detecting biomaterials in solutions are attractive because of their simplicity and low-cost. In this section we discuss various electrochemical biosensors based on CNTs. In the first part we discuss the assessment criteria for different biosensors. We will present many biosensor applications for the detection of various biomolecules in the second part.

2.4.2.1 Assessment criteria of sensors

When designing CNT-based biosensors for practical application, several measurement parameters are of particular importance. Detection range is the most essential one, which determines the sensitivity, specificity and dynamic range required by the specific applications. For example, the normal level of glucose in human veins is 3.89-6.11 mmol/L and the fasting plasma glucose level at or above 7.0 mmol/L is diagnosed as diabetes. Therefore a practical glucose sensor should cover a detection range from a few μ mol/L to 15 mmol/L. A cholesterol sensor should be sensitive in the range of 50-400 mg/dL (1.3-10.4 mmol/L), because the desirable level of LDL

cholesterol is considered to be less than 100 mg/dL (2.6 mmol/L) and a patient who has a level of higher than 240 mg/dL (>6.2 mmol/L) of cholesterol is running a high risk of heart disease. As some biomolecules, like enzymes, degrade over time, a biosensor with high stability is a vital characteristic. Of course, specificity, sensitivity, accuracy, response time and reproducibility, etc, are also very critical to electrochemical sensors.

2.4.2.2 Electrochemical biosensors

We list CNT based glucose biosensors in Table 2-2, and CNT-based DNA biosensors in Table 2-3. Other biomolecule-functionalized electrochemical biosensors are summarized in Table 2-5. Biosensors without biomolecule-functionalization are summarized in Table 2-4. Several common biochemical species that CNT-based electrochemical biosensors detect are described below in detail.

Table 2-2 Summary of CNT-based electrochemical glucose biosensors and their important parameters

No. & Ref.	Electrodes	Design Principles	Sensitivity [(mmol/L) ⁻¹]	Linear Range [mmol/L]	Response Time [s]	Stability
G1 [52]	CuNP-SWNT-Nafion/GCE and CuNP-SWNT-Nafion/Cu	Nanoparticle decoration	256 μ A	2.5×10^{-4} -0.5	10	
G2 [28]	Nafion/Gox/PtNP/CNT/graphite	Nanoparticle decoration, direct adsorption	14 μ A	0.1-13.5	<5	73.5% after 22 days
G3 [53]	GOx/PtNP-SWNT-Nafion/GCE	Nanoparticle decoration, direct adsorption	2.11 μ A	0.0005-5	3	
G4 [39]	GOx/MWNT-array/Au	Oriented modification, direct adsorption	1.75 μ A	0.05-13	<16	96.3% after 1 month, 94.4% after 2 month, and 91.2% after

G5 [44]	GOx/PtNP-Silicate-SGC-MWNTPE	Nanoparticle decoration, direct adsorption	1.11 μ A	1-25	<15	3 month 90% after 3 days, and 80% after 1 month
G6 [83]	POAP-GOx/FePc-MWNT/GCE	Entrapment	0.735 μ A	0.0005-4	<8	120 days
G7 [51]	GOx/PNR-cMWNT (LBL)/GCE	Direct adsorption	0.6 μ A	0.05-10	<10	Constant in first 17 days, and 85% after 1 month
G8 [19]	GOx-MWNT-Nafion/GCE	Entrapment	0.33 μ A	0.025-2	<3	
G9 [40]	GOx-Ppy/MWNT-array/Au	Oriented modification, Entrapment	0.31 μ A	2.5-20		70% after 3 days
G10 [30]	MWNT-array/GCE	Oriented modification	0.22 μ A	0.002-11	<10	
G11 [82]	GOx-SGC/MWNT/BP PG	Entrapment	0.196 μ A	0.2-20	<5	3 weeks
G12 [43]	GOx/Teflon-MWNT	CNT composite electrode, direct adsorption	0.14 μ A	2-12	25	
G13 [78]	GOx-PDDA·MWNT(LBL)/PSS/PDDA/MPS/Au	Entrapment	44 nA	0.058-5	<8	82% after 5 weeks
G14 [77]	GOx-MWNT(LBL)/graphite	Entrapment	39 nA	0.5-15	6.7	
G15 [81]	GOx-FMC-BSA-MWNT-SGC/GCE	Entrapment	18 nA	0.05-20	25	96% after 110 days
G16 [45]	GOx-CuNP-MWNTPE, GOx-IrNP-MWNTPE	CNT composite electrode, nanoparticle decoration, direct adsorption	8.3 nA (Cu), 7.1 nA (Ir)	1.8-12 (Cu), 0-20 (Ir)	10 (Cu), 12 (Ir)	Constant in 2 months, and 24% after 6 months
G17 [34]	GOx-cMWNT-array/Si	Oriented modification, covalent attachment	~2.5 nA	0.08-30	20-30	
G18 [84]	Ppy-GOx-cMWNT/GCE	Entrapment	2.33 nA	0.2-50	15	

The blanks in the columns indicate that these data were not available in corresponding references. If not indicating “oriented modification” in the column of “Design principles”, “non-oriented modification” is a default design principle.

C carboxylized, BPPG basal plane pyrolytic graphite, BSA bovine serum albumin, FePc iron phthalocyanine, FMC ferrocenemonocarboxylic acid, GCE glassy carbon electrode, GOx glucose Oxidase, LBL layer-by-layer technique, MPS 3-mercaptopropylsulfonic-acid, NP Nanoparticle, PDDA poly(dimethyldiallylammonium chloride), MWNTPE MWNT paste electrode, PNR poly(neutral red), POAP poly-*o*-aminophenol, Ppy polypyrrole, PSS poly(sodium 4-styrenesulfonate), SGC sol-gel composite,

Table 2-3 Summary of CNT-based electrochemical DNA biosensors

Objective	No.	Sensors	Design Principles	Ref.
DNA hybridization	D1	DNR; ssDNA-cMWNT/GCE	Covalent attachment	[86]
	D2	ssDNA-Ppy/cMWNT/GCE	Entrapment	[87]
	D3	$\text{Ru}(\text{bpy})_3^{2+}$; ssDNA-cMWNT-array-SiO ₂ /Si	Oriented modification, covalent attachment	[35-37]
	D4	ssDNA/cMWNT-DNA/CPE	Covalent attachment	[88]
	D5	DNR; cMWNT-Ppy/GCE; ssDNA/RSH/MNP	CNT composite electrode	[50]
	D6	MWNT/GCE; probe-ssDNA-MNP; target-ssDNA-ALP		[89]
	D7	MB; ssDNA-cMWNT-array/Au	Oriented modification, covalent attachment	[33]
	D8	DNR; ssDNA-cMWNT-PtNP-Nafion/GCE	Covalent attachment	[90]
	D9	MWNT/GCE; probe-ssDNA1-cCNT-ALP; probe-ssDNA2-MNP		[91]
	D10	MWNT/GCE; probe-ssDNA1/PSS/ALP-PDDA(LBL)/SWNT; probe-ssDNA2-MNP		[92]
DNA and nucleic acids	D11	SWNT/GCE		[26]
	D12	MWNTPE	CNT composite electrode	[49]
	D13	MB; DNA/MWNT-chitosan/graphite	Direct adsorption	[93]

If not indicating “oriented modification” in the column of “Design principles”, “non-oriented modification” is a default design principle.

c carboxylized, *ALP* alkaline phosphatase, *CPE* carbon paste electrode, *DNR* daunomycin, *GCE* glassy carbon electrode, *LBL* layer-by-layer technique, *MB* methylene blue, *MNP* magnetite nanoparticle, *MWNTPE* MWNT paste electrode, *NP* nanoparticle, *PDDA* poly(diallyldimethylammoniumchloride), *PPy* polypyrrole, *PSS* poly(sodium 4-styrenesulfonate), *RSH* mercaptoacetic acid, ssDNA single-stranded DNA

Table 2-4 Summary of biomolecule-free CNT-based biosensors for various biological molecules

Analyte	Occurrence	Electrodes	Ref. No.
L-Cysteine	Biological system	Pt/CNT/graphite	[6]
Cytochrome <i>c</i>	Biological system	aSWNT/GCE	[23]
		AuNP/MWNT/DHP/Au	[6]
Dopamine	Brain blood	tissue, CNT/bromoform/glass-tube	[46]
		MWNT-Nafion/CFE	[15]
		PSS/SWNT/GCE	[6]
Folic acid	Tissue, products	food MWNT/Au	[24]
Glutathione	Biological system	CNT-array	[31]
Indole-3-acetic acid	Plant cells	MWNT/GCE	[6]
Lincomycin	Pharmacy	MWNT-DHP/GCE MWNT-SDBS/GCE MWNT-Nafion/GCE	[6]
Morphine	Blood, fluids	body MWNT/GCE	[29]
NADH	Living cells	MWNT/GCE	[14]
		TB/MWNT/BPPG	[21]
		AC/MWNT/BPPG	[21]
		TBO-CHIT-MWNT/GCE	[6]
		AZU-CHIT/MWNT/GCE	[6]
		CNTEC	[94]
Nitric oxide	Biological system	Nafion/MWNT/GCE	[6]
		Myb/MWNT/GCE	[6]
Phenolic compounds	Water, products	food MWNT-Nafion/GCE	[16]
Procaine	Pharmacy	MWNT/GCE	[20]
Theophylline	Pharmacy	cMWNT/GCE	[22]
Quercetin	Flavor, pharmacy	MWNT/Ch/graphite	[27]
Rutin	Plants	MWNT- β -CD/GCE	[95]
		SWNT/Au	[25]
Thiocholine	Environment	CNT/GCE	[6]

a activated, *AC* azure C, *AZU* Azure dye, *BPPG* basal plane pyrolytic graphite, *CD* cyclodextrin, *CFE* carbon fiber electrode, *Ch* choline, *CHIT* chitosan, *CNTEC* CNT-epoxy composite, *DHP* dihexadecylphosphate, *GCE* glassy carbon electrode, *Myb* myoglobin, *NP* nanoparticle, *PSS* poly(styrene sulfonic acid) sodium salt, *SDBS* sodium dodecylbenzenesulfonate, *TB* toluidine blue, *TBO* toluidine Blue O

Table 2-5 Summary of bimolecular-functionalized CNT-based biosensors

Analyte	Occurrence	Biomolecule functionalized on electrode	Electrodes	Design Principles	Ref. No.
Cholesterol	Blood	Cholesterol oxidase (ChOx)	PDDA-ChOx(LBL)/cMWNTs/Au	Entrapment	[79]
			ChOx/MWNT/SPE	Direct adsorption	[96]
			ChOx-SGC/PtNP/CNT/graphite	Nanoparticle decoration, entrapment	[54]
			ChOx/PVA/MWNT-array/Si	Oriented modification, direct adsorption	[32]
Choline	Tissues	Choline oxidase (ChOx)	ChOx-SGC/MWNT/Pt	Entrapment	[97]
Dopamine	Brain tissue, blood	DNA	DNA/CNTPE	CNT composite electrode	[47]
DNA	Bioassays	ssDNA	See Table 2-3		
Glucose	Blood, body fluids	Glucose oxidase (GOx)	See Table 2-2		
Lactate	Human sweat	Lactate oxidase (LOx)	LOx/cSWNT/GCE	Direct adsorption	[98]
			LOx/cSWNT/Si/ITO		
Organophosphate compounds	Agriculture, environment	Acetylcholinesterase (AChE)	LOx/CNTPE	CNT composite electrode, direct adsorption	[48]
			AChE/MWNT/SPE	Direct adsorption	[75]
		Organophosphorus hydrolase (OPH)	PDDA-AChE(LBL)/MWNT/GCE	Entrapment	[6]
Phenolic compounds	Water, food products	Polyphenol oxidase (PPOx)	OPH/MWNT-Nafion/GCE	Direct adsorption	[17]
		Tyrosinase (Ty)	PPOx/CNTPE	Direct adsorption	[48]
Putrescine	Tissue, pharmacy	Putrescine oxidase (POx)	Nafion/Ty/SWNT/GCE	Direct adsorption	[76]
			Glutaraldehyde/POx/APTES-MWNT-Nafion/GCE	Entrapment	[18]

If not indicating “oriented modification” in the column of “Design principles”, “non-oriented modification” is a default design principle.

c carboxylized, *APTES* γ -aminopropyltriethoxysilane, *CNTPE* CNT paste electrode, *GCE* glassy carbon electrode, *ITO* indium tin oxide, *LBL* layer-by-layer technique, *NP* nanoparticle, *PDDA* poly(diallyldimethylammoniumchloride), *PVA* polyvinyl alcohol, *SGC* sol-gel composite, *SPE* screen-printed electrode

2.4.2.2.1 Glucose

Glucose is the principal circulating sugar in the blood and the major energy source of the body. A high fasting blood sugar level is an indication of prediabetic and diabetic conditions. As a result, a tight monitoring of blood glucose level is one of the most frequently performed routine analyses in clinics and hospitals.

Conventionally, enzyme GOx is used in biosensors to detect the concentration of glucose. GOx catalyzes the oxidation of β -D-glucose into D-glucono-1,5-lactone, while oxygen (O_2) acts as the final electron acceptor and is then reduced to hydrogen peroxide (H_2O_2) whose presence can be electrochemically detected. The concentration of glucose is determined by the resulting oxidative current on the electrode.

We compiled the design and performance characteristics of reported CNT-based glucose sensors in a descent order of sensitivity in Table 2-2. It should be noted that since surface area of the electrodes are not reported in most of these papers the total electrode current is referred here as sensitivity.

One can see that most sensitive glucose biosensors were decorated with metallic nanoparticles. The sensor with Cu Nanoparticle (G1) exhibited the highest sensitivity of $256 \mu A/(mmol/L)$ as shown in Figure 2-17a. But the linear range from 2.5×10^{-4} to 0.5 mmol/L was much lower than the clinical requirement. Pt nanoparticle-decorated sensor G2, G3 and G5 showed preferable linear detection range. Figure 2-17b illustrated the responses of sensor G5 to glucose with and without Pt nanoparticle attachment. Both G2 and G3 used a pre-selective membrane Nafion to improve the

selectivity of these sensors. The difference is that G3 utilized Nafion as solubilizing agent of CNTs, while a thin Nafion layer was coated on the surface of CNT-modified electrode in G2. Compared with other nanoparticles decorated CNT-based glucose biosensors (G1, G3, G5 and G16), G2 showed a superior performance with relatively high sensitivity and clinically compatible detection range.

Figure 2-16 (a) The performance of sensor G1 with CuNP-SWNT-Nafion/GCE (refer to Table 2-2) in amperometrically detecting glucose of different concentrations, 0.5, 1.0, 5, 20, 50, 100 $\mu\text{mol/L}$ at 0.65 V vs. Ag/AgCl (3 mol/L NaCl). (Inset) addition of 0.5 $\mu\text{mol/L}$ and 1.0 $\mu\text{mol/L}$ of glucose, respectively. Reprinted from [52] with permission. (b) Real-time monitor of successive addition of 2 mmol/L glucose at the biosensors (i) with Pt nanoparticles and (ii) without Pt nanoparticles measured at 0.1 V vs. SCE. (Inset) the calibration curve for the glucose addition. Reprinted from [44] with permission.

Immobilization of GOx on the electrode surface using entrapment methods (electropolymerization and encapsulation) was also commonly adopted. G6 immobilized GOx on a poly-o-aminophenol (POAP) electropolymerized electrode surface. GOx was immobilized in a Nafion matrix in G8. Both G9 and G18 entrapped GOx within an electropolymerized PPy film, but G18 exhibited a much lower sensitivity. This could be attributed to the fact that the MWNTs were in direct contact with the substrate of G9, while the CNTs were just suspended and loosely contacted with the substrate of G18. G11 and G15 both encapsulated GOx into a sol-gel

composite, and the resulted sensitivities were 196 and 18 nA/(mmol/L), respectively. In G13 and G14, LBL technique was utilized to entrap GOx with CNTs at the surface of the electrode. In this category of sensors, G11 is more suitable for clinical applications.

In term of the response time, Pt Nanoparticle-decorated sensors S2 and S3 demonstrated the fastest response of less than 5 s with high sensitivity. Some biosensors prepared by entrapment of GOx, namely G8 and G11, also showed a fast response, whereas, the sensors without GOx, such as G1 and G10, had relatively slow response.

2.4.2.2.2 Dopamine

Dopamine is an essential neurotransmitter for normal functioning of the central nervous system. It is also used as a medication that acts on the sympathetic nervous system, producing effects such as increased heart rate and blood pressure. Obviously, precise determination of dopamine in brain tissues is demanded in clinical diagnoses. The first reported biosensor using CNTs modified electrode was a dopamine biosensor by Britto et al. [46]. Figure 2-18a depicts the differential pulse voltammetry (DPV) response of this sensor for various concentrations of dopamine. CNT-modified electrodes, combined with negatively charged pre-selective membrane, including Nafion [15] and poly(styrene sulfonic acid) (PSS) [6], were used to detect dopamine in the presence ascorbate and ascorbic acid. Hocevar et al. invented a disposable dopamine microsensor utilizing MWNT and Nafion modified carbon fiber microelectrode to achieve a linear detection range from 2 to 20 $\mu\text{mol/L}$ and a

detection limit of 70 nmol/L [15]. The dopamine sensor based on PSS/SWNT/GCE exhibited good performance, such as a large dynamic range (16 nmol/L-600 μ mol/L) and a low detection limit (8 nmol/L) [6]. A novel DNA immobilized CNT composite electrode was used to detect dopamine with an ultralow detection limit of 0.021 nmol/L [47] (Figure 2-18b). Polyphenol oxidase (PPOx)-modified CNT paste electrode was also used to detect dopamine with a detection limit of 1 μ mol/L [48].

Figure 2-17 (a) DPV responses (left) and the corresponding calibration plot (right) of dopamine in PBS at a MWNT composite electrode. Marks from No. 1 to 6 corresponded to 0, 200, 400, 600, 800, 1000 mmol/L addition of dopamine. Reprinted from [46] with permission. (b) The calibration curve of square-wave (SW) stripping voltammetry of dopamine at various concentrations: (i) 0, 10, 20, 30, 40, 50, 60, 70, 80 and 100 mg/L; and (ii) 0, 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.1 and 0.11 μ g/L at optimal conditions. (Inset) (i) anodic and cathodic SW stripping voltammograms; (ii) SW anodic and CV voltammograms. Reprinted from [47] with permission.

2.4.2.2.3 DNA

DNA is the genetic material that holds the inherited instructions for growth, development, and cellular functioning. The development of an effective DNA-sensing system, therefore, is of great interest. Besides traditional DNA detection techniques such as fluorescent, radiochemical and chemiluminescent methods, electrochemical methods are attractive for their simple and low-cost solutions to DNA analysis ([99] and references within).

The use of CNT in electrochemical DNA sensors has recently attracted many researchers. A number of such sensors reported in the literature are listed in Table 2-3. They have been utilized to detect DNA [26, 49, 93] or DNA hybridization [33, 35-37, 50, 86-92].

One of the commonly used methods to prepare CNT-modified sensors for DNA hybridization detection was to attach ssDNA onto carboxylized-CNT modified electrode (e.g., D1-D4, D7, D8 in Table 2-3). Sensors of this kind can report a current signal when the complementary DNA sequence (target) hybridizes with the immobilized ssDNA (probe). The first of such sensors (D1 in Table 2-3) was based on a ssDNA-modified MWNT/GCE. ssDNA of 24 base long was detected using DPV in the presence of the electroactive intercalator daunomycin (DNR). The average anodic current of DNR was linear with the concentration of complementary ssDNA in the range of 0.2 nmol/L to 50 nmol/L with a detection limit of 0.1 nmol/L. Owing to its excellent selectivity, this sensor can report mismatch of even a few bases. The hybridization of less than 10⁶ DNA targets can be measured by combining the MWNT nanoelectrode array (MWNTNEA) electrodes (D3 in Table 2-3) with Ru(bpy)₃²⁺ mediated guanine oxidation [35]. When dealing with the long single-

stranded PCR amplicon with a large number of inherent guanine bases, the detection limit was further lowered to under ~ 1000 target DNAs [36]. Sensor D8 (Table 2-3) realized a detection limit of 0.01 nmol/L for target DNA by using CNTs to promote electro-transfer reactions and platinum nanoparticles for its high catalytic activities, and employing DNR as an indicator for hybridization reaction (Figure 2-19). Using methylene blue (MB) as a redox indicator, a DNA-hybridization sensor (D7 in Table 2-3) was fabricated on self-assembled MWNTs with covalently attached probe DNAs, as shown in Figure 2-20.

Figure 2-18 DPV voltammograms of Pt nanoparticles decorated ssDNA-MWNT/GC electrodes for different concentrations of target DNA: (a) 2.25×10^5 pM; (b) 2.25×10^4 pM; (c) 2.25×10^3 pM; (d) 2.25×10^2 pM; (e) 2.25×10^1 pM; (f) 0.0 pM. (Inset) the corresponding logarithmic calibration plot. Reprinted from [90] with permission.

Figure 2-19 Schematic of the preparation of ssDNA-MWNT-array modified Au electrodes and the detection of target ssDNA sequences in the presence of an indicator, methylene blue (MB). Reprinted from [33] with permission.

DNA-hybridization sensors were also developed in the absence of any indicator. D2 (Table 2-3) detected DNAs on a probe DNA-doped PPy film deposited onto MWNT/GCE via AC impedance measurement. When hybridization occurred, a decrease of impedance value was observed. To construct sensor D4 (in Table 2-3), carboxylized MWNTs were first linked onto a carbon paste electrode (CPE) via hybridization between bridging DNA molecules. And then the covalent binding of the probe DNAs to the MWNTs was followed. Such sensor provided a larger surface area for DNA immobilization and consequently exhibited a detection limit down to 10 pg/mL.

Magnetite nanoparticle (MNP) incorporated CNT sensors were demonstrated for DNA hybridization detection. For example for D5 in Table 2-3, a MWNT/PPy-modified GCE detected the DNA hybridization by capping the ssDNA probes with mercaptoacetic acid (RSH)-coated MNPs. It showed superior hybridization

selectivity thus the ability to discriminate mismatched DNA sequences. The degree of hybridization relates to the peak reduction current of the indicator - DNR. The detection limit of target DNAs was as low as 2.3×10^{-14} mol/L. Wang and his group developed several enzyme-based electrochemical sensors (D6, D9 and D10 in Table 2-3) for the same purpose. In the example of D6, MNPs attached with probe ssDNA were used to receive the target ssDNA tagged with alkaline phosphatase (ALP). The hybridization was reported by the enzymatic activities of ALP using a MWNT/GCE. The hybridization information could be acquired from the enzymatically liberated products on a MWNT/GCE. CNTs played a dual-amplification role in both recognition and transduction events for sensors D9 and D10 in Table 2-3. In these applications, the CNTs not only were loaded with various enzyme ALP tags for hybridization detection, but also helped to retain and accumulate the product of the enzymatic reaction. Such sensors could detect DNA down to 80 copies (5.4 amol/L). The difference between D9 and D10 was that the ALP tracer was immobilized on CNTs by LBL method in D10.

Other CNT modified electrodes for DNA detection are also listed in Table 2-3: SWNT/GCE (D11), MWNTPE (D12), and DNA/MWNT-chitosan/graphite electrode (D13).

2.4.3 Field-effect transistors based on SWNTs

SWNT based field-effect transistors (CNTFETs) have recently emerged as novel candidates for molecular electronics and biosensors. SWNTs are one-dimensional structures whose conductance is extremely sensitive to electronic perturbations

produced by variations of surface potential because all of the current flows at the surface of the nanotubes. While SWNT serves as the conducting channel exposing directly to the sensing environment, CNTFET devices are highly responsive to the binding events of specific molecules as well as other subtle chemophysical changes of the immediate surrounding environment. CNTFETs have been used to sense various chemical gases such as NO_2 , NH_3 and etc. [59, 100, 101], biocatalytic processes, biological species and events and so on. CNTFETs have been used to detect these species in two different ways. One is the chemiresistor configuration in which the real-time conductance change of CNT is monitored during analytes addition, while the gate voltage is fixed to the ground or certain level. The other way is to monitor the field-effect modulated conductance after introduction of the analytes. This kind of sensors sometimes is referred as chemFET.

In the following, we enumerate various papers utilizing CNTFET in biosensing applications, and also compile these biosensors and some of their aspects in Table 2-6.

Table 2-6 Summary of the biosensors based on CNTFETs

Objective	Biomolecule functionalized SWNTs	on	With a linker layer? (Y/N)	Ref.
Protein recognition	Biotin, SpA, U1A	Y		[63]
	Biotin	Y		[58]
	hCG	N		[64]
	HA	Y		[73]
	α -PSA	N		[62]
	Anti-copper oxLDL	Y		[85]
	Thrombin aptamer	Y		[69]
	PSA-AB	Y		[71]
	SpA, hCG	N		[65]
DNA hybridization	PNA	Y		[72]
	ssDNA	N		[61]
	ssDNA	N		[66]
Enzymatic study	GOx	Y		[60]
	Starch	N		[67]
Protein adsorption	Cytc	N		[102]
	SA	N		[59]
	SA, IgG	N		[103]
Others	Cell membrane	N		[59]

α -PSA anti-pig serum albumin, *cytc* cytochrome c, *GOx* glucose oxidase, *hCG* human chorionic gonadotropin, *IgG* immunoglobulin G, *oxLDL* oxidized low density lipoprotein, *PNA* peptide nucleic acid, *PSA-AB* anti-prostate-specific antigen monoclonal antibody, *SA* streptavidin, *SpA* staphylococcal protein A, *ssDNA* single-stranded DNA

2.4.3.1 Protein recognition

Most of exploited biological applications of CNTFETs are to recognize specific protein. Antibodies, which selectively bind to the corresponding antigens, are usually used as the recognition receptors in CNTFET biosensors.

In its first reports application, Chen et al. [63] found that Tween-coated SWNTs exhibited excellent resistance to non-specific binding of various proteins. Taking advantage of this, CNTFETs coated with biotinylated Tween, staphylococcal protein A (SpA)-Tween and U1A antigen-Tween could real-time monitor the specific binding of streptavidin, IgG and 10E3 down to 1 nmol/L, respectively. The

interferences from the non-specific binding of other proteins were eliminated. Response of such device to 10E3 is depicted in Figure 2-21a. Star and his coworkers applied CNTFET devices to detect specific protein binding. A PEI/PEG polymer coating layer was used to prevent non-specific binding of proteins and as the molecular linker between SWNTs and the receptor proteins, biotin [58]. The biotin-streptavidin binding events were observed from the shift of transfer characteristics of the CNTFETs (Figure 2-21b). Another example for label-free detection of biomolecules was to differentiate low density lipoprotein (LDL) cholesterol between the reduced (native LDL) and the oxidized state (oxLDL) on an anti-copper oxLDL antibody conjugated CNT network-based FET, in which a PEI/PEG layer was appeared as the linker [85]. Complementary detection of prostate-specific antigen (PSA) was achieved by utilizing p-type CNTFETs and n-type In₂O₃ nanowire based FETs both anchored with anti-PSA monoclonal antibody (PSA-AB) via linking molecules [71]. The antibody, anti-pig serum albumin (α -PSA), was directly immobilized on SWNTs through non-specific adsorption without linking molecules [62]. Subsequent binding of the antigen, PSA, was investigated from the real-time monitor of the characteristic changes of CNTFETs. Considering their high specificity, relatively low-cost and capability of reversible denaturation, aptamers, which are artificial oligonucleotides, were used as an alternative to protein-based sensing elements [69]. CNTFET bound by 15-mer ssDNA aptamer via CDI-Tween was used to probe blood-clotting factor thrombin, achieving a low detection limit around 10 nmol/L.

Figure 2-20 (a) The Conductance vs. time curve shown that a recombinant human autoantigen functionalized CNTFET exhibited specific response to ≤ 1 nmol/L 10E3 mAbs. (Inset) the same device shown selectivity that reject the interference polyclonal IgG at a much larger concentration of 1 μ mol/L (Inset). Reprinted from [63] with permission. (b) Transfer characteristic change of a biotinylated polymer-coated CNTFET before and after exposing to streptavidin. Reprinted from [58] with permission.

In order to further understand the biosensing mechanisms of the specific protein recognition by CNTFET, Chen et al. conducted a series of control experiments by examining the effects of blocking selected areas of the devices on sensing properties [64]. They concluded that protein adsorption induced modulation in Schottky barrier occurring at the contacts between SWNTs and metallic electrodes dominated the measured biosensing signal. And the contribution from the exposed SWNTs was negligible if the adsorbed species were not highly charged. With this knowledge in mind, Byon and Choi purposefully modified the device geometry to increase the

Schottky contact area [65]. This modification was implemented by evaporating metallic source/drain electrode at a tilted angle using a shadow mask. In comparison with the detection limit in the sensing of proteins or protein-protein interactions demonstrated in the previous works [63, 64], which is ca. 100 pmol/L to 100 nmol/L, the devices with increased Schottky area could detect proteins at much lower concentration 1 pmol/L.

An alternative architecture, in which protein receptor hemagglutinins (HA) was immobilized on the back-gate of CNTFET via linking molecules instead of SWNTs channel, was proposed to detect anti-HA binding [73]. The detection limit of anti-HA was estimated to be 5×10^{-8} mg/mL, better than enzyme-linked immunosorbent assay (ELISA) system.

2.4.3.2 DNA hybridization

Nowadays, the development of genome diagnosis has been a subject with great interest. Label-free electronic methods, including the use of CNTFET based biosensors, are believed to be promising for sensitive, selective and inexpensive detection of DNA hybridization (Figure 2-22). The first SWNT transistor used for this purpose was developed in association with covalently immobilized amino modified peptide nucleic acid (PNA) oligonucleotides onto the Au surface of the CNTFET back gate via a self-assembled monolayer (SAM) [72]. This device could effectively detect the complementary DNA at an extremely low concentration of 6.8 fmol/L. Star et al. utilized CNT network FETs as selective detectors for DNA immobilization and hybridization [61]. The probe DNAs were non-covalently adsorbed on the SWNT

network instead of the back gate region. The devices were used for the label-free detection of DNA hybridization at picomolar to micromolar concentrations. It was found that the addition of Mg^{2+} during hybridization could improve the sensitivity of DNA detection probably by increasing the extent and overall efficiency of DNA hybridization on SWNTs. The mechanism of DNA detection using CNTFET devices, however, is still under debate. Star et al. suggested a charge-based mechanism [61]. In contrast, Tang and his coworkers demonstrated that DNA hybridization on the contact regions of the CNTFET caused a more significant contribution to the acute electrical conductance change, probably due to the modulation of energy level alignment at the contact of SWNTs and Au electrodes [66]. More experiments are still needed to clarify this issue.

Figure 2-21 Real-time monitoring of 15mer DNA hybridization in PBS on an ssDNA functionalized CNTFET. Two liquid cells were used in parallel for simultaneous drop adding 5 μL of complementary (dark grey) and mismatched (light grey) target oligo solutions to 500 μL of buffer. Reprinted from [66] with permission.

2.4.3.3 Enzymatic study

With GOx attached to the nanotube sidewall through linking molecules, a liquid-gated FET device was used for the detection of glucose (Figure 2-23) [60]. It was observed

that the immobilization of GOx induced a downward shift of the transfer characteristics (the source-to-drain current I_d versus the gate voltage V_G) of the FET sensor, which was probably due to a change in the capacitance of the tube. The addition of 0.1 mmol/L glucose solution increased the conductance of enzyme functionalized CNTFETs, but the exact mechanism was not explained. An alternative approach was used to detect the enzymatic degradation of starch on CNTFET [67]. Instead of enzyme, the substrate of an enzymatic reaction, starch, was attached to the devices surface directly, leading to a shift in the transfer characteristics of devices. After incubation of these devices in aqueous buffer solutions of enzyme amyloglucosidase (AMG), the curve of source-to-drain current versus gate voltage almost completely recovered to the same as measured before deposition of starch, suggesting that nearly all the starch were hydrolyzed to glucose and then washed away by buffer solution. AMG alone would not affect the device characteristics and the adsorbed starch could not be washed off by buffer solution.

Figure 2-22 Real-time monitoring of the GOx functionalized CNTFET to glucose. Arrows showed the addition of 2 μ L milli-Q water and 2 μ L 0.1 mmol/L glucose to the device. (Inset) the same measurement on a control CNTFET without GOx. Reprinted from [60] with permission.

2.4.3.4 Protein adsorption

Noncovalent adsorption of proteins, such as cytochrome c [102] and streptavidin [59, 103], IgG immunoglobulin G (IgG) [103], could also be simply detected by SWNT or SWNT-network based FET devices. Such non-specific binding on bare SWNTs alters the electrical characteristics of devices, presumably due to the electrostatic influence from the charged group on the protein molecules.

2.4.3.5 Others

Bradley et al. integrated a complex biological system, the cell membrane of *Halobacterium salinarum*, with CNTFET device, and found that both of them preserved their properties and functions [59]. Furthermore, the charge distribution in this biological system was investigated.

2.5 Noise analysis of CNT device

CNT possesses many novel properties which prompt its usage in a wide range of electronics applications, including nanometer-scale devices, thin-film transistor, and chemical and biological sensors. However, CNT based devices have an undesired property that they exhibit unexpected large electrical noise. Collins and his colleagues [104] firstly reported that in a wide variety of CNT based devices, including 1D individual isolated nanotubes, 2D thin films of interconnected nanotubes and 3D bulk nanotube mats, a large component of $1/f$ noise could be found (Figure 2-24). From the observation that a single empirical expression could describe the noise for all sample,

they suggested a common noise-generating mechanism proportional only to the number of nanotubes in the conductor.

Figure 2-23. Voltage noise power S_V vs. frequency for a single SWNT in three values of applied bias current. The dot line is the thermal noise limit $S_V = 4kTR$.

Snow and his research group [105] further explore the scaling behavior of $1/f$ noise in 2D CNT network devices. They also used an empirical expression,

$$S_V = \frac{AV^2}{f^b}$$

to calculate the noise amplitude A . They found that the noise scaled inversely with device size for devices with a given resistance. The noise amplitude was also found to be almost inversely proportional to the source-drain current with fixed V_{DS} but changing V_G (Figure 2-25). They proposed that field-induced charge fluctuations in the gate oxide is one possible causes.

Figure 2-24 The scaled noise amplitude A (circles) and the drain current (line) for a typical device plotted versus the gate bias applied to the Si substrate. The noise has maximum value when the device achieves a minimum off-state current and switches from p-type conduction to n-type conduction at $V_G = 1.6$ V.

Reza et al. [106] studied low-frequency noise over the 77-300 K temperature range and observed $1/f$ noise spectra coupled with Lorentzian shaped spectra. Because the suspended and supported nanotubes had same level of noise in their experiments, it is concluded that the nanotube oxide layer is not a significant source of excess noise. But the generation-recombination nature of the measured noise indicated that carrier number fluctuation is more dominated part than mobility fluctuations. Similarly, Briman et al. [59] also concluded that the carrier number fluctuations was the source of $1/f$ noise by applying gate potential through conducting liquid and avoiding SiO_2 -nanotube interaction contributed low frequency noise. Lin et al. [107] have conducted more comprehensive study by applying devices with different switching mechanisms, carrier types and channel lengths. The systematic study of current fluctuations in low-frequency region showed that these nano-devices exhibited significant $1/f$ type noise and for all devices, the $1/f$ noise level increased with device resistance R as the gate varied (Figure 2-26a), which is the same with aforementioned Snow's finding [105]. In addition, Lin et al. found that $1/f$ noise level is inversely proportional to the channel

length for SB-CNTFETs (Figure 2-26b) and the noise amplitude A was correlated with carrier number in the CNT (N) with the relation of $A \propto 1/N$. According to their assessment using Hooge's Empirical Rule

$$A = \frac{a_H}{N}$$

The intrinsic noise strength α_H of CNT was comparable to most bulk materials and the significant noise amplitude A in CNT devices were attributed to the small number of carriers.

Figure 2-25 (a) The drain current (left axis) and $1/f$ noise amplitude A (right axis) as a function of V_G of an SB-CNFET. The solid and dash lines are simulation results assuming a $1/f$ noise parameter $\alpha_H = 2 \times 10^{-3}$. (b) Normalized current noise power spectrum (S_I/I^2) of two CNTFETs with channel length of $7 \mu\text{m}$ (L) and $0.5 \mu\text{m}$ (S).

However, Ishigami and coworkers [108] predicted that the mobility fluctuation was the dominant mechanism for the noise in CNTFET. They conducted the experiments utilizing a CNTFET with individual semiconducting SWNTs and observed that the $1/f$ noise amplitude is inversely proportional to $|V_G - V_{th}|$ ($1/A \propto |V_G - V_{th}|$) (Figure 2-27). Then they substituted the carrier number N in Hooge's Empirical Rule by the total number of carriers in a 1D FET in the on states $N \propto |V_G - V_{th}|$, they got that the α_H is independent of gate voltage, which was corresponding to $1/f$ noise in MOSFETs

models based on mobility fluctuations. They also found that $1/f$ noise amplitude is inversely proportional to channel length and furthermore, it would not be affected by the surface adsorbates. Liu et al. [6] also suggested that the amplitude of $1/f$ noise was more likely to correspond to mobility fluctuation rather than number fluctuation for the narrow channel CNTs operating in strong inversion region with a small source-drain bias.

Figure 2-26 $1/A$ plotted against V_G . The solid line is a linear fit to the data.

Different with Ishigami and coworkers' finding [108] that the noise amplitude coefficient A in air is significantly smaller than that in ultra high vacuum, Vijayaraghavan et al. [69] reported an contrary finding: the $1/f$ type resistance fluctuation (noise) in both semiconducting and metallic SWNT devices with Ti/Au-contacts decreased while their resistance increased when putting devices in vacuum (Figure 2-28). And after brought back to ambient, the noise level and resistance of samples would recover to their original values. They concluded that the $1/f$ noise of semiconducting SWNTs (s-SWNT) might originate from their contacts since the Schottky contact dominated the total resistance of s-SWNT, and SB height fluctuation and/or effective doping fluctuation of CNT at the extended contact regions may be the possible mechanisms. They also reported that the s-SWNT devices had much higher

noise amplitude compared to m-SWNT ones, which was in agreement with Reza et al.'s observation [109]. In addition, Reza demonstrated that electrical annealing, which would cause Joule heating at contacts by current flow, would improve the conductance and lower noise level, which further shown that the contact part was the dominant source of $1/f$ noise.

Figure 2-27 the noise amplitude $A=S_I/I^2 \times f$ at ambient (lines 1 and 1') and in vacuum (line 2) for (a) m-SWNT and (b) s-SWNT devices. Line 1' shows A for m-SWNT after 24 h of the exposure to the atmosphere.

P. Avouris's group [110] explored the role of the contact region in $1/f$ noise property of CNTFET. They found that the type of contact metal had no significant effect on the $1/f$ noise of devices. Although devices with Pd contact had much larger channel current in comparison with Ti ones, their $1/f$ noise level was nearly the same. They explained that while the transport of an SB-CNTFET was dominated by the tunneling through the SB, the carrier number of holes inside the SWNT remained independent of SB height for a given $(V_G - V_{th})$, and $1/f$ noise was consequently not determined by

the contacts as they proposed previously that the noise amplitude was inversely proportional to the carrier numbers inside the channel. In addition, in order to reduce the intrinsic device noise level, they applied a tube transistor with multiple SWNT channel in parallel [111].

Chapter 3 Device Fabrication

In this chapter, we use the AC dielectrophoresis (ACDEP) method to manipulate the SWNTs and electrical breakdown method to selectively burn off metallic SWNTs. The ACDEP and electrical breakdown method will be discussed in details in this section.

3.1 Experimental setup

The high-purity SWNTs (95%) powder was purchased from Materials and Electrochemical Research Corporation. The as-prepared SWNT has average diameter of 1.4nm (obtained from Raman shift curves), and length of 10-50 μm . The SWNTs are in the form of bundles due to the aggregation nature of SWNTs which has high aspect ratio. The percentages of s- and m-SWNTs are around 60% and 40%, respectively. Figure 3-1 shows the TEM images and the AFM image of the tubes suspended in deionized (DI) water. On an average, the bundle is very big and wrap around to each other. Therefore, further treatment to the suspension is needed before device fabrication.

Figure 3-1 (Left) TEM image of SWNT bundles. Scale bar is 20nm. (Right) Enlarged view of SWNT bundles. Scale bar is 10nm.

The treatment is implemented in two steps. At first, SWNTs, surfactant (such as sodium dodecylsulfate (SDS) and Triton X100) and deionized water were mixed together. Then this suspension was treated with ultrasonic agitation. The SWNT bundles are found to become much smaller after this process. Unfortunately, the SWNTs are also severely shortened. The dispersion of the SWNTs depends on the type of surfactants, as well as the time duration of ultrasonic agitation. The detailed relationship between the dispersion and the agitation time is not clear yet. The concentration of the SWNTs in the suspension is around 0.1~0.5mg/L; but this value is not critical for the method. After that, the centrifugation at 10,000 rpm for 1 hr was followed. The upper 80% of the suspension was decanted for the second round of centrifugation. The usage of centrifugation processes is to remove some large particles and strongly aggregated CNT bundles. After that, an usage of a well dispersed suspension can be shown in connecting the SWNTs to the electrodes.

The substrate is a silicon wafer capped with a thermally grown SiO_2 layer. The parameters of the substrate are shown in Table 3-1. The metallic electrodes on the substrate are deposited using standard lithography and E-beam technology. The electrodes consist of an Au layer on the top of a Ti layer, which is used to increase the

adhesion between the Au layer and SiO₂ surface. The thicknesses of Au and Ti are typically 50 and 20 nm, respectively. Photos of the electrodes made from two different mask patterns and the schematic structure of the substrate with electrodes are shown in Figure 3-2. Figure 3-2a shows the mask with cross patterns and Figure 3-2b shows the mask with parallel patterns. Any pair of electrodes in the cross mask or parallel mask could be used as a “source” and “drain” electrodes shown in Figure 3-2c. The distance between two electrodes in cross mask varies from 1 to 4 μm , and that of the parallel mask is between 1 and 5 μm .

Table 3-1 Substrate parameters

Parameters	Data
Size (inch)	4
Type	P
Crystal orientation	<100>
Resistivity ($\Omega\text{-cm}$)	0.01-0.02
Thickness (μm)	500-550
Dielectric thickness (nm)	500, 200, 100 or 20 (thermally grown SiO ₂)
Remark	Prime silicon wafer, single side polish with a primary flat, thermal oxide on both side

Figure 3-2 (a) the photo of a cross-electrodes made from a mask with cross patterns. (b) The photo of a seven-electrodes made from a mask with parallel patterns. (c) Schematic structure of the substrate with patterned electrodes.

3.2 ACDEP method

With the SWNTs suspension and the substrate with predefined electrodes, we now proceed to the manipulation of the SWNTs. The method is systematically described

by Li et al. [112]. Let us take the cross-electrodes as an example. The setup of the ACDEP method is shown in Figure 3-3a. The suspension was agitated in the ultrasonic cleaner for 10mins and then dropped onto the electrodes, on which an AC bias was applied. The peak-to-peak voltage of the applied AC bias is between 4 and 16 V, depending on the electrode distance, while the frequency of the AC bias was 6~10 MHz. During the experiment, the AC bias was ceased several times to measure the resistance between the two electrodes. If such resistance decreased significantly compared to that before the AC bias was applied, say, from several $M\Omega$ to tens of $K\Omega$ or a few hundred $K\Omega$, SWNTs are likely to bridge the electrodes. Once the SWNT connection is confirmed, the AC bias was switched off immediately. After that the substrate was rinsed with DI water to wash away the excess CNT suspension and then blown dry with nitrogen gas. The number of SWNTs between the electrodes is determined by the deposition time and SWNT concentration of the suspension. The longer the deposition time, the more the SWNTs are deposited. The case for parallel electrode could be seen in Figure 3-3d.

Figure 3-3 (a) SEM image of Ti/Au cross-electrodes on a Si wafer. AC bias voltage is applied between two adjacent electrodes, as indicated in the figure. AFM images for SWNTs bridging the adjacent electrodes for a deposition time of (b) 50s and (c) 300s, respectively. The black arrows indicate the direction of the electric field. (d) The AFM image of SWNTs bridging through parallel electrodes by AC-DEP method.

The mechanism of ACDEP method is as follows. Two forces can drive CNTs in the suspension to the electrodes. The first is the electrophoretic force due to charge, the second is the dielectrophoretic force due to the dielectric constant difference between CNTs and the solvent medium. The time-averaged dielectrophoretic force can be expressed approximately as follows:

$$\frac{\mathbf{r}}{F} \propto \mathbf{e}_m \frac{\mathbf{e}_p - \mathbf{e}_m}{\mathbf{e}_p + 2\mathbf{e}_m} \nabla E_{rms}^2 \quad (3)$$

where ϵ_m and ϵ_p are the dielectric constant for the solvent medium (IPA) and the SWNTs, respectively, E_{rms} is the average electric field strength. $\epsilon_m = 18.3\epsilon_0$ for IPA as solvent and $\epsilon_p = 2000\epsilon_0$, $2 \sim 5\epsilon_0$, $15\epsilon_0$ for m-SWNTs, s-SWNTs and graphite,

respectively. Since the high frequency AC bias is used here, the electrophoretic force did not affect the motion of the SWNTs because of time averaging effect. Because the permittivity of the SWNTs is larger than the other contaminations (for example, amorphous carbon) in the suspension, contaminations were rarely found between electrodes under the high frequency bias.

3.3 M-SWNTs breakdown process

As there are 40% of m-SWNTs in the suspension, most of the bridged SWNTs bundles in between two electrodes are a mixture of m- and s-SWNTs. Since the conductance of semiconducting SWNTs display strong dependence on the gate voltage, we can switch off these semiconducting SWNTs by adjusting the gate voltage V_G so that most of current will pass through m-SWNTs after the semiconducting SWNTs are switched off. With a sufficiently high V_{DS} , a large current passes through the m-SWNTs and generates enough heat to burn them off, leaving the semiconducting SWNTs essentially intact. Thus the I_{ON}/I_{OFF} of the devices increases. The high I_{ON}/I_{OFF} indicates that most of the current are contributed by s-SWNTs and almost all of the m-SWNTs are burnt off. After the electric breakdown process, only s-SWNTs left behind so that CNTFET exhibits strong semiconducting property with high I_{ON}/I_{OFF} .

The mechanism for the electrical breakdown is as follows. Heat generated by large current causes oxidation at the sites of the defects on the SWNTs. The m-SWNTs may be not burnt off together at one time. The authors suggest that the outmost m-SWNTs in the bundle are likely to be bunt off first due to being fully exposed to

oxygen, while the inner m-SWNTs are more stable and need a higher current to burn them off.

3.4 Top-gated CNTFET fabrication

For top-gate SWNT-FET, top insulating layer (SiN_x) deposition by PECVD and then 2nd round lithography and E-beam deposition was needed to achieve this structure (Figure 3-4). For DWNT-FET with back-gate or top-gate configuration, the fabricating process was the same with SWNT ones.

Figure 3-4 Schematic of CNTFET with top-gate configuration

Chapter 4 Results and Discussion

4.1 Organophosphate detection

Organophosphorus (OP) compounds are among the most toxic substances and they are thus commonly used as pesticides, insecticides and chemical warfare agents [113]. There has been growing demand for reliable on-site monitoring of OP compounds. Common laboratory-based analytical techniques for detecting OP compounds primarily include either gas or liquid chromatography. Both processes are expensive and time-consuming [114]. In the past decade, biosensors based on inhibition of acetylcholine esterase (AChE) have been widely used for detecting OP compounds. Unfortunately, such inhibition biosensors typically have very poor selectivity and do not function on a real-time basis. They are only for single use due to the irreversible inhibition of enzyme activity.

Recently, fast and direct detection of OPs is possible by applying the biocatalytic action of organophosphorus hydrolase (OPH), where OPs were used as the sensor substrates. As a result, OPH is extremely attractive for the potential application in detecting OP compounds [115]. The CNT-based OPH amperometric biosensors have been reported recently for organophosphates [17, 75], but they are still based on MWNTs modified electrochemical detection.

In this project, we demonstrate the first OPH-functionalized SWNT based electronic biosensor for real-time OPs detection, such as paraoxon in our experiment (Figure 4-

1b). This biosensor is based on the enzymatic reaction of paraoxon, which is different with most of other CNTs based electronic biosensors because the sensor function of these biosensors, developed on SWNTs, were based on the conductance change of SWNT induced by binding events, such as antigen-antibody binding and DNA hybridization.

4.1.1 Experimental details

Similar with the fabrication processes described in the last chapter, 1 mg commercial SWNTs with 95% purification (MER Inc.) were firstly suspended in 100 ml deionized water with 1 wt% sodium dodecyl sulfate (SDS). The suspension was ultra-sonicated for 2 hrs, followed by centrifuged at 10,000 rpm for 1 hr. The upper 80% of the suspension was decanted for the second round of centrifugation. After that, the well-dispersed suspension was ready for connecting the SWNTs to the electrodes. The SWNT sensors were fabricated on p-type silicon wafers with a 500-nm-thick SiO₂ layer. A pair of 20-nm Ti/40-nm Au electrodes was patterned on the SiO₂ layer using conventional e-beam deposition and photo-lithography processes. AC dielectrophoresis method was used to assemble SWNTs to the electrode pairs [56, 116]. After a 2 μ l droplet of the SWNT suspension was introduced to the device area, an AC bias with 10V peak-to-peak voltage at a frequency of 6MHz was applied for 1 min. In order that the biomaterials can well adsorb on the surface of the SWNTs, the devices were rinsed with deionized water and soaked in it for overnight to completely remove SDS residuals [6, 117]. Selective electrical breakdown process [57] was applied to remove metallic SWNTs and ensure a better electric contact between the

semiconducting SWNTs and electrodes. From Figure 4-1a, one can see well aligned SWNT bundles bridging the electrode pairs.

Organophosphorus hydrolase was used to functionalize the SWNT bundles through non-specific binding. A trace volume of OPH solution (in 0.01M pH 7.4 phosphate buffer) was introduced onto the SWNTs by a pipette as shown in Figure 4-1b. After one hour the samples were rinsed with deionized water to remove unbound enzyme and buffer residuals and dried with nitrogen.

Figure 4-1 (a) SEM picture of a typical SWNT sensor. Well aligned SWNT networks connect the electrodes. The scale bar is 1 μm. (b) Schematic of paraoxon detection based on an OPH functionalized SWNT electronic sensor.

The electrical properties of the SWNT sensors were characterized using a precise semiconductor parameter analyzer (HP 4156B) at room temperature. During the measurements, the voltage difference between the electrodes was kept at 200 mV.

4.1.2 Results and discussion

The non-specific binding (NSB) of OPH on the SWNTs was confirmed by atomic force microscopy (AFM) images shown in Figure 4-2a. Before OPH immobilization, the height of the SWNTs was constant over its length. While, after OPH immobilization, the average height was found to increase by 3 to 5 nm. This increment in the height is in good agreement with OPH dimension of a few nanometers observed by Lei et al [118]. The spontaneous adsorption of OPH is attributed to the strong hydrophobic interaction between the SWNTs and enzyme [68, 119, 120].

OPH NSB can be further verified from the downward shift in the curves of source-drain conductance vs. gate voltage of the SWNT sensors before and after OPH binding as shown in Figure 4-2b. The gate voltage V_G was applied to the silicon substrate. This phenomenon can be interpreted as follows. First of all, the adsorbed enzyme could induce a significant scattering potential and act as carrier scattering sites along the SWNTs [58], leading to a decrease in the conductance. Secondly, it has also been reported that protein adsorption can reduce the work function of gold electrodes [121]. As a result, the height of the Schottky barriers (SB) between the metallic electrode and SWNTs is increased and the resistance to hole transport in the SWNTs is also increased, thus a decrease in channel conductance. Electron donation of amine groups of OPH is the third possible mechanism [59].

Figure 4-2 (a) AFM images of a typical SWNT sensor before and after OPH immobilization. The scale bar is 1 μm. (b) Curves of source-drain conductance vs. gate voltage of the SWNT sensor before and after OPH immobilization.

Preliminary result shown in Figure 4-3 suggests OPH-functionalized SWNT sensors are sensitive to paraoxon. In order to eliminate the influence of pH change on the conductance due to the enzymatic hydrolysis of paraoxon, all samples were prepared in 0.01M pH 7.4 phosphate buffer solution and all measurements were conducted in the same buffer. The device was first wetted with 1 μl buffer. The addition of 1 μl buffer did not cause any significant conductance change of the wetted SWNT sensors.

However, when 1 μL of 50 μM , 200 μM and 1 mM paraoxon in phosphate buffer was injected using a pipette, the conductance of the sensors showed a rapid decay to a new saturated conductance. The appeared steep increase when adding paraoxon may be caused by the injection action, but since we measured the response according to the decreased scale of conductance, such sudden increases only have a little bit affection on our measurement. Figure 4-3 inset a showed the relative conductance change of the device as a function of calculated final concentration of paraoxon. The nonlinear response to paraoxon concentration might be attributed to saturation kinetics of enzymatic reaction.

Figure 4-3 Real-time response of an OPH functionalized SWNT sensor to phosphate buffer and different concentrations of paraoxon. The SWNT channel of the sensor was immersed in 1 μL buffer initially. The p-type silicon was connected to ground. Inset shows relative conductance change of the device as a function of OP concentration.

After the device was heated at 80 $^{\circ}\text{C}$ for 1 hr to inactivate the enzyme, it showed an insignificant response to 1 mM paraoxon (Figure 4-4a). Additionally, the as-prepared

CNTFET without immobilized OPH showed an insignificant response to 1mM paraoxon as well (Figure 4-4b). Both of control experiments suggest that OPH does play a key role in the detection of paraoxon.

Figure 4-4 (a) The response of a device with inactive OPH to paraoxon. (b) The response of as-prepared CNTFET without OPH to paraoxon.

We also test the re-usability of the devices. The responses of another OPH functionalized SWNT sensor to the buffer and paraoxon buffer solution, respectively, were examined and they showed similar characteristics as the previous device (Figure 4-5). After the device was rinsed and blown dry with N_2 , the second round of measurement was conducted. One can see that before paraoxon addition, the baselines of the two round experiments were nearly overlapped. Interestingly, the device was

still active to respond to paraoxon in the second round test. In comparison with the first round, the relatively small and slow response could be caused by the fact that some non-covalently immobilized OPH molecules were washed away during rinsing process before the second round detection. Furthermore, in tens of devices we fabricated, more than half of them responded to paraoxon, and the malfunction ones may be caused by inactive OPH, showing that the reproducibility of the sensor is accepted and could be improved further.

Figure 4-5 the response of another OPH functionalized SWNT sensor to phosphate buffer and paraoxon. After the first round test, the device was rinsed and blown dry with nitrogen. Before the second round real-time measurement, 1 μ l phosphate buffer was used to wet the SWNT channel. The p-type silicon was connected to ground.

The mechanism of the conductance decreasing with paraoxon addition is still under investigation. We suppose that the sensing signal may come from the hydrolyzed products, or OPH molecules themselves. OPH hydrolyzes paraoxon to generate *p*-

nitrophenol (PNP) and diethyl phosphate. According to our experimental results, PNP increases the conductance (Figure 4-6a) while diethyl phosphate decreases the conductance (Figure 4-6b). Interestingly, the mixture of same concentration of PNP and diethyl phosphate only cause a decrease in the conductance as shown in Figure 4-6c. From these observations, we hypothesize that hydrolyzed products could contribute to the conductance change. Furthermore, it has been suggested that in the catalytic reaction OPH undergoes deformation [60], resulting the change of charge status on the surface of enzyme. This deformation could not only affect charge transfer of enzyme molecules to the bulk part of SWNTs, but also further change the height of SB at the contact region between SWNTs and metallic electrodes, since CNTFET is basically a SB-FET [122] and the adsorbates on the contact region may affect the conductance of CNTFET through SB height modulation. Since the exact mechanisms of OPs detection by OPH functionalized CNTFET are not clear yet, more experiments with optimized device structure are needed, for example, control experiments on devices with only contact region or channel region exposed so that the effects of contact part and bulk part of SWNTs during the OPs sensing could be distinguished.

Figure 4-6 (a) Real-time response of the device to PNP, one of the hydrolysis products of paraoxon. 1 μL phosphate buffer was dropped on SWNTs before the addition of PNP. The addition of PNP caused conductance increase. (b) Real-time response of the device to diethyl phosphate, another hydrolysis product of paraoxon. 1 μL phosphate buffer was dropped on SWNTs before the addition of diethyl phosphate. The addition of diethyl phosphate caused conductance decrease. (c) After the addition of 1 μL phosphate buffer to the SWNTs, a mixture with same concentration of PNP and diethyl phosphate was added, which is simulated to the hydrolysis products of paraoxon catalyzed by OPH. The net effect of PNP and diethyl phosphate shows the same trend as seen in Figure 4-3.

In conclusion, we have demonstrated a novel biosensor for real-time organophosphate detection using enzyme as the molecular recognition elements and SWNT bundles as the transducer. The real-time electrical conductance response of the sensors to the addition of paraoxon is attributed to the enzymatic hydrolysis. Changes of charge status of enzyme and the “electron” or “hole” doping effect of enzymatically hydrolyzed products are likely to be the dominant factors for the conductance response. Compared to the electrochemical detection method, the novel biosensors could serve as a simple and low-cost platform with real-time and re-usability

biosensing capability. Further functionalizing SWNT like selective polymer decoration may be utilized to improve the selectivity of our devices.

4.2 Nitrophenol compounds detection

This CNTFET based chemical sensor is different with most of other reported counterparts, such as chemical sensors for nitrogen dioxide [100, 123, 124], ammonia [59, 100, 124], carbon dioxide [125], dimethyl methylphosphonate (DMMP) [126, 127], etc., because in most of these cases, CNT based sensors were mainly used for the gas phase detection instead of the analytes in liquid, especially in aqueous samples, which are more complex due to the interference of the solvents used. Although Star et al. [128] reported to detect benzene derivatives in organic solvent cyclohexane, they only measured the transfer characteristic shift of these devices with different analytes but they did not show the dynamic variety of the device performance during experiments.

In earlier work, when analyzing one of the hydrolysis products of paraoxon, PNP, we found that addition of such nitrophenol compound could increase the conductance of as-prepared CNTFET (without OPH). In addition, Nitrophenol compounds, because of its toxicity, are listed as U.S. Environmental Protection Agency priority pollutants. Acute (short-term) inhalation or ingestion of nitrophenols in humans causes headaches, drowsiness, nausea, and cyanosis, etc. Therefore, there is an urgent demand to develop analytical and real-time devices to monitor nitrophenols for environmental control [129]. Chromatographic, electrochemical and immunoassay techniques, and microbial biosensors have been developed for monitoring

nitrophenols [129-131]. Although their sensitivity and selectivity are reasonable for practical applications, these methods are either time-consuming or expensive, or require skilled person to operate. Therefore, their application is limited.

In this project, we present SWNT-based devices for real-time nitrophenol detection in aqueous samples. The developed devices exhibit a sensitive concentration-dependent conductance response to nitrophenols and good re-usability in the real-time format. The detection mechanisms are discussed in detail.

4.2.1 Experimental details

Figure 4-7a shows the chemical structures of nitrophenol compounds, 2-nitrophenol, 3-nitrophenol, 4-nitrophenol (Sigma-Aldrich), which are used to characterize the device response. In order to eliminate pH change induced conductance variation, all the chemicals were prepared in 0.01M pH 7.4 phosphate buffers. Phenol, purchased from Sigma-Aldrich, which has similar structure as nitrophenols but without nitro group, was used in control experiments with a concentration of 10mM by dissolving in phosphate buffers.

Figure 4-7 (a) Chemical structures of nitrophenol compounds used in the experiments. (b) Schematic of the SWNT device and experimental setup in the nitrophenol detection. (c) Transfer characteristic of an as-prepared SWNT device. Inset: the SEM image of the device. The scale bar is 1 μm.

The experimental setup is shown in Figure 4-7b. The details of the device fabrication have been described in Chapter 3 [6]. The presented devices have a top-contact and bottom-gate structure configuration. For each device, the source-drain SWNT conductance (S) was characterized as a function of gate voltage V_G using a precise semiconductor parameter analyzer (HP 4156B) under ambient laboratory conditions. Our as-prepared device showed p-type characteristic (Figure 4-7c). The voltage difference between the source-drain electrodes V_{DS} was kept at 200mV. When measuring the transfer characteristic of the devices, the V_G was swept between -20V and +20V, while the p-type silicon used as a back-gate was connected to the ground during the real-time monitoring. The volume of applied aqueous samples was very

small in all experiments, so the sample could be held on the device without any problem of spilling off.

4.2.2 Results and discussion

We firstly use our SWNT devices to detect nitrophenols in aqueous sample (Figure 4-7). Typical real-time responses of a SWNT device to blank buffer, 10mM phenol in phosphate buffer and 4-nitrophenol in phosphate buffer were shown in Figure 4-8a. The conductance of the device did not change significantly with the addition of the blank buffer and phenol. Note that the variations exhibited in addition of the blank buffer and phenol are reasonable in the CNT devices, as there might be more or less surfactant residues around SWNTs or imperfect contacts between SWNTs and metallic electrodes, etc. The solution injecting action may introduce noise as well. However, the response to blank buffer and phenol is negligible compared to the response to the subsequent addition of 0.5 μ L 1mM 4-nitrophenol. As shown in Figure 4-8a, the addition of 4-nitrophenol caused a sharp increase in the conductance. Similarly, 2-nitrophenol and 3-nitrophenol also lead to a rise in the conductance, as shown in Figure 4-8b. A control experiment was conducted to measure the leakage current between the source and drain by dropping the nitrophenol solutions on bare devices without SWNTs. Only a negligible leakage current was detected (data not shown). Therefore, the results above indicate that the nitro groups do play a key role in the variation of the SWNT conductance.

Figure 4-8 (a) Real-time responses of the SWNT device to buffer, phenol and 4-nitrophenol, respectively. 1.5 μ L buffer was dropped onto the device before measurement. After introducing buffer and phenol in phosphate buffer, 0.5 μ L 1 mM 4-nitrophenol in buffer solution was injected. (b) Real-time responses of the SWNT device to the phosphate buffer solution of 2-nitrophenol, 3-nitrophenol and 4-nitrophenol, respectively.

In addition, the device, first wetted with 1 μ l buffer, exhibited the concentration-dependent conductance change to nitrophenols, as shown in Figure 4-9. One can see that, when 0.5 μ l of 50 μ M, 100 μ M, 250 μ M, 0.5 mM, and 1 mM 4-nitrophenol in phosphate buffer were introduced to the device consecutively, the response of the device ($\Delta S/S_0 \times 100\%$) was nearly linear to the calculated final concentration of 4-nitrophenol in phosphate buffer (see the inset of Figure 4-9).

Figure 4-9 Real-time responses of a typical SWNT device to consecutive additions of 0.5 μL 4-nitrophenol in phosphate buffer with concentration of 50 μM , 100 μM , 250 μM , 0.5 mM , and 1 mM , respectively. The SWNT channel of the device was immersed in 1 μL buffer initially. The calculated final concentrations of 4-nitrophenol after each injection are indicated in the figure. Inset: The relative conductance change of the device versus 4-nitrophenol concentrations.

The reusability of the SWNT device, important for its practical use, is also studied as follows. Figure 4-10 shows the responses of another SWNT device to the blank buffer and 4-nitrophenol buffer solution. Normalized data obtained from this and previous devices indicate similar response characteristics. Before each test, 2 μL phosphate buffer was used to wet the SWNT channel. After the first round test, the device was refreshed by rinsing it with deionized water and blown-dry with nitrogen, and then the test was repeated. One can see that the device still showed good response to 4-nitrophenol. No significant difference in the response of conductance to 4-nitrophenol in two rounds of tests could be found.

Figure 4-10 Two-round measurements for the re-usability of a SWNT device. Before each test, 2 μL phosphate buffer was used to wet the SWNT channel. After introducing 0.5 μL buffer, 0.5 μL 20 μM 4-nitrophenol in buffer solution was injected. The device was rinsed and blown dry with nitrogen after the first round test.

The detection mechanism is still under argument. First, charge transfer between the nitro group and SWNTs could contribute to the increase in conductance. When the SWNT channel is immersed in aqueous samples, because H_2O molecule was reported to have weak or even negligible electron-donating nature [132, 133], the devices are still p-type [69]. As the hydroxyl group ($-\text{OH}$) only has a comparably weak electron-donating capability with H_2O molecule [128, 134] and adsorption of benzene only induces minor changes in the electrical properties of SWNTs suggested by theoretical calculation [135, 136], the conductance variation caused by the charge transfer of phenol and benzene ring of phenol to SWNTs is believed to be insignificant in the aqueous solution, consistent with our experimental result in Figure 4-8a Compared to water molecule and phenol, the nitro group ($-\text{NO}_2$) is usually of nearly maximal electron-withdrawing power [134]. Moreover, as the nitrophenol molecules with aromatic structure can stack on SWNTs through π - π interaction like benzene and

phenol, in addition to the strong electron withdrawing capability of nitro groups, the carrier transfer between the SWNTs and adsorbed molecules in the close proximity of SWNTs is more effective, and subsequently increases the hole density in the SWNT channels and its conductance as well. Second, modification of the Au-CNT interface due to chemicals adsorption may also play an important role [101]. Because the SWNT based device is considered to be a Schottky barrier (SB) device [10], it is possible that the adsorbates on the interface region increase the work function of Au [137], or decrease the SB height for hole transport in SWNTs, leading to an increase of conductance. Third, the electrostatic effect could be another concern as the chemical compounds we used (Figure 4-7a) are negatively charged in operating solution since the hydroxyl group could be ionized in solution. However, due to the weak ionization constant K_a of hydroxyl group, the concentration of negative charged molecules is very low in the solution. In addition, the small Debye length ($\sim 3\text{nm}$ in 10mM ionic concentration) [138] makes these charged molecules less effective to affect the carrier density in SWNTs. As a result, the electrostatic effect could be minor in comparison with other effects. The fact that the phenol molecules which have no nitro group only cause insignificant conductance change supports the above mentioned hypothesis. More careful experiments on special device structures with passivated channel or contact region will be carried out to study the influences of the contacts. Additionally, all experiments are conducted in simulated water sample in this research. In order to apply this method to real water sample, further strategies such as nitrophenol selective polymer decoration of SWNTs and ionic concentration control using buffer solution have to be utilized to provide better immunity to interferences from environmental samples.

In summary, we have demonstrated the possibility to utilize the SWNT device as effective sensor for fast, low-cost, sensitive, and real-time nitrophenols detection. Our results showed that the developed sensors could distinguish phenolic compounds with or without nitro group, and exhibit a concentration-dependent conductance response and good re-usability for nitrophenol detection even at this early stage. Charge transfer between the nitro group and SWNTs and the metal-nanotube interface modification are hypothesized to be the possible sensing mechanisms. Aiming to extend our devices to commercial-available sensor applications, we are currently investigating on different device configurations and functionalization methods to optimize the sensitivity and improve the chemical selectivity of our SWNT-based devices.

4.3 Low frequency noise characterization of CNTFETs

From our previous works, we found the CNT has a promising potential to be used for the fast, low-cost, sensitive and real-time nano-scale electronic sensor applications. But how to improve the sensing sensitivity is a realistic problem to be solved. During our experiments, we realized that some of devices exhibited significant noise, causing deteriorating signal-to-noise ratio. Therefore, noise analysis for CNT device becomes an urgent demand to develop further high-performance sensor devices.

In the past years, the noise properties of CVD-grown individual isolated SWNTs, thin SWNT films and bulk nanotube mats based devices have been discussed by several groups [6, 59, 69, 104-111]. They all found that at low frequency region, the $1/f$ noise is the dominated component. But the mechanism of such noise in CNT devices is still

in argument. Some researchers believed that the number fluctuation of channel carriers is the main mechanism contributing to the $1/f$ noise, which is similar to MOSFETs [59, 107, 110, 111]. But others thought that the noise was due to mobility fluctuation rather than number fluctuation [6, 108].

Here we reported noise measurement and analysis in CNTFET devices fabricated with AC dielectrophoresis technique, including both isolated SWNT devices and DWNT ones.

4.3.1 Experimental details

The details of the device fabrication was similar to that giving in Chapter 3 [6].

During the experiments, the samples were mounted onto a sample holder with a copper platform and three probes (Figure 4-11a). For back-gate CNTFET, two of them could act as the source and drain probe respectively, while copper plate could be used to connect the back gate of the device. For top-gate CNTFET, the three probes connected to the source, drain and top-gate pad of the device respectively. The electrical characterization of CNTFET devices was conducted by HEKA EPC 10 clamp amplifier inside a cage (Figure 4-11b) under ambient laboratory conditions. During the real-time monitoring, the top-gate or back-gate voltage could be set from -10V and +10V, while source-drain voltage was set below 1V. The sampling rating provided by this equipment could reach to 100 kHz.

Figure 4-11 (a) sample holder used to mount devices. The three probes on the top of copper plate could be used as source, drain and top-gate probe while the copper plate could be used to connect the back-gate of device. (b) Samples were putted into a cage with copper nets to prevent external interference.

4.3.2 Results and discussion

We firstly mounted the CNT device onto the sample holder and put them into the cage. Then typical real-time responses of the device in one second were collected, for example, the response of a back-gate DWNT-FET was shown in Figure 4-12. Since such device had exposed SWNT channel and consequently a p-type characterization, the channel current had larger value when back-gate voltage was applied with a large negative bias. Note that in a logarithmic scale, the relative current fluctuation $\Delta I_d/I_d$ could be evaluated by the vertical spreading of current data points. Thus we could see that at a constant source-drain voltage $V_{DS}=400$ mV, the relative current fluctuation $\Delta I_d/I_d$ rose significant when a back gate voltage increased to more positive value. However, we could see that the relative current fluctuation $\Delta I_d/I_d$ shows little dependence on the absolute current level and the drain voltage. According to Lin's report [107], this meant that the observed current fluctuation ΔI_d is not due to the thermal noise which is current dependent like $\Delta I/I \propto I^{-1}$ or the shot noise which is proportional to $I^{0.5}$ like $\Delta I/I \propto I^{0.5}$. In fact, the current fluctuation ΔI_d is proportional to

I_d and $\Delta I_d/I_d$ only depended on the back gate voltage. The real-time response of n-type top-gate CNTFET was vice versa since the oxygen molecules were expelled from CNT during PECVD SiN_x coating and the device exhibited an n-type characterization.

Figure 4-12 Real-time monitoring of the channel current of a typical device in one second. The green, orange, purple and blue traces corresponded to $V_{DS} = 400$ mV, 300 mV, 200 mV and 100 mV, respectively.

After collecting real-time response data, we used the data processing software Igor to calculate the current noise power spectra density (PSD) $S_{I_{ds}}$ at various gate bias as shown in Figure 4-13. At a finite source-drain bias, the noise PSD varied as $f^{-\beta}$, thus the noise was referred as $1/f$ noise. We can see that such $1/f$ noise was much larger than the thermal Nyquist level $S_I = 4k_B T/R$, which was further confirmed our previous conclusion that the observed noise was not caused by the thermal noise.

Figure 4-13 the calculated current noise PSD for a DWNT-FET at various gate voltages. The source-drain voltage V_{DS} was kept at 100mV. The red dot line was calculated thermal noise.

As studied in other papers [105, 107], the current $1/f$ noise PSD of CNTFETs is proportional to the square of the dc current I^2 , which is expressed by an empirical expression $S_I/I^2 = A/f^\beta$, where A is the noise amplitude and $\beta \sim 1$. Thus we normalized the noise power spectrum by I_{DS}^2 , as shown in Figure 4-14a. The normalized PSD increased by two orders when the back-gate voltage increased from -10V to 10V, which was in agreement with the trend of $\Delta I_d/I_d$ shown in Figure 4-12. Moreover, the normalized PSD S_I/I^2 measured at a fixed gate voltage but various source-drain voltages coincident with each other (Figure 4-14b). In other words, the normalized noise is almost independent of the applied drain bias in the linear regime, meaning that the device current noise PSD S_I was proportional to I_d^2 at linear regime at a constant V_G . This finding suggests that the noise most likely originates from the channel [139].

Figure 4-14 (a) Normalized noise PSD in a DWNT-FET device. The solid green line shows the $1/f$ dependence of the noise PSD. (b) Noise normalized PSD for a SWNT-FET device at a fixed $V_G = 0$ V but various drain bias $V_{DS} = 50, 100, 150, 200$ and 250 mV.

Because the $1/f$ noise behavior could be described by

$$S_I = \frac{AI^2}{f^b}$$

We could get

$$\lg\left(\frac{S_I}{I^2}\right) = -b \lg f + \lg A$$

Therefore, by applying linear fit in logarithmic scale of both S_I/I^2 and f , we could get the amplitude A of $1/f$ noise and the β value. We plot the channel current and $1/f$ noise amplitude A as a function of V_G of the DWNT-FET in Figure 4-15. One could see that the noise amplitude is inversely proportional to the channel current. In other word, when the channel current decreases with increasing V_G , the noise amplitude A increases monotonically.

Figure 4-15 the channel current (left axis) and $1/f$ noise amplitude A (right axis) as a function of V_G of a p-type DWNT-FET in ambient. The source-drain voltage is set at 100mV.

After measuring many SWNT-FETs and DWNT-FETs with top-gate or back-gate configuration, we found that the $1/f$ noise amplitude A in all these devices is inversely proportional to the channel current I_{DS} . Figure 4-16 shows the noise amplitude A as a function a channel resistance of all devices. It shows that DWNT devices have relatively small noise amplitude than the SWNT devices at a given channel resistance. The mechanism of such difference is still under investigation now. The contact properties between DWNT-FET and SWNT-FET could be one of reasons.

Figure 4-16 Plot of noise amplitude A versus the sample resistance for various SWNT and DWNT devices.

In summary, the noise characteristics of CNTFET devices at different drain bias and gate bias reveal that at low-frequencies the noise behavior is $1/f$ type and shown little dependence on the drain bias. We also observed that the DWNT-FET devices had

smaller noise amplitude compared to SWNT-FET devices at a given source and drain resistance.

Chapter 5 Conclusions and Recommendations

5.1 Conclusions

In this thesis, I have mainly studied the biological and chemical sensor applications of CNTFETs in liquid phase. The noise characterization of this kind of devices is also carried out. This project in the past two years was cover a wide range, consisted of experimental setup implementation, device design, fabrication and characterization, and furthermore, experimental data analysis to establishment of sensing mechanism.

As discussed in previous sections, the major findings and achievements of this project are summarized as follows:

1. Successfully fabricated CNTFETs using AC DEP and electrical breakdown technique. Such CNTFETs with back-gate and top-contact geometries exhibited good semiconducting performance and were further utilized in biological and chemical sensor applications.
2. Demonstrated a novel CNT real-time organophosphate detector, in which enzyme is used as the molecular recognition elements and a SWNT bundle is used as the transducer. A near linear relationship between the respond conductance and the concentration of one type of organophosphates, paraoxon, is confirmed. The real-time electrical conductance response of the sensors to the addition of paraoxon is attributed to the enzymatic hydrolysis. Changes of charge status of enzyme and the “electron” or “hole” doping effect of

enzymatically hydrolyzed products are likely to be the dominant factors for the conductance response.

3. Studied the sensing ability of our CNTFET devices to nitrophenol compounds and found such CNTFET sensors could distinguish phenolic compounds with or without nitro group, while exhibited a concentration-dependent conductance response and good re-usability for nitrophenol detection. We suggest that charge transfer and SB modification are considered to be the main sensing mechanism.
4. Investigated the noise characterization of CNTFET device at low frequency region (<2 kHz). The $1/f$ noise was found to be the dominated component at this frequency region. It is suggested that such observed current fluctuation is not due to the thermal noise or the shot noise. In fact, normalized current noise PSD only depended on the back gate voltage. Furthermore, by applying Hooge's empirical law to calculate the noise amplitude of $1/f$ noise in CNT based devices, we found that the DWNT-FETs have smaller noise amplitude compared to SWNT-FETs when their resistance are comparable.

Some key challenges for this project are as follows:

1. Our present top contacted CNTFETs have its channel and contacts freely exposed to biological and chemical environments. Thus, CNTs can interact with foreign species though either charge transfer to/from the channel or barrier modulation at the contact. To passivate the channel or contacts would be necessary to understand the sensing mechanism.
2. Relatively high current fluctuation exists in our SWNT and DWNT devices probably due to the carrier mobility fluctuation or number fluctuation of total transport carriers presented in the system. The poor adhesion of CNTs on

metallic electrodes through van der Waals force could be also one of reasons. Such noise affects our device performance and signal-to-noise ratio seriously in some cases.

5.2 Recommendations for future work

During my experiments, some key challenges still exist. First of all, the selectivity and sensitivity of our sensing devices needed further improvement. Secondly, our present top contacted CNTFETs have its channel and contacts freely exposed to/from biological and chemical environment. Thus, the interaction with foreign species can occur by either charge transfer to the channel or barrier modulation at the contacts. Last, the mechanism of the current fluctuation exhibited in our CNT based devices needs to be clarified.

According to the above discussion, possible implementations are listed as follows:

1. Functionalization of SWNTs with specific biological or chemical materials should be implemented in order to improve the sensitivity and selectivity of our SWNT sensors. For example, using polymer to decrease non-specific binding and modification of CNT with specific probes (peptide-polymers), respectively, that can provide better immunity to interferences.
2. CNTFETs with passivated channel or contact region should be fabricated so that the roles of channel and contact region during sensing experiments could be clarified.

3. Device structure and experimental configuration should be optimized to improve the overall performance of our sensor devices. For example, multiple sensors may be used as a sensor network to detect various species at the same time.
4. More noise characterization of various types of CNT devices should be conducted and more convincing data should be collected in order to find the mechanism for the $1/f$ noise, i.e. carrier mobility fluctuation or number fluctuation of total transport carriers in SWNTs.

Author's Publication

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