Carbon nanotube based electronic detection of biomolecules and chemicals

Salila Vijayalal Mohan Hari Krishna

2015

Salila Vijayalal Mohan Hari Krishna. (2015). Carbon nanotube based electronic detection of biomolecules and chemicals. Doctoral thesis, Nanyang Technological University, Singapore.

<https://hdl.handle.net/10356/62152>

<https://doi.org/10.32657/10356/62152>

NANYANG
TECHNOLOGICAL
UNIVERSITY

**CARBON NANOTUBE BASED ELECTRONIC
DETECTION OF BIOMOLECULES AND CHEMICALS**

SALILA VIJAYALAL MOHAN HARI KRISHNA
SCHOOL OF MECHANICAL AND AEROSPACE
ENGINEERING

2015

CARBON NANOTUBE BASED ELECTRONIC DETECTION OF BIOMOLECULES AND CHEMICALS

SALILA VIJAYALAL MOHAN HARI KRISHNA

SALILA VIJAYALAL MOHAN HARI KRISHNA

School of Mechanical and Aerospace Engineering

A thesis submitted to the Nanyang Technological University

in partial fulfilment of the requirement for the degree of

Doctor of Philosophy

2015

Acknowledgements

First and foremost, I would like to thank my ex-supervisor, Prof. Zheng Lianxi, for giving me an opportunity to embark on this journey of PhD in the area of nanotechnology. These four years have undoubtedly been the toughest phase of my life as I kept encountering several hurdles both personally and academically. Nevertheless, every time I look up to Prof. Zheng, he has given me priceless suggestions, constant encouragement, and timely guidance, which have largely been the source of my strength during these strenuous phases. Prof. Zheng has been a true role model for me for his simple attitude towards work and life. I am deeply indebted to him, and without his guidance, I would not have been able to improve in various aspects of research and life. I also sincerely thank my current supervisor Prof. Wong Chee How, who has been instrumental in my thesis submission process following Prof. Zheng's departure from NTU. He has been kind and I am extremely grateful to him for lending a helping hand in my troubled times.

I would also like to express my deepest gratitude to my past and present group members Dr. Sun Genzhi, Dr. Zhan Zhaoyao, Ms. An Jianing, Dr. Zhou Jinuyuan, Dr. Zhang Yani, Dr. Liu Yang, Mr. Reinack Hansen and Dr. Raj Kumar for their friendship and continuous support throughout this period. Also, my sincere thanks to the technical staff of MMC lab 1, Mr. Hoong Sinpoh, Mr. Pek Soo Siong, Mr. Ho Kar Kiat, and Mr. Nordin Bin Abdul Kassim for their assistance in clean room with

various experimental processes. I also thank my MMC lab mates for creating a positive atmosphere in the office.

Special thanks to my dearest friend, Mr. Paruthi Pradhapan, who has trusted me more than myself and backed me at every stage, right from joining NTU till submission of thesis. He has supported and helped me to come out of uncountable predicaments.

Last, but not the least, I thank my parents and brother for their endless love and belief in me. Also, I thank all other friends for their sustained love, moral support and well wishes for me.

Table of Contents

Acknowledgements	I
Table of Contents	III
List of Figures.....	VI
List of Tables.....	XIV
Abstract.....	XV
Chapter 1: Introduction	1
1.1 Background and Motivation	1
1.2 Objectives	5
1.3 Scope and Organization of Thesis	6
Chapter 2: Literature Review	8
2.1 Nanoelectronic Bio/Chemical Sensors.....	8
2.2 Carbon Nanotube.....	9
2.2.1 Basics of Carbon Nanotube	9
2.2.2 Synthesis of CNTs.....	11
2.2.3 Electronic Band Structure of CNTs	11
2.2.4 CNTs in Sensing Applications	14
2.3 CNT-Based Electronic Bio/Chemical Sensing.....	15
2.3.1 CNT Field-Effect Transistor	17
2.3.1a Transistor Model	19
2.3.1b Modes of Operation	21
2.3.2 Types of FET Sensing Mechanisms	24
2.3.3 CNT Chemiresistor	28
2.3.4 Factors Affecting CNT-Based Electronic Bio/Chemical Sensing	29
2.3.4a Molecular Factors	30
2.3.4b Device Factors	35
2.4. Summary.....	39

Chapter 3: Experimental.....	42
3.1 Growth of SWCNT	42
3.2 Device Fabrication	44
3.3 Characterization Methods	46
3.3.1 Scanning Electron Microscopy (SEM)	46
3.3.2 Atomic Force Microscopy (AFM)	47
3.3.3 Resonance Raman Spectroscopy	48
3.3.4 Electrical Characterization.....	50
3.4 Classification Tool.....	51
Chapter 4: Effect of Pyrene Derivative Functionalization and Channel Length of CNT-Based FETs in Nucleic Acid Hybridization Detection	57
4.1 Introduction.....	57
4.2 Pyrene Derivative Functionalization of CNT	59
4.3 Mechanism of Nucleic Acid Hybridization Detection.....	61
4.4 Effect of Functionalization	65
4.4.1 Without Junction	65
4.4.2 With Junction	66
4.5 Effect of Channel Length	68
4.6 Conclusions.....	81
Chapter 5: Effect of SsDNA Sequence on the Electrical Response of CNT-Based FETs in Dopamine Detection	83
5.1 Introduction.....	83
5.2 SsDNA Decoration of SWCNT	85
5.3 Effect of Surface Modification.....	86
5.4 Mechanism of SsDNA-DA Interaction Detection.....	90
5.5 SsDNA Sequence Dependent Response.....	92
5.6 Conclusions.....	97
Chapter 6: β-Cyclodextrin-Decorated CNT-Based Chemiresistors for Detecting Host-Guest Interactions	99

6.1 Introduction.....	99
6.2 β-CD Decoration of CNT.....	101
6.3 Mechanism of Host-Guest Interaction Detection.....	102
6.3.1 Determination of 9-ACA	104
6.3.2 Determination of DCFNa.....	105
6.3.3 Determination of Curcumin	107
6.4 Effect of Surface Modification.....	108
6.5 Selectivity Using Conductance Correlation.....	112
6.5.1 Autocorrelation Function	113
6.5.2 Two-Point Correlation Function	116
6.6 Conclusions.....	119
Chapter 7: Conclusions and Future Work	121
7.1 Conclusions.....	121
7.2 Future Work	125
List of Publications	127
References	130

List of Figures

- Figure 2.1** The typical structure of a (a) SWCNT, and (b) MWCNT, respectively.¹⁹. 10
- Figure 2.2** (a) A graphite lattice showing the chiral vector ($\vec{C}_h$) with the unit vectors $\vec{a}_1$ and $\vec{a}_2$. (b) The structures of an armchair, zigzag and chiral nanotube.²¹ 10
- Figure 2.3** The 3-D Band structure of a graphene sheet shows the intersection of the valence and the conduction bands at the Fermi points. The enlarged image of the Brillouin zone is also shown. Here k_x and k_y denote the reciprocal space vectors along x-and y-axis.²⁶ 12
- Figure 2.4** Schematic diagrams of (a) 1-D band structure of SWCNTs obtained using zone-folding approximation on 3-D graphene structure showing the allowed energy states represented by the lines and (b) the energy dispersion relation for a typical metallic (left) SWCNT with the lines passing through the Fermi point and a semiconducting (right) SWCNT with no lines passing through it.²⁷ The density of states (DOS) of a (c) metallic (13,1) and (d) semiconducting (10,5) SWCNT calculated using a tight binding model.²⁸ 13
- Figure 2.5** Flow diagram of a typical electronic bio/chemical sensing setup. 16
- Figure 2.6** (a) Schematic diagram of a SWCNT in a back-gated FET configuration with source, drain and gate electrodes.⁴⁸ The typical (b) output (I_D - V_{DS}) and (c) transfer (I_D - V_G) characteristics of a CNT-based FET. 18
- Figure 2.7** Schematic diagrams showing (a) the metal Fermi level (E_{fm}), semiconductor Fermi level (E_{fs}), semiconductor conduction band energy (E_{cs}) and

semiconductor valence band energy (E_{vs}), and (b) the formation of Schottky barrier due to Fermi level alignment between the contact metal and semiconducting CNT....22

Figure 2.8 Schematic diagrams of a p-type Schottky barrier (a) at $V_G=0$ V (OFF state), and (b) at $V_G< 0$ V (ON state), when the band alignment causes a shifting of the Fermi level resulting in hole tunneling.....22

Figure 2.9 Schematic diagrams of a p-type bulk-effect in CNT FET (a) at $V_G=0$ V (OFF state), where the shaded region indicates the modulation of only bulk by the gate, and (b) $V_G< 0$ V (ON state), when the holes accumulate in the CNT.....23

Figure 2.10 Typical FET transfer curves of the four possible sensing mechanisms following CNT-biomolecule interaction. (a) Electrostatic gating/charge transfer, (b) Capacitance modulation, (c) Schottky barrier modulation and (d) Mobility modulation. Adapted from ref.⁷24

Figure 2.11 (a) FET transfer curves before (solid line) and after streptavidin (dotted line) exposure showing charge transfer mechanism.⁶⁵ (b) FET transfer curves of aptamers-modified thrombin detection showing the contribution of capacitance effects.⁷⁷ (c) A comparison of the FET transfer curves of junction-exposed (left) and channel-exposed (right) device before probe DNA immobilization, after probe immobilization, and upon target DNA hybridization demonstrating Schottky barrier modulation. The image of the corresponding photoresist capped region obtained using optical microscope is shown in the respective inset.⁷¹ (d) DNA detection using network SWCNT FET exhibiting mobility modulation mechanism. The schematic diagram of DNA on SWCNT network FET (left), the transfer curves before and after DNA addition (middle), and the plot of % mobility change vs. DNA concentration for devices with different on/off ratio (right) are shown.⁷⁴27

Figure 2.12 (a) Schematic diagram of a chemiresistor setup for cyclohexanone sensing with the chemical structures of the functionalization entities. (b) The normalized conductance of a CNT chemiresistor functionalized with a tri-functional selector and exposed to various concentrations of cyclohexanone. The inset shows normalized conductance vs. concentration calibration curve.⁸¹28

Figure 2.13 A schematic diagram showing the various covalent surface functionalization routes on a CNT.⁸²30

Figure 2.14 Schematic diagrams of some noncovalent functionalization entities such as (a) zinc porphyrin, (b) pyrenecyclodextrin and (c) pyrene/CdSe nanoparticles decorated on a SWCNT used in a FET configuration for bio/chemical sensing.¹⁹31

Figure 2.15 Schematic diagrams showing the strategy involved in (a) making surface responsive by ssDNA-decoration,⁹⁴ (b) preventing non-specific binding of biotin on SWCNT by using Triton-X 100 and PEG, and (c) improving the selectivity of biotin-streptavidin binding using biotin-amidocaproic acid 3-sulfo-*N*-hydroxysuccinimide ester linker in a SWCNT FET.³32

Figure 2.16 (a) Plots of on/off ratio (left) and mobility (right) vs. channel length of network-based CNT FET showing opposite trends.¹⁰¹ (b) The schematic diagram of CNT-based FET employing single SWCNT (left), horizontally aligned SWCNTs (middle) and network SWCNT (right) as the conduction channel, respectively. (c) (Left) Plot showing improvement in on/off ratio with network length, and (right) high mobility of a 325 μm long individual (inset) CNT-based FET. (d) (Left) Conductance vs. time of semiconducting (1,2) and metallic (3) CNT FET during the adsorption of the protein cytc. The arrow indicates the start of the introduction of cytc into the buffer solution. (Right) Plot of the relative change of conductance vs time.⁶³ (e) (left) Conductance vs. gate voltage and (right) conductance response vs. time plots of a p-

type silicon nanowire FET demonstrating higher sensitivity in the subthreshold regime when used as used as a pH sensor.¹⁰⁹37

Figure 3.1 (a) Stages of CNT growth, (b) CVD apparatus, and (c) flow diagram illustrating CNT growth steps.43

Figure 3.2 Schematic diagrams (a) of fabrication process route **A** for FETs with channel length $>50\text{ }\mu\text{m}$ and **B** for FETs with channel length $<50\text{ }\mu\text{m}$, and (b) a typical chemiresistor setup.45

Figure 3.3 SEM images of (a) CNT array in the range of millimeters, (b) high density random network CNT and (c) as-fabricated CNT FETs with short (few μm), long (few hundreds of μm) and ultralong (few mm) channel.46

Figure 3.4 (a) AFM image and (b) height profile of a long individual SWCNT. (c) The histogram plot of the diameter distribution of the as-grown SWCNTs.....47

Figure 3.5 The Raman spectrum of a 1 cm long SWCNT showing RBM at $\sim 129.7\text{ cm}^{-1}$ and G band with G^- and G^+ peaks at 1590 cm^{-1} and 1603 cm^{-1} , respectively. The inset shows the Raman mapping image of the SWCNT.....49

Figure 3.6 (a) A typical MLP architecture. (b) Schematic diagram of ANN showing the input, hidden and output layers with ‘ w ’ and ‘ b ’ denoting the weights and bias, respectively.52

Figure 3.7 A flow chart illustrating the general steps involved in feature extraction and classification of CNT FET/chemiresistor sensor data using ANN.54

Figure 4.1 A schematic setup for cDNA/cRNA detection using SWCNT FET. Here, cDNA/cRNA represents the complementary target ssDNA/ssRNA, and DNA-

DNA/DNA-RNA represents the double-stranded hybrids formed by base pairing between probe DNA and cDNA/cRNA.61

Figure 4.2 I_D - V_{DS} curves of pyrene-functionalized long channel SWCNT FET ($L=300\ \mu\text{m}$) showing the various functionalization steps for (a) cDNA and (b) cRNA detection, respectively. The gate voltage was kept at $-24\ \text{V}$62

Figure 4.3 I_D - V_G curves of pyrene-functionalized long channel SWCNT FET ($L=300\ \mu\text{m}$) with only channel exposed to (a) cDNA and (b) cRNA, respectively. The ‘before cDNA/cRNA’ step corresponds to the recording obtained after probe DNA, EA, and Tween 20 incubation steps. The ‘after cDNA/cRNA’ step represents the recording after incubation with cDNA/cRNA. The arrow marks indicate the direction of gate voltage sweep.63

Figure 4.4 I_D - V_G curves of pyrene-functionalized long channel SWCNT FET ($L=300\ \mu\text{m}$) with channel and junction exposed to (a) ncDNA and (b) cDNA/cRNA. The ‘before ncDNA’ step corresponds to the recording obtained after probe DNA, EA, and Tween 20 incubation steps. The ‘after ncDNA’ step represents the recording after incubation with ncDNA. The arrow marks indicate the direction of gate voltage sweep.64

Figure 4.5 I_D - V_G curves of unfunctionalized long channel SWCNT FET ($L=300\ \mu\text{m}$) for cDNA/cRNA detection with (a) only channel exposed, and (b) channel and junction exposed. The ‘before cDNA/cRNA’ step corresponds to recording after probe DNA and Tween 20 incubation steps. The arrow marks indicate the direction of gate voltage sweep.65

Figure 4.6 Schematic diagram of (a) B-form (DNA-DNA) and A-form (DNA-RNA) helixes. Chemical structures of (b) nucleoside with ribose/deoxy ribose sugar and (c) pyrene butanoic acid succinimidyl ester (PASE), respectively.68

Figure 4.7 The variation in the conductance response of channel and junction-exposed ($\Delta G_{on}/G_{on}$) devices and only channel-exposed ($\Delta G_{ch}/G_{ch}$) devices with L for (a) cDNA and (b) cRNA detection, respectively. The negative sign on the y-axis indicates the decrease in magnitude of conductance after hybridization. The solid lines are a guide to the eye.69

Figure 4.8 (a) The relative change in peak transconductance ($\Delta g_{mp}/g_{mp}$) following exposure to cDNA and cRNA, respectively. The change in threshold voltage (ΔV_{th}) and hysteresis gap (ΔH) following (b) cDNA and (c) cRNA hybridization, respectively for different L . The additional subscripts ‘f’ and ‘r’ in V_{th} represent the threshold voltages for the forward and reverse gate voltage sweep, respectively. The negative and positive sign of the threshold voltage shift indicates the leftward and rightward shift in the transfer curve. A positive ΔH indicates rise in hysteresis whereas, a negative sign indicates reduction in hysteresis. The change in all electrical parameters induced by hybridization was obtained with respect to the ‘before cDNA/cRNA’ I_D - V_G curve. The solid lines are a guide to the eye.71

Figure 4.9 $\Delta\phi$ vs. L for (a) forward and (b) reverse sweeps in the linear and near-threshold regimes. K vs. L for (c) forward and (d) reverse sweeps in the linear and near-threshold regimes. The solid lines are a guide to the eye.75

Figure 5.1 Schematic diagram of ssDNA-decorated SWCNT FET for DA detection.85

Figure 5.2 I_D - V_G curves of (a) bare SWCNT FET and (b) (GA)₂₂-decorated SWCNT FET after exposure to DA, UA and DA-UA solution mixture. The arrow marks indicate the direction of gate voltage sweep.87

Figure 5.3 Summary of the sequence dependent variation in FET electrical parameters induced by DA and solution mixture of DA and UA. (a) $\Delta G_{on}/G_{on}$, (b) $\Delta g_{mp}/g_{mp}$, (c) ΔV_{th} , and (d) ΔH . – sign on the y-axis in (a) and (b) indicates the drop in the respective

parameters with respect to the ssDNA functionalized state. – and + on the y-axis in (c) and (d) indicate the left shift in V_{th} and increase in H , respectively, with respect to the ssDNA functionalized state. The additional subscript ‘f’ in V_{th} represents the threshold voltages obtained from the forward gate voltage sweep.....93

Figure 5.4 (a) Mean squared error (MSE) and (b) training state plot of the MLP classifier for a 4-input feature and 8-output class classification.....96

Figure 6.1 The chemical structures of (a) mono-(6-ethanediamine-6-deoxy)- β -cyclodextrin and (b) 3, 4, 9, 10-perylene tetracarboxylic acid (PTCA). (c) A schematic setup of β -CD-decorated CNT chemiresistor for host-guest interaction detection. ... 102

Figure 6.2 I_D - V_{DS} characteristics following PTCA functionalization and CD decoration steps in a CNT chemiresistor. 103

Figure 6.3 (a) $(G-G_0)/G_0$ vs. time and (b) $(G-G_0)/G_0$ vs. concentration plots of PTCA linked β -CD-decorated CNT chemiresistor for increasing concentration of 9-ACA. (c) The chemical structure of 9-ACA. The arrows indicate the starting time of the introduction of 9-ACA for each concentration. 104

Figure 6.4 (a) $(G-G_0)/G_0$ vs. time and (b) $(G-G_0)/G_0$ vs. concentration plots of PTCA linked β -CD-decorated CNT chemiresistor for increasing concentration of DCFNa. (c) The chemical structure of DCFNa. The arrows indicate the starting time of the introduction of DCFNa for each concentration. 106

Figure 6.5 (a) $(G-G_0)/G_0$ vs. time and (b) $(G-G_0)/G_0$ vs. concentration plots of PTCA linked β -CD-decorated CNT chemiresistor for increasing concentration of curcumin. (c) The chemical structure of curcumin. The arrows indicate the starting time of the introduction of curcumin for each concentration..... 107

Figure 6.6 $(G-G_0)/G_0$ vs. time plots of β -CD-decorated CNT chemiresistor with no PTCA linkage for increasing concentration of (a) 9-ACA, (b) DCFNa, and (c) curcumin, respectively.	109
Figure 6.7 I_D vs. time plots of bare CNT chemiresistor for increasing concentrations of (a) 9-ACA, (b) DCFNa, and (c) curcumin, respectively.	112
Figure 6.8 Plots of (a) R_k vs. k and (b) $\log R_k$ vs. k upto 10 s for the three host-guest systems (9-ACA, DCFNa and curcumin) at a guest concentration of 1 nM for a β -CD-decorated CNT chemiresistor with PTCA linkage. R_k vs. k plots for different guest concentrations within the linear detection range for (c) β -CD-9-ACA, (e) β -CD-DCFNa and (g) β -CD-curcumin host-guest systems, respectively. Plots of $\log R_k$ vs. k upto 10 s for (d) β -CD-9-ACA, (f) β -CD-DCFNa and (h) β -CD-curcumin host-guest systems, respectively, for different guest concentrations within the linear detection range.....	115
Figure 6.9 (a) $A(t)$ vs. time graphs for different host-guest systems (9-ACA, DCFNa and curcumin) at guest concentration of 1 nM for a β -CD-decorated CNT chemiresistor with PTCA linkage. Plots of $A(t)$ vs. time for (b) β -CD-9-ACA, (c) β -CD-DCFNa and (d) β -CD-curcumin host-guest systems, respectively, for different guest concentrations within the linear detection range.	117
Figure 6.10 (a) The mean squared error (MSE) and (b) training plot of MLP-based classification. The classification method used the correlation functions (R_k and $A(t)$) obtained at a guest molecule concentration of 1 nM as input patterns for classifying the conductance response into three host-guest system classes, i.e., 9-ACA, DCFNa and curcumin.	118

List of Tables

Table 2.1 Summary of various kinds of CNT-based sensors.....	15
Table 2.2 A summary of CNT-based FET/chemiresistive sensor for detection of various biomolecules and chemicals.....	39
Table 3.1 Summary of the MATLAB functions used to perform MLP classification and the tasks performed by them..	56
Table 4.1 Summary of the observed responses and mechanisms of SWCNT FET of three different channel lengths (a) with and (b) without the presence of CNT-metal junction for hybridization detection in the presence and absence of pyrene linker. +/- sign for I_D and H indicate increase/decrease in these parameters after hybridization. +/- sign for V_{fth} and V_{rth} indicate positive/negative shift in these parameters following hybridization.	80
Table 5.1 Summary of MLP-based classification of electrical responses of different ssDNA-decorated SWCNT FETs before and after interaction with DA for homo base sequences, repeated base sequences and a combination of both.	97
Table 6.1 Summary of the detection range, LOD, sensitivity and R^2 for β -CD-decorated CNT chemiresistors in the detection of 9-ACA and DCFNa with and without PTCA linker. Curcumin was not detected by chemiresistors without PTCA linkage, and therefore, has been neglected from the table.	110
Table 6.2 Range of values of the two-point correlation function, $A(t)$, for 9-ACA, DCFNa and curcumin detection in their respective linear detection range.	118

Abstract

Most current nanostructure-based sensors for detecting biomolecules and chemicals rely on time-consuming optical detection principles, require large sample volume, or involve complex data analysis. This has compelled the need to explore an electronic alternative to bio/chemical sensing. The highly sensitive surface and size compatibility of carbon nanotubes (CNTs) with bio/chemical systems, and the charged nature of bio/chemical species have been the cardinal reasons for adopting CNTs as the transducing surface in electronic platforms such as field-effect transistors (FETs) and chemiresistors. Along the development of this new type of devices, two major issues are identified to be related to sensitivity and selectivity. For most interested molecules, bare-CNT devices show very poor response. This requires scientists to modify CNT surfaces to enhance the device performance. Even for surface modified devices which exhibit strong response, how to translate the device outputs into molecular recognition (receptor-target interaction) is another challenge, because different targets bond differently with different receptors, and display different electronic sensing mechanisms depending both on the molecular nature and device parameters.

In this thesis, we design two types of devices (CNT FET/chemiresistor) to study the sensing mechanisms, the effects of surface modification and device structure on the transduction outputs in detecting three types of typical biomolecular and chemical entities. Particularly, individual and network CNTs were successfully grown using chemical vapor deposition (CVD) process under optimized conditions and

fabricated into FETs/chemiresistors. The surface modification was extensively studied in terms of the role of functionalization entities, the effect of different receptors in identifying a single target, and the effect of one receptor in identifying different targets. By using various non-covalent surface modification entities such as pyrene butanoic acid succinimidyl ester (PASE), single-stranded DNA (ssDNA) and 3, 4, 9, 10-perylene tetracarboxylic acid (PTCA), we detected a wide range of biomolecular and chemical targets including DNA and RNA, DA, 9-ACA, DCFNa and curcumin. For studying the effect of device parameter, we analyzed the impact of FET channel length on nucleic acid hybridization detection.

From the studies pertaining to electronic detection of molecular recognition, the results are divided into the following categories. Firstly, with respect to the electronic sensing mechanism, the FET-based detection exhibited a combination of charge transfer, carrier scattering and charge trapping mechanisms, which were apparent from the change in transistor electrical parameters including conductance, transconductance, threshold voltage and hysteresis gap; while chemiresistor-based detection exhibited an increase/decrease in conductance. Secondly, surface modification not only improve the sensitivity and selectivity of the detection, but also enable CNT sensors to detect wide range of receptor-target interactions such as hydrogen bonding, electrostatic/polar interactions and host-guest complex formation. Pyrene-derivative functionalization improved the selectivity in detecting DNA-DNA hybridization and DNA-RNA hybridization. SsDNA decoration improved the FET

response to DA, and enhanced its selectivity in the presence of UA. PTCA linker improved the device response, sensitivity, limit of detection (LOD), and selectivity of β -cyclodextrin (CD)-decorated CNT chemiresistors in identifying different host-guest interactions. Finally, with respect to device parameter, FETs with channel length in the range of a few hundred micrometers displayed better response for hybridization detection compared to FETs with few micrometer or millimeter long channels. The 300 μm long channel FETs make use of their excellent coverage area, freedom from contacts, thereby showing better response compared to micrometer-channel FETs. In addition, they do not suffer from the very high channel resistance hindering the detection sensitivity compared to millimeter-channel FETs.

Chapter 1: Introduction

1.1 Background and Motivation

The growing demands for better health and environmental safety have pushed the need for better chemical and biological recognition platforms. The unique size- and shape-dependent properties, high surface-to-volume ratio, and tunable surface properties of nano-scaled materials offer many fold improvement in sensitivity, selectivity, and response time. However, current nanomaterial-based bio/chemical sensing techniques mainly rely on optical detection methods, which are time consuming, expensive and require labelling. To overcome these limitations, an electronic, economical, and label-free alternative approach for bio/chemical sensing is required.

Single walled carbon nanotube (SWCNT) is a one-dimensional (1-D) nanomaterial with ultrahigh surface-volume ratio, excellent electronic properties and size compatibility with bio/chemical systems.^{1,2} The molecular recognition of bio/chemical species involves charge transfer or other electrostatic interactions during receptor-target interaction, which allows the use of an electronic transduction platform employing CNTs as the sensitive elements to detect surface molecular recognition processes. Moreover, CNTs allow surface modification, which encourages their use as multifunctional sensors.³ In this regard, CNT-based field-effect transistors (FETs) and chemiresistors present simple multifaceted elementary units for constructing electronic bio/chemical sensing devices.⁴⁻⁶

Detections of various bio/chemical molecules using CNT FETs/chemiresistors have been reported by employing several receptors exhibiting different sensing mechanisms, which are evaluated by the change in the transistor electrical parameters.⁶⁻⁸ The outcome of the sensing is evaluated in terms of the reproducibility of the sensing mechanism and the sensor performance. In the FET-based detection of nucleic acids, the presence or absence of CNT-metal junction largely dictates the dominant sensing mechanism during sensing.⁹ In gas sensing using CNT FETs, majority of the target analytes (gases) fails to induce any response on bare CNT devices. In several cases that the devices exhibit minor effects on the response, bare CNT FETs are unable to distinguish between gases with similar structures, which highlight poor specificity and selectivity. However, it was observed that CNT FET gives a detectable signal when the target binds with the nucleic acid immobilized on the CNT.¹⁰ Considering the same example of CNT FET-based gas sensing, it was observed that structural variations in the receptor (different nucleic acid sequences) produce different responses for a particular target (gas), which shows the specificity of molecular recognition. Also, in nucleic acid-decorated CNT FETs, different targets (gas) yield different transduction outputs for the same receptor molecule (nucleic acid) and certain receptors exhibited better response to a particular target compared to others, which highlights the sensor selectivity. Clearly, the above example demonstrates the variety of concerns that electronic detection faces with respect to response, sensitivity, specificity, and/or selectivity of molecular recognition. It hints at

the role of device structure and CNT surface modification in rectifying the issues. These issues also form part of other bio/chemical sensing applications. Herein, we use detailed examples to present these challenges and the motivation behind the suggested potential solutions to overcome these hurdles. These examples are particularly selected from the major bio-engineering areas including genetic, diagnostic, and environmental applications, in order to demonstrate versatile potentials of the CNT sensors.

Nucleic acids like deoxyribo nucleic acid (DNA) and ribo nucleic acid (RNA) are key components in genetic engineering. Both of them possess charged nature and nanometric dimensions, which allow the use of a single SWCNT with the similar size for their hybridization detection. Previous CNT FET-based hybridization detection suffered from lack of response due to non-specific bonding, contact interference, and lack of specificity and selectivity in discriminating DNA-DNA and DNA-RNA duplexes when short unfunctionalized SWCNTs were used as channels.^{9,10} Long SWCNTs have exhibited excellent mobility,¹¹ which could improve device response, and CNT surface modification by functionalization approaches³ could enhance receptor immobilization, thereby improving the specificity and selectivity of detection. Therefore, understanding the effect of channel length and functionalization on the specificity and selectivity of hybridization detection is necessary.

Dopamine (DA) is an important molecule in disease diagnosis. Abnormal levels of DA can hamper brain functions including learning, memory formation, message transfer in the central nervous system and pathological processes of

Parkinson's disease, schizophrenia, attention deficit hyperactivity disorder (ADHD) and restless legs syndrome (RLS). Molecular recognition of such a neurotransmitter biomolecule using CNT electronic sensors in previous studies suffer from poor response and selectivity due to the presence of an interferent like uric acid (UA).¹² Hence, there is a need for a functionalization approach, which not only recognizes DA, but selectively screens UA from giving rise to false signals. Single-stranded DNA (ssDNA) is one such functionalization biopolymer with good wrapping tendency on CNTs and ability to distinguish and detect a variety of polar analytes based on its sequence.¹³ The possibility of various sequence combinations makes the FET response sequence dependent, which urges the need to analyze the impact of different CNT-ssDNA systems on the electronic detection of DA.

Certain class of chemicals such as 9-anthracenecarboxylic acid (9-ACA),¹⁴ diclofenac sodium (DCFNa)¹⁵ and curcumin,¹⁶ which are important for environmental and health safety, fail to produce any response on bare CNT devices. Literature reveals that these molecules form good complexes with β -cyclodextrin (β -CD),¹⁷ which in conjunction with CNTs have demonstrated excellent molecular recognition capabilities.¹⁸ For better detection, efficient β -CD immobilization is crucial, which is possible through CNT surface modification.³ Hence, it is necessary to study the influence of surface modification on the device response. As the same receptor (β -CD) identifies different targets, the selectivity of the sensors in discriminating the host (β -CD)-guest (target) interactions needs evaluation.

In general, for the aforesaid electronic detection of molecular recognition of different targets, factors such as CNT surface modification and device structure play significant roles in CNT-receptor and/or receptor-target interaction, which defines particular sensing mechanisms, and consequently determines the specificity and selectivity of molecular recognition. Therefore, studying the influence of surface modification and behind sensing mechanisms for different molecular recognition processes, as well as the influence of device parameters on the electronic transduction outputs, form the research interests investigated and reported in this thesis.

1.2 Objectives

Based on the background and motivation, the objectives of this research thesis are listed as follows:

- i) Grow individual as well as network CNTs, and fabricate them into FETs/chemiresistors.
- ii) Study the surface modification, sensing mechanisms, and influence of device parameters of CNT-based FETs/chemiresistors in various bio/chemical sensing applications.
- iii) Study the effect of CNT-receptor interaction on the device response to a specific molecular recognition using different receptors.
- iv) Study the receptor-target interaction of different targets using a single receptor.

1.3 Scope and Organization of Thesis

Since a particular application has its own specific challenges, the thesis is organized according to applications rather than objectives directly, but above-mentioned objectives will constitute the major research focus in each application.

Chapter 1 gives a brief background and motivation behind this work. All objectives pertaining to the goal are listed and discussed.

Chapter 2 presents the literature survey conducted as a part of this work. It includes an introduction and review of CNT basics, CNT-based electronic sensors, sensor concepts related to CNT-based FET/chemiresistors for bio/chemical sensing applications, and a brief summary of the literature review.

Chapter 3 describes the experimental details of CNT growth, FET/chemiresistor fabrication, characterization techniques, and data/pattern classification tool used.

Chapter 4 covers the sensing mechanism of individual CNT FET-based detection of DNA-DNA and DNA-RNA hybridization. The effect of device structure (channel length) and CNT surface modification (pyrene derivative functionalization) on the FET response to different receptor-target interactions (DNA-DNA and DNA-RNA hybridization) is also discussed.

Chapter 5 investigates the sensing mechanism of ssDNA-decorated CNT FETs in DA detection in the presence of UA. This chapter discusses the effect of CNT-receptor interaction (CNT-ssDNA) on the FET response to molecular recognition (ssDNA-DA) for different surface modifications (ssDNA sequences).

Chapter 6 deals with the detection of host-guest interactions using β -CD-decorated CNT chemiresistors for chemical sensing. It involves the study of different receptor-target interactions (β -CD-9-ACA, β -CD-DCFNa and β -CD-Curcumin), and the effect of surface modification (PTCA) on the performance of a CNT chemiresistor.

Chapter 7 summarizes the experimental observations and results, and gives the conclusions. It also includes recommendations for future work.

Chapter 2: Literature Review

2.1 Nanoelectronic Bio/Chemical Sensors

A bio/chemical sensor responds to chemical or biological stimuli and converts it into a measurable analytical quantity. It comprises recognition, transduction and detection units, which recognize and transform the measurable signal for detection, recording and processing. Affordable mass production and high sensitivity are prerequisites for sensors. However, most current techniques are optical-based such as mass spectrometry and labelled fluorescence. These sensors suffer from difficulty in size miniaturization. Hence, the use of nanostructures as transduction units in bio/chemical sensors nanoscale devices has taken precedence. Reducing the size of a structure to nanometric dimension increases the surface to volume ratio considerably, which leads to the dominance of surface phenomena over bulk. Thus, use of nanostructures in bio/chemical sensors reduces the size of the transducer unit, which reduces power consumption, allows large scale integration, increases sensitivity and selectivity, provides better specificity and signal to noise ratio durability, decreases response time, allows multi-analyte detection and requires less sample volume.

Most biomolecular and chemical recognition processes involve ion movement, electrostatic interactions, and/or charge transfer, which opens a door for direct electronic detection as an alternative to optical characterization. In the last decade, the use of nanostructure-based electronic approaches to detect biological and chemical species has received a lot of attention in pharmaceutical, genetic, biomedical, and drug

related applications. Specifically, field-effect transistors (FETs) and chemiresistor based on carbon nanotubes (CNTs) merges the excellent electronic property of CNT, which is sensitive to charge variations on its surface during molecular recognition, with the electronic readout platform of FET/chemiresistor to give a faster route to bio/chemical sensing.^{1,4,5}

In the succeeding sections, we will briefly review the CNT fundamentals, and the structure, operation, mechanism, and bio/chemical sensing applications of CNT-based FETs/chemiresistors. Subsequently, we will identify the issues related to CNT-based electronic detection of bio/chemical molecular recognition.

2.2 Carbon Nanotube

2.2.1 Basics of Carbon Nanotube

CNTs are classified as single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs).¹ A SWCNT resembles a rolled-up sheet of graphene in a tube structure with diameter in the range of 1-2 nm (Figure 2.1a). A MWCNT structure resembles a concentric set of SWCNTs with diameter ranging from 10–100 nm (Figure 2.1b). Using two indices, n and m , corresponding to the graphene unit lattice vectors, the type of a SWCNT can then be identified. These integer indices along with a chiral vector determine the direction along which the graphene sheets are rolled to form a SWCNT.

Figure 2.1 The typical structure of a (a) SWCNT, and (b) MWCNT, respectively.¹⁹

The chiral vector is given by, $\vec{C}_h = n\vec{a}_1 + m\vec{a}_2$, where $\vec{a}_1$ and $\vec{a}_2$ are the graphene unit lattice vectors as shown in Figure 2.2a. If $n=m$, the nanotubes are commonly known as armchair nanotubes,²⁰ and if $m=0$, the nanotubes are called zigzag. The remaining combinations of n and m form chiral or helical nanotubes.

Figure 2.2b shows the types of CNT structures formed in different orientations.

Figure 2.2 (a) A graphite lattice showing the chiral vector ($\vec{C}_h$) with the unit vectors $\vec{a}_1$ and $\vec{a}_2$. (b) The structures of an armchair, zigzag and chiral nanotube.²¹

The CNT diameter (d) and the chiral angle (θ) can be estimated using the equations given below:

$$d = \frac{\sqrt{3}}{\pi} a_{cc} \sqrt{m^2 + mn + n^2} \quad (2.1)$$

$$\theta = \tan^{-1}[\sqrt{3}m(2n + m)] \quad (2.2)$$

where a_{cc} is the nearest neighbour carbon atom distance (~0.142 nm).²²

2.2.2 Synthesis of CNTs

The three methods usually employed to grow CNTs are arc discharge, laser ablation and chemical vapor deposition. The carbon arc-discharge method uses an arc ignited between two graphite electrodes at a high temperature in an atmosphere of either argon or hydrogen.²³ In the laser ablation method, an intense laser pulse is focused onto a surface containing carbon kept in a gaseous chamber filled with helium gas.²⁴ This results in the evaporation of carbon, and its subsequent condensation to yield fullerenes. The chemical vapor deposition (CVD) process typically involves the use of a catalyst particles heated to a high temperature (350°C–1000°C).²⁵ A carbon source is supplied at high temperature to the chamber containing the catalyst particles, which cause the carbon to saturate and precipitate in the form of CNTs.

2.2.3 Electronic Band Structure of CNTs

Since SWCNT is the rolled form of graphene, the one-dimensional (1-D) SWCNT's band structure is derived from the two-dimensional (2-D) energy dispersion (E - k) relationship of the graphene sheet quantized along the circumference. The interaction of energy states near the Fermi level (E_f), i.e., the energy of the highest occupied

electronic state at 0 K, determine the electronic properties of a material. In a 2-D structure, graphene has the carbon atoms arranged in a hexagonal lattice, with each atom having a sp^2 configuration. The $2s$, $2p_x$ and $2p_y$ orbitals form σ and σ^* bonds in the plane whereas, the $2p_z$ orbital overlaps with other $2p_z$ orbitals to form delocalised π and π^* bonds perpendicular to the graphene plane. These π bonds govern the electronic properties of the SWCNT.

Figure 2.3 The 3-D Band structure of a graphene sheet shows the intersection of the valence and the conduction bands at the Fermi points. The enlarged image of the Brillouin zone is also shown. Here k_x and k_y denote the reciprocal space vectors along x-and y-axis.²⁶

Graphene is a semiconductor with zero band gap. For a SWCNT, the wave vector (k) is defined in two directions-one along the nanotube axis ($k_{||}$) and the other along the circumferential direction ($k_{\perp}$). According to the 3-D band structure of graphene, including the tight binding approximations, the bonding and anti-bonding bands touch each other at six different points, which form the corners (k points) of Brillouin zone (Figure 2.3). However, for the remaining k values, there exists a semiconductor-type energy band gap. Upon adding the effects of electron confinement

to the graphene band structure, the energy levels are quantized and satisfy the periodic boundary condition given by,

$$k_{\perp} \cdot C_h = 2\pi j \quad (2.3)$$

where j is an integer and C_h represents the chiral vector discussed in section 2.2.1.

These 1-D sub bands are continuous along the tube axis, and for an infinite SWCNT length, k is continuous along the axis of the nanotube. The above condition allows only specific $k_{\perp}$ states during the formation of SWCNT from graphene.

Figure 2.4 Schematic diagrams of (a) 1-D band structure of SWCNTs obtained using zone-folding approximation on 3-D graphene structure showing the allowed energy states represented by the lines and (b) the energy dispersion relation for a typical metallic (left) SWCNT with the lines passing through the Fermi point and a semiconducting (right) SWCNT with no lines passing through it.²⁷ The density of states (DOS) of a (c) metallic (13,1) and (d) semiconducting (10,5) SWCNT calculated using a tight binding model.²⁸

Applying one-fold approximation to the energy dispersion of graphene enables the use of allowed $k_{\perp}$ states to obtain the 1-D structure of SWCNTs. Figures 2.4a and

2.4b show the 1-D structure of SWCNTs obtained using zone folding and the 1-D energy dispersions for a metallic and a semiconducting SWCNT. For a (n, m) nanotube, if $|n-m|=3i$, where i is an integer, the nanotube will be metallic because the permitted $k_{\perp}$ states pass through the k -points resulting in a zero band gap. On the other hand, if $|n-m|\neq 3i$, the allowed $k_{\perp}$ states will not pass through the k -points resulting in a band gap, and thereby the nanotube is semiconducting. Consequently, armchair (n, n) nanotubes are always metallic, but zig-zag $(n, 0)$ and chiral nanotubes can be either metallic or semiconducting. The absence of band gap in a metallic SWCNT leads to a finite density of states (DOS) at E_f (Figure 2.4c) while the presence of a band gap results in no DOS at E_f for semiconducting SWCNT (Figure 2.4d). The electron confinement in 1-D SWCNTs results in series of sub-bands appearing as discrete energy level peaks or spikes in their DOS, which are called van-Hove singularities (Figures 2.4c and d). At the Fermi energy ($E=0$), the DOS is constant for metallic nanotubes while it is zero for semiconducting nanotubes due to the existence of band gap.

2.2.4 CNTs in Sensing Applications

The ability to use CNTs as a sensor material is attributable to:

- i) nanometer size providing the possibility of miniaturization of devices, sensor array fabrication and construction of highly localized sensing units,
- ii) ultra-high surface to volume ratio making it highly sensitive to external stimuli,
- iii) low power consumption.

Various forms of CNT have been used as sensors to detect a wide range of stimuli displaying different output responses. Table 2.1 summarizes the various applications of CNT sensors.

Table 2.1 Summary of various kinds of CNT-based sensors.

Type of sensor	Input stimuli	Output response	Type of CNT
Chemical ⁶	Gas molecules, organic vapor	Conductance change, gate threshold shift	Individual, network
Biochemical ^{29,30}	Biomolecules (liquid phase)	Conductance change, gate threshold shift	Individual, network
Electromechanical ^{31,32}	Pressure, displacement strain	Conductance change	Individual
Pressure ^{33,34}	Pressure	Conductance change	CNT block
Resonant cantilevers ^{35,36}	Molecules (mass loading)	Resonance frequency change	Double-walled CNT, MWCNT
Doubly clamped resonators ^{37,38}	Molecules (mass loading), strain	Resonance frequency change	Individual
Optical ³⁹⁻⁴¹	Photons, light	Photocurrent	Individual

2.3 CNT-Based Electronic Bio/Chemical Sensing

Molecular recognition forms the basis for bio/chemical sensing. It involves the event of binding of an immobilized chemical/biological component (receptor) with an analyte (target) on an active surface (transducer). The complementarity between the

receptor and the analyte forms the crux of bio/chemical detection. The role of the transducer is to recognize this binding event and convert it into a useful measurable signal. Most current chemical/biosensing using nanostructures include amperometry,⁴² potentiometric,⁴³ electrochemical impedance spectroscopy⁴⁴ and assay based procedures⁴⁵. Besides being time consuming and expensive, these methods involve multi-step procedure, complex labeling procedures, use of multiple reagents and complex data analysis. This has reinstated the necessity for a rapid, electronic, label-free and real time approach for bio/chemical detection.

Figure 2.5 Flow diagram of a typical electronic bio/chemical sensing setup.

The electronic detection using CNT-based devices offers the following advantages.

- i) It ensures size compatibility with the target molecules because the CNT diameter is directly comparable to the size of single biomolecules and to the electrostatic screening length in physiological solutions,

- ii) SWCNTs have only surface carbon atoms, which make them highly sensitive to even minute charge variations in their immediate environment. Since majority of the bio/chemical reactions and processes involve charge transfer and electrostatic interactions, merging electronics with bio/chemical phenomenon allows fast real-time detection.
- iii) CNTs have excellent chemical stability, and modifiable ends and sidewalls, which encourage functionalization and fabrication of multifunctional sensors.

In a CNT-based electronic sensor, the receptor-target binding occurring on the nanotube surface is converted into an electrical signal (voltage and/or current) by the CNT (transducing element) to detect a bio/chemical species as shown in Figure 2.5. Field-effect transistors (FETs) and chemiresistors are the two most popular electronic transduction platforms for detection of bio/chemical molecular recognition.

2.3.1 CNT Field-Effect Transistor

FETs are one of the simplest means to make use of the exceptional electronic properties of CNTs for sensor applications.^{4,5,29} In a FET configuration, the nanotube resting on a substrate forms the conduction channel flanked on either sides by source and drain electrodes as shown in Figure 2.6a, which is analogous to the metal-oxide-semiconductor field-effect transistors (MOSFETs).^{46,47} The modulation in the electronic transport of a SWCNT because of surface charge variations forms the basis for their use as electronic sensors.

In a FET configuration, the gate voltage (V_G) controls the formation of charge carriers in the CNT channel and the drain voltage (V_{DS}) provides the potential difference across the channel for the carriers to flow from source to drain and constitute the output drain current (I_D). The two types of current (I)-voltage (V) characteristics obtained using transistor measurements are the output (I_D - V_{DS}) and transfer (I_D - V_G) characteristics as shown in Figures 2.6b and 2.6c, respectively.

Figure 2.6 (a) Schematic diagram of a SWCNT in a back-gated FET configuration with source, drain and gate electrodes.⁴⁸ The typical (b) output (I_D - V_{DS}) and (c) transfer (I_D - V_G) characteristics of a CNT-based FET.

As-grown CNTs are p-type due to oxygen adsorption during growth.⁵ Therefore, a positive V_G attracts the minority carriers, i.e., electrons towards the CNT surface, which depletes the channel of holes, causing the FET to remain in an OFF

state. As V_G becomes negative, the holes are attracted towards the surface resulting in the formation of an inversion region, which conducts upon application of a suitable V_{DS} . The threshold voltage (V_{th}) determines the transition from the OFF to the ON state. For $|V_G| \ll |V_{th}|$, the device is in subthreshold or weak inversion regime, where minority carriers govern the transport properties. For $|V_G| \gg |V_{th}|$, the FET enters the strong inversion regime comprising the majority carriers (holes). The moderate inversion region marks the transition between the two regions. In the moderate and weak inversion regimes, the behaviour of the charge carriers is different from that in the strong inversion region because of the comparable magnitude of the transverse gate electric field (E_G) and the longitudinal drain-source electric field (E_{DS}).

2.3.1a Transistor Model

According to FET theory,¹¹ under a low bias the CNT FET behaves like a voltage controlled resistor. The drain current in the deep Ohmic region of the output characteristic is given by,

$$I_D = \mu_{eff} \frac{C}{L^2} \left[(V_G - V_{th}) V_{DS} - \frac{V_{DS}^2}{2} \right] \quad (2.4)$$

where I_D is the drain current, V_{DS} is the drain bias voltage, L is the length of the nanotube, C/L is the capacitance per unit length of the nanotube, V_{th} is the threshold voltage, V_G is the gate-source voltage and μ_{eff} is the effective mobility. For $|V_{DS}| \ll |(V_{th} - V_G)|$, Eq. (2.4) reduces to

$$I_D = \mu_{eff} \frac{C}{L^2} [(V_G - V_{th}) V_{DS}] \quad (2.5)$$

The capacitance per unit length of the nanotube is modelled by cylinder on a planar substrate and is given by

$$\frac{C}{L} = \frac{2\pi\epsilon_0\epsilon_r}{\ln\left(\frac{2t_{ox}}{r}\right)} \quad (2.6)$$

where ϵ_0 is the permittivity of free space ($8.8542 \times 10^{-12} \text{ Fm}^{-1}$), ϵ_r is the dielectric constant of SiO_2 gate insulator (~ 3.9), t_{ox} is the SiO_2 thickness, and r is the radius of the nanotube.⁴⁹⁻⁵² Some of the transistor parameters obtained from the transfer and output characteristics are discussed below.

Conductance (G) is the instantaneous slope of the output characteristics at a constant V_G such that

$$G = \frac{\partial I_D}{\partial V_{DS}} \quad (2.7)$$

Transconductance (g_m) is the instantaneous slope of the transfer characteristics at a constant V_{DS} . It determines the sensitivity of the FET and is defined as

$$g_m = \frac{\partial I_D}{\partial V_G} \quad (2.8)$$

Subthreshold swing (S) is the reciprocal of the change in logarithmic value of I_D for a change in gate voltage. It is used to estimate the speed of transition from “ON” to the “OFF” state. A low subthreshold swing is desirable for fast switching and is highly useful parameter in digital applications.⁵³

$$S = \left(\frac{\partial \log I_D}{\partial V_G} \right)^{-1} \text{ in mV/decade} \quad (2.9)$$

Threshold voltage (V_{th}) is the voltage, which separates the ON state from the OFF state in a FET. A low V_{th} reduces the voltage required to turn ON the device.

Hysteresis gap (H) is the difference between the threshold voltages obtained from the forward and reverse gate voltage sweeps. It is not an intrinsic property of the FET, but arises due to contribution from other factors like interface traps, charge traps, dipoles etc.⁵⁴

Mobility, in general, is a measure of the response of the charge carriers to an applied electric field. It is defined as

$$\mu = \frac{v}{E} = \frac{e\tau}{m^*} = \frac{\sigma n}{e} \quad (2.10)$$

where v is the drift velocity of charge carriers, E is the applied electric field, σ is the conductivity, and ne is the charge density. Mobility is further defined in two ways for a transistor- the effective mobility (μ_{eff}),^{11,55-57} which is closest to the intrinsic value of the nanotube without including any device attributes given by,

$$\mu_{eff} = \frac{L^2}{C} \frac{G}{(V_{th} - V_G)} \quad (2.11)$$

and conventional device field-effect mobility (μ_{fe}),^{11,55-57} which includes the device attributes like contact resistance, parasitic resistance, surface effects, etc., and is given by

$$\mu_{fe} = \frac{L^2}{C} \frac{g_m}{V_{DS}} \quad (2.12)$$

For random network based FETs, L^2/C is replaced by L/WC where W is the channel width and $C (= \epsilon_r \epsilon_o / t_{ox})$ is capacitance per unit area.

2.3.1b Modes of Operation

CNT-based FETs show both Schottky Barrier and MOSFET-like bulk effects.

Figure 2.7 Schematic diagrams showing (a) the metal Fermi level (E_{fm}), semiconductor Fermi level (E_{fs}), semiconductor conduction band energy (E_{cs}) and semiconductor valence band energy (E_{vs}), and (b) the formation of Schottky barrier due to Fermi level alignment between the contact metal and semiconducting CNT.

When a semiconducting CNT encounters a metal electrode, an alignment of their respective Fermi levels (Figure 2.7a) at equilibrium occurs, which results in the formation of a depletion zone in the semiconductor at one junction. This zone acts as an obstacle to current flow in one direction resulting in a rectifying behaviour. Such FETs based on carrier tunnelling through the barrier as shown in Figure 2.7b are called Schottky barrier FETs.⁵⁸⁻⁶⁰

Figure 2.8 Schematic diagrams of a p-type Schottky barrier (a) at $V_G=0 \text{ V}$ (OFF state), and (b) at $V_G<0 \text{ V}$ (ON state), when the band alignment causes a shifting of the Fermi level resulting in hole tunneling.

The existence of Schottky barriers at the CNT-metal electrode junction causes an asymmetric variation of the drain current for opposite gate bias voltages. Figures 2.8a and 2.8b show the schematic representations of Schottky barrier operation. A FET operates as a Schottky barrier FET when the barrier blocks its current flow and carrier transport depends on overcoming this tunnelling barrier. This Schottky barrier height is band gap dependent, which in turn, is inversely related to the diameter of the nanotube.⁶⁰ As a result, large diameters have smaller barrier heights. Therefore, a proper choice of contact materials like Pd with CNT diameters >2 nm will reduce the Schottky barrier influence.⁶¹

Figure 2.9 Schematic diagrams of a p-type bulk-effect in CNT FET (a) at $V_G=0$ V (OFF state), where the shaded region indicates the modulation of only bulk by the gate, and (b) $V_G<0$ V (ON state), when the holes accumulate in the CNT.

Figures 2.9a and 2.9b show the schematic representations of a basic p-type bulk-mode operation. In this mode, the electrostatic potential of a SWCNT is modulated by an applied gate voltage, which causes the accumulation/depletion of charge carriers in the CNT during the ON/OFF state.⁶²

2.3.2 Types of FET Sensing Mechanisms

The current transport in SWCNT channel is extremely sensitive to the adsorptions/reactions occurring on its surface, which is readily detectable through an electronic readout. The transistor I - V characteristics can identify the molecular recognition through various sensing mechanisms. There are four widely accepted sensing mechanisms investigated by Heller *et al.*⁷: i) charge transfer/electrostatic gating, ii) Schottky barrier modulation, iii) capacitance modulation and iv) mobility modulation. Each mechanism has its own characteristic effect on the transfer curves as seen in Figures 2.10a-d.

Figure 2.10 Typical FET transfer curves of the four possible sensing mechanisms following CNT-biomolecule interaction. (a) Electrostatic gating/charge transfer, (b) Capacitance modulation, (c) Schottky barrier modulation and (d) Mobility modulation. Adapted from ref.⁷.

A charge transfer/electrostatic gating mechanism is reflected in the form of a shift in FET threshold voltage to either more positive values indicating electron withdrawal from the SWCNT or more negative values as a consequence of electron donation to the SWCNT.^{63,64} The experiments by Bradley *et al.*⁶⁵ showed the detection of streptavidin using a SWCNT FET based on charge transfer mechanism (Figure 2.11a). According to this report, ~4000 amine groups per streptavidin on interaction with SWCNT resulted in the transfer of 0.04 electrons into the SWNT valence band, while Hu *et al.*⁶⁶ observed the opposite effect and attributed it to electrolyte gating.

The capacitance changes⁶⁷ occur in liquid gated FETs because of the change in gate capacitance following the adsorption of biomolecules (Figure 2.11b). The low permittivity of the biomolecules compared to the electrolyte alters the gate capacitance. In general, the quantum capacitance dominates the CNT-electrolyte interfacial capacitance.⁶⁸ Therefore, the reduction in electrostatic capacitance will be apparent only when the surface has full biomolecule coverage. The inhibition of the binding of the ions from the electrolyte onto the CNT reduces the electrical conductance.

In a Schottky barrier modulation mechanism, the adsorption of biomolecules affects the metal electrode and causes local modulation of the metal work function, which alters the band alignment at the CNT-metal junction.^{69,70} This results in an asymmetric shift in drain current for opposite gate biases, which is a characteristic of Schottky barrier mechanism.⁶³ Experiments conducted by Gui *et al.*⁷¹ for DNA

hybridization detection indicate the dominance of metal work function modulation (Figure 2.11c). Similarly, biosensing experiments on the interaction of proteins with unpassivated SWCNT FETs demonstrated the dominance of Schottky barriers modulation rather than SWCNT-protein interaction.⁷²

In the mobility modulation mechanism, the adsorbed molecules act as scattering potentials and suppress current flow in both p- and n-branches of conduction, resulting in the changes in mobility. Mobility change occurs in FETs dominated by diffusive transport, especially, in long channel FETs. According to Star *et al.*,⁷³ polymer–biotin functionalized FETs showed a reduced slope indicating reduction in mobility following protein detection. According to Fu *et al.*,⁷⁴ ultrasensitive detection of DNA based on the mobility changes is possible using high on/off ratio CNT network (Figure 2.11d).

In general, electrostatic gating/charge transfer^{75,76} and Schottky barrier modulation^{70,71} are two most predominant FET mechanisms in biosensing applications.

Figure 2.11 (a) FET transfer curves before (solid line) and after streptavidin (dotted line) exposure showing charge transfer mechanism.⁶⁵ (b) FET transfer curves of aptamers-modified thrombin detection showing the contribution of capacitance effects.⁷⁷ (c) A comparison of the FET transfer curves of junction-exposed (left) and channel-exposed (right) device before probe DNA immobilization, after probe immobilization, and upon target DNA hybridization demonstrating Schottky barrier modulation. The image of the corresponding photoresist capped region obtained using optical microscope is shown in the respective inset.⁷¹ (d) DNA detection using network SWCNT FET exhibiting mobility modulation mechanism. The schematic diagram of DNA on SWCNT network FET (left), the transfer curves before and after DNA addition (middle), and the plot of % mobility change vs. DNA concentration for devices with different on/off ratio (right) are shown.⁷⁴

2.3.3 CNT Chemiresistor

A chemiresistor is a simple electronic sensor that responds to the change in resistance introduced by the binding of analytes. Chemiresistors offer several potential advantages such as low cost, low power consumption, rapid and label-free detection of chemicals/biomolecules, and highly accurate resistance measurements.⁷⁸⁻⁸⁰

Figure 2.12 (a) Schematic diagram of a chemiresistor setup for cyclohexanone sensing with the chemical structures of the functionalization entities. (b) The normalized conductance of a CNT chemiresistor functionalized with a tri-functional selector and exposed to various concentrations of cyclohexanone. The inset shows normalized conductance vs. concentration calibration curve.⁸¹

Figures 2.12a and 2.12b show the schematic diagram of a CNT chemiresistor setup on a glass substrate, and conductance vs time plots (conductance response vs. concentration shown in inset) for cyclohexanone sensing, respectively, reported by Frazier *et al.*⁸¹ The tri-functional selector performs three functions: the first is to promote noncovalent bonding with SWCNT through the bis(trifluoromethyl) aryl

group. The second is to bind to ketones through two-point hydrogen bonding with the aid of thiourea group and to detect cyclohexanone. The final function uses the triethoxysilane (TES) group to create a polymer network structure, besides reacting with the hydroxyl groups on the glass surface to immobilize both SWCNT and receptor. The gas sensing is marked by a peak in the conductance response, which shows the rise in resistance following the introduction of cyclohexanone. The decrease in conductance was attributed to a combination of interaction of cyclohexanone's dipole with holes as a result of oxidative (air oxidation) doping, swelling of the network causing the tunnelling barriers to widen and/or the alterations in the energetics of intertube conduction pathways induced by dipoles following absorption of cyclohexanone.⁸¹ After attaining the peak value, the response subsides to its stable base line state showing the recovery of the sensor. The normalized conductance peaks increases with increasing concentrations of cyclohexanone.

2.3.4 Factors Affecting CNT-Based Electronic Bio/Chemical Sensing

The performance of CNT-based electronic detection of molecular recognition is dependent on two important factors:

- i) Molecular factors such as CNT-receptor (receptor immobilization) and receptor-analyte interaction.
- ii) Device factors such as CNT-metal junction, device architecture, type of CNT and device operation regime.

2.3.4a Molecular Factors

To ensure effective receptor immobilization, and subsequent efficient receptor-target interaction, surface modification of the transducer surface is necessary. Broadly, the surface modification techniques are divided into two major types based on the nature of interaction of the functionalization entity with the SWCNT surface, namely, covalent and non-covalent methods.

Figure 2.13 A schematic diagram showing the various covalent surface functionalization routes on a CNT.⁸²

Covalent functionalization involves the application of modification to the ends or sidewalls of the nanotube by introducing functional groups.⁸³⁻⁸⁵ The different functional groups cater to different types of receptor moieties. Some of the commonly used reactions to introduce functional groups include fluorination, cycloaddition,

cyclopropanation, nucleophilic carbenes addition, diazotization, and reduction reactions.^{84,86-88} Figure 2.13 shows the various covalent functionalization routes.

Figure 2.14 Schematic diagrams of some noncovalent functionalization entities such as (a) zinc porphyrin, (b) pyrenecyclodextrin and (c) pyrene/CdSe nanoparticles decorated on a SWCNT used in a FET configuration for bio/chemical sensing.¹⁹

Non-covalent approaches involve the adsorption of molecules on the CNT surface based on π - π interactions, electrostatic and van der Waals forces, which preserve the surface properties of the nanotube.⁸⁹ Polymer adsorption,⁹⁰ *in-situ* catalytic polymerization,⁹¹ *in-situ* electrochemical polymerization⁹² and adsorption of molecules with large π -systems⁹³ are some of the routes for non-covalent

functionalization. Figures 2.14a-c show some non-covalent functionalization schemes used in SWCNT FETs for bio/chemical sensing.

The surface modification could enhance molecular recognition on CNT by

- i) making the surface responsive,
- ii) preventing non-specific interactions, and
- iii) improving the specificity and selectivity of molecular recognition.

Figure 2.15 Schematic diagrams showing the strategy involved in (a) making surface responsive by ssDNA-decoration,⁹⁴ (b) preventing non-specific binding of biotin on SWCNT by using Triton-X 100 and PEG, and (c) improving the selectivity of biotin-streptavidin binding using biotin-amidocaproic acid 3-sulfo-N-hydroxysuccinimide ester linker in a SWCNT FET.³

All bio/chemical species do not readily interact with CNT and give reproducible signals. Hence, it is necessary to make the surface responsive to the molecule of interest. Biopolymers such as single-stranded DNA (ssDNA) interact with

CNT through π -stacking and are used in the detection of a wide variety of analytes in vapour/gaseous state, which otherwise have no effect on CNT (Figure 2.15a).^{10,13}

SWCNT FET-based detection of biotin-streptavidin interaction by Shim *et al.*³ revealed that coating SWCNT with Triton X and polyethylene glycol (PEG) prevented the non-specific interactions of streptavidin on CNT (Figure 2.15b). In addition, in SWCNTs coated with Triton and amine-terminated PEG, the PEG covalently binds with succinimidyl group in biotinamidocaproic acid 3-sulfo-*N*-hydroxysuccinimide ester (Figure 2.15c). This functionalization scheme improved the selectivity of streptavidin recognition while eliminating non-specific interactions. Similarly, the linker molecules such as 1-pyrenebutanoic acid succinimidyl ester (PASE)⁹⁵ can adsorb on the CNT sidewalls through π - π interactions as well as covalently form amide linkages with the amine groups of target analytes including ferritin, streptavidin, and biotinyl-3,6-dioctanediamine through its succinimidyl ester group, and improve the specificity of detection.⁶⁷

In general, the immobilization of receptors on CNT is based on chemical interactions such as covalent bonding and cross-linking, as well as physical interactions such as adsorption, entrapment, confinement, and encapsulation between the functionalization entity and receptor.⁹⁶ The type of interaction between the receptor and target analyte determines the transduction output. Some of the common receptor-target interactions are given below:

- i) Non-polar molecules because of the poor solvation of the molecular surface exhibit hydrophobic interaction.^{96,97} The lack of polarity in such molecules results in their aggregation in aqueous solution and exclusion of water molecules, which is known as the hydrophobic effect. Since every nonpolar molecule is hydrophobic, this type of interaction is not specific.
- ii) Electrostatic forces include both attractive and repulsive interactions depending on charge carried by the receptor and target.^{96,98} Molecules carrying the same charges tend to repel each other while opposite charges exhibit attractive forces. This interaction depends on the electrical charge and the ionic strength of the medium and is nonspecific. Electrostatic interaction is strong as well as long-ranged.
- iii) Polar interactions occur because of dipole-dipole interactions between the receptor and analyte.^{10,96} Dipole–dipole interactions are attractive intermolecular forces between two molecules. These interactions are a type of electrostatic interactions between the permanent dipoles of different molecules, which align the molecules to increase the attraction (intermolecular bonding). These interactions are weaker and short-ranged.
- iv) Hydrogen bond involves the attraction between H and electronegative atoms such as N, O and F in the receptor and analyte.^{71,96} The presence of both acidic and basic sites in molecules is enough for hydrogen bonding. It is oriented but not specific.

- v) Complex formation occurs due to the sharing of external electron orbitals between the host (receptor) and guest molecule (analyte) partners.^{96,99} It is highly oriented and closely depends of the chemical nature of the partner, so that it is specific.

2.3.4b Device Factors

The device factors affecting the sensing mechanism include the CNT-metal junction, device architecture, type of CNT, and the operation region of the FET.

The CNT-metal junction may give rise to unwanted false signals, which makes signal analysis difficult. In this case, passivation of the electrodes could be beneficial.^{100,101} However, in some cases, the Schottky area is more sensitive to certain molecule, which suggests that covering the channel region could yield better device response.⁷¹

The device parameter (channel length, channel width and network density) affects the sensitivity of detection (Figure 2.16a).¹⁰²⁻¹⁰⁴ Longer channels reduce the incubation time leading to a faster response, but very long channels may also degrade the sensitivity of the sensor. Therefore, it is necessary to optimize the device parameters to strike a balance between response time, sensitivity and incubation period. The presence of CNT-CNT interconnections with both metallic (M) and semiconducting (S) tubes in network-based FETs results in the sensing mechanism of these network FETs to be different from individual CNT-based FETs.¹⁰⁵ In particular, a high device on/off ratio and mobility are prerequisites of transistors for good

response to biodetection. However, the coexistence of M and S CNTs makes on/off ratio and mobility of the FETs to be dependent on network density and channel length. Based on the percolation model,^{106,107} each SWCNT in a network behaves as a conducting path. To optimize the performance of network SWCNT-based FET, it is necessary for the total network density to be above the percolation threshold and the density of metallic CNTs to be below the percolation threshold.¹⁰⁸

The other aspect of device architecture includes the use of either single nanotubes or network CNTs (Figure 2.16b). The difference in structure allows the operation of the sensor as FET as well as chemiresistor. Single SWCNT-based devices have superior sensitivity, but suffer from device to device variability, poor reproducibility, and low efficiency because the tube chirality and diameter differ during each SWCNT growth run, despite the growth conditions being unchanged, which alters the electronic transport properties of the device. Even with the current advancements in SWCNT growth, obtaining nanotubes with exactly the same chirality and diameter is still challenging, which in turn, affect the reproducibility and repeatability of SWCNT based devices. However, individual SWCNTs are particularly useful in detecting molecules approaching nanometer size such as nucleic acids (~0.34 nm) because of their better size compatibility with DNA, RNA etc. compared to larger molecules such as proteins, carbohydrates, lipids etc.

Figure 2.16 (a) Plots of on/off ratio (left) and mobility (right) vs. channel length of network-based CNT FET showing opposite trends.¹⁰¹ (b) The schematic diagram of CNT-based FET employing single SWCNT (left), horizontally aligned SWCNTs (middle) and network SWCNT (right) as the conduction channel, respectively. (c) (Left) Plot showing improvement in on/off ratio with network length, and (right) high mobility of a 325 μm long individual (inset) CNT-based FET. (d) (Left) Conductance vs. time of semiconducting (1, 2) and metallic (3) CNT FET during the adsorption of the protein cytc. The arrow indicates the start of the introduction of cytc into the buffer solution. (Right) Plot of the relative change of conductance vs time.⁶³ (e) (left) Conductance vs. gate voltage and (right) conductance response vs. time plots of a p-type silicon nanowire FET demonstrating higher sensitivity in the subthreshold regime when used as a pH sensor.¹⁰⁹

Network CNTs contain interconnected nanotubes, which despite the presence of different diameter, chirality, and length distribution of CNTs, result in a more uniform and reproducible system because of statistical averaging.¹¹⁰ In addition, networks can be easily grown on a silicon substrate using catalyst or by casting from a dispersed SWCNT solution.^{111,112} They have larger coverage area, higher uniformity, lower noise and higher reproducibility, which is inexpensive and suited for detection of larger sized molecules (see Figure 2.16c).¹⁰¹

The type of CNT determines the sensing mechanism. Metallic CNTs are insensitive to molecular detection since charge transfer does not significantly affect the charge density at the Fermi level,¹¹³ but semiconducting SWCNTs show large variations in conductance and transconductance following molecular adsorption as shown in Figure 2.16d,⁶³ which is dependent on the chirality and diameter of the CNT. Reduction of CNT diameter will improve its sensitivity because of higher surface to volume ratio.

The gate bias operational region of the FET has a profound impact on the sensing mechanism. According to studies by Gao *et al.*,¹⁰⁹ the subthreshold regime exhibited the highest sensitivity to biosensing with a high signal to noise ratio (Figure 2.16e), while studies by Heller *et al.*¹⁰⁵ revealed a large conductance response in this regime.

From the above discussions, it is clear that CNT-based FETs/chemiresistors have been used to detect a wide variety of target analytes using different receptors.

Table 2.2 lists a summary of some of CNT-based electronic molecular recognition of different molecules using various receptors.

Table 2.2 A summary of CNT-based FET/chemiresistive sensor for detection of various biomolecules and chemicals.

Receptors	Targets
DNA, RNA, aptamers	DNA/RNA, ⁶⁹ gases, ¹³ adenosine triphosphate (ATP), ¹¹⁰ proteins, ⁷⁷ toxins ¹¹¹
Enzymes	Reduced nicotinamide adenine dinucleotide (NADH), ¹¹² carbohydrates, ¹¹³ toxin, ¹¹⁴ cell activity ^{115,116}
Antibodies	Microorganism, ¹¹⁷ steroid, ¹¹⁸ protein, ¹¹⁵ biomarker ¹¹⁹
Hormones	Pollutants ⁷⁶
Polydiacetylene, hexafluoroisopropanol phenyl-1-pyrenebutyramide	Chemical warfare agents ^{111,120,121}
Lipids	Ions ¹²²

2.4. Summary

The CNT properties, the types of CNT-based electronic sensors, and the sensor concepts associated with electronic detection of bio/chemical molecular recognition using CNT FET/chemiresistor have been reviewed. Overall, for effective electronic detection of molecular recognition, attention has to be devoted to two areas of CNT FET/chemiresistor-based electronic detection of molecular recognition:

- i) Surface modification of SWCNTs enhances receptor immobilization, increases the accessibility of receptors to target analyte, and prevents non-specific

adsorption, which are requisites for good specificity and sensitivity of molecular recognition (receptor-target interaction). On the other hand, selectivity of a molecular receptor is determined by how differently it interacts with different analytes, which is influenced by CNT-receptor interaction as well as receptor-target interaction. The stability of transduction is determined by the sustainability of the surface modification, which depends on the nature of the interaction between the receptors and functionalization entities. Therefore, it is necessary to investigate the effect of surface modification on the sensing mechanism.

- ii) A stable device structure is essential to obtain a constant and predictable signal, provide a surface for reliable functionalization, and understand the effect of molecular variables on the sensor response. The efficacy of the SWCNT-based FETs in detecting molecular recognition depends on the number of receptor-target interactions occurring on the SWCNT surface. Ultralong channels could confine more such interactions on the CNT, but they suffer from high channel resistance. Similarly, in SWCNT network-based FETs, the coexistence of metallic and semiconducting tubes makes the device on/off ratio and mobility dependent on network density and channel length.^{101,123-125} Therefore, it is necessary to optimize the device parameters (network density and channel length) to construct bio/chemical sensors for efficient electronic detection of molecular recognition.

This thesis involves the study of CNT FET/chemiresistor-based electronic detection of different molecular recognition processes such as DNA-DNA/DNA-RNA hybridization (hydrogen bonding), DNA-dopamine interaction (electrostatic/polar) and cyclodextrin-chemical interaction (host-guest complex formation) Moreover, in each chapter of this thesis, we focus on the influence of surface modification or device structure, or both on the transduction mechanism. In particular, the study of the effect of CNT surface modification on bio/chemical detection is the molecular factor discussed in this thesis, which covers one or more of the following aspects:

- ❖ The influence of functionalization moiety on the device response, specificity, and/or selectivity.
- ❖ The impact of CNT-receptor binding on the electrical response to molecular recognition based on the differences in interaction of different receptors with one analyte.
- ❖ The differences in transduction output of receptor-target interaction using different targets, but same receptor.

With respect to the device architecture, the effect of channel length and the influence of contacts of individual SWCNT-based FET for hybridization detection form the device factors investigated in this thesis.

Chapter 3: Experimental

3.1 Growth of SWCNT

Chemical vapor deposition (CVD) was used to grow SWCNT with ethanol as the source of carbon. Figures 3.1a-c show the stages of CNT growth, the apparatus used for CVD and a flow diagram illustrating CNT growth steps. Given below are the steps involved in CNT growth.

- i) *Temperature ramp:* Before the start of experiment, the tube was flushed with argon (Ar) for a few minutes in order to eliminate the residual air. The sample was placed in the middle of the quartz tube, and the furnace was heated continuously at a constant rate to the required growth temperature.
- ii) *Catalyst pre-treatment or annealing:* As the temperature reached the set point, the sample was annealed under hydrogen (H_2) environment for 30 minutes. The sintering of the iron (Fe) thin film along with reduction by H_2 results in the formation of catalyst nanoparticles at this temperature. These nanoparticles decompose the carbon source and initiate CNT growth upon its introduction into the tube.
- iii) *Growth phase:* After the annealing, the carbon source was introduced into the furnace starting the CNT growth, which lasted for the required duration.
- iv) *Cooling:* The sample was taken out after the furnace was cooled to room temperature. Different growth parameters, such as the growth temperature, the

growth duration, the value of reactant gas flow etc. control the diameter, length, and density of the nanotubes.

Figure 3.1 (a) Stages of CNT growth, (b) CVD apparatus, and (c) flow diagram illustrating CNT growth steps.

SWCNTs were grown on n^+ -doped silicon (Si) capped by a 1 μm dielectric layer of thermally grown silicon dioxide (SiO_2). The wafers had a resistivity of 0.001-0.005 $\Omega\text{-cm}$ and a Si layer thickness of 525 μm . One typical recipe to grow long SWCNTs is described here, which is similar to our previous works.^{62,79,126,127} Gas-flow-guided ethanol CVD was used to obtain horizontally-aligned ultralong SWCNTs. 0.01 M FeCl_3 solution was used as the catalytic precursor. Using a dip pen, we applied the catalyst solution at the end of the Si/ SiO_2 substrate and placed the substrate in a 1-

inch quartz tube furnace. The end of the substrate containing the catalyst faced the direction of the gas flow. The temperature of the furnace was ramped upto 950°C under a flow of 120 sccm argon (Ar) and 30 sccm hydrogen (H₂). At this temperature, the catalyst complex decomposes and reduces into Fe nanoparticles. Ar and H₂ flow were reduced to 6 sccm and 4 sccm after 10 minutes, followed by the introduction of ethanol vapor by bubbling 20 sccm Ar through ethanol (20°C) to begin the CNT growth. The ethanol supply was stopped after 40 minutes. Thereafter, the furnace was allowed to cool down to room temperature under ~120 sccm Ar.

To obtain CNTs in a high density network configuration, we increased the concentration (0.1 M) of FeCl₃ catalyst solution, increased the pre-treatment time to 20 minutes, Ar and H₂ flow were increased to 12 sccm and 8 sccm, respectively, and the growth period was raised to 50 minutes.

3.2 Device Fabrication

The fabrication of FET requires the deposition of Ti/Au (10/60 nm) onto the substrates containing the CVD-grown CNTs. Depending on the length of the channel needed for fabrication, two different methods were employed to deposit source and drain electrodes.

For fabrication of short-channel FETs with channel length <50 µm, a standard photolithography and lift-off process was used. For fabrication of devices with channel length >50 µm, Ti/Au was deposited through shadow mask facilitated electron-beam evaporation. The two methods are illustrated schematically in Figure 3.2a. Selective

photoresistive capping using photolithography was used to cover the CNT-electrode junction.

Figure 3.2 Schematic diagrams (a) of fabrication process route **A** for FETs with channel length $>50 \mu\text{m}$ and **B** for FETs with channel length $<50 \mu\text{m}$, and (b) a typical chemiresistor setup.

For fabrication of a chemiresistor, a $2 \text{ mm} \times 3.5 \text{ mm}$ CNT network recording chamber area with source and drain electrodes at the two opposite edges of the CNT

network was created using silver paint, and silicone rubber was used to insulate the two CNT-electrode junctions (Figure 3.2b).

3.3 Characterization Methods

3.3.1 Scanning Electron Microscopy (SEM)

We used SEM (Jeol, JSM-7600F) to observe the morphology of CNTs over a large area with an acceleration voltage of 1 kV and magnification around $25\times$ to show the existence of CNTs. SEM was used to analyze the length and density distributions of CNTs. Figures 3.3a-c show the SEM images of CNT array, CNT network, and the fabricated FETs of different channel lengths.

Figure 3.3 SEM images of (a) CNT array in the range of millimeters, (b) high density random network CNT and (c) as-fabricated CNT FETs with short (few μm), long (few hundreds of μm) and ultralong (few mm) channel.

3.3.2 Atomic Force Microscopy (AFM)

AFM (Asylum Research, Cypher AFM) was used to obtain the height profile in the tapping mode. The AFM tip moves along the sample containing the CNT to give the height profile. The difference in height profile between the substrate and the top of the CNT surface gives the CNT diameter.

Figure 3.4 (a) AFM image and (b) height profile of a long individual SWCNT. (c) The histogram plot of the diameter distribution of the as-grown SWCNTs.

Figures 3.4a and 3.4b show the AFM image and height profile of a SWCNT, respectively. The two colored dots in Figure 3.4b are the markers corresponding to the height profile of the substrate and top of SWCNT surface. The difference between

these markers gives the diameter of the SWCNT, which was ~ 1.51 nm. Figure 3.4c shows the diameter distribution of as-grown CNTs. The average diameter of the SWCNTs was ~ 1.55 nm.

3.3.3 Resonance Raman Spectroscopy

Raman spectroscopy is a fast and effective method for characterizing the as-grown CNTs. CNTs can be spatially resolved in Raman mapping images, with respect to morphology and consistency. The radial breathing mode (RBM) signals and G bands signal in combination with confocal imaging can be used for assessing the semiconducting nature of the CNTs.¹³³ Three important features from the Raman spectrum, which aid in probing the structural information of SWCNTs, include the low frequency radial breathing mode (RBM), the defect-induced D-band at ~ 1300 cm^{-1} and the tangential stretching G-band observed between 1500 and 1600 cm^{-1} . The RBM represents the coherent vibration of carbon atoms in the radial direction, and appears in the range 150-300 cm^{-1} . The D band is a result of a double resonance process, which is observed in the 1300-1400 cm^{-1} range.¹³⁴ The stretching of the C-C bond is reflected as a G band with a single sharp peak at ~ 1582 cm^{-1} in graphite. However, because of the quantum confinement of phonon wave vector along the SWNT circumferential direction and the symmetry-breaking effects associated with SWNT curvature, the G band in SWCNTs exhibits a double-peak feature known as G^+ and G^- components.¹³⁵ Therefore, the appearance of D band and the intensity (I_n) ratio of D band and G band

(I_D/I_G) can be taken as fingerprints for identifying defects in SWCNTs and evaluating the extent of chemical functionalization in a carbon material.¹³⁴

We used a Raman spectrometer (Renishaw, via Microscope) combined with a confocal imaging microscope to obtain Raman image in our experiments. The laser power used was <1 mW to avoid any heating effects and an excitation wavelength of 633 nm was used to characterize the as-grown CNTs. The laser beam was focused onto the substrate containing the CNTs with a 100× objective, which provides a 1 μ m excitation spot size. The Raman spectrum was collected and integrated thrice using an integration time of 10 s.

Figure 3.5 The Raman spectrum of a 1 cm long SWCNT showing RBM at ~ 129.7 cm^{-1} and G band with G^- and G^+ peaks at 1590 cm^{-1} and 1603 cm^{-1} , respectively. The inset shows the Raman mapping image of the SWCNT.

Figure 3.5 shows a typical Raman spectrum with G band and RBM signals of a long CNT with its Raman mapping image in the inset. The SWCNT with a RBM frequency at 129.7 cm^{-1} is assigned to be semiconducting within the resonance window. The peak at 1328 cm^{-1} can be assigned to the A_{1g} breathing mode of the

disorder graphite structure (i.e., the D band). The E_{2g} structure mode of graphite (i.e., the G band), is seen as G^- and G^+ peaks at 1590 cm^{-1} and 1603 cm^{-1} , respectively. The twin peak feature demonstrated the semiconducting characteristic of the SWCNT, which is in agreement with literature.¹³³⁻¹³⁵ The I_{D}/I_{G} of as-grown SWCNTs was ~ 0.087 , which is consistent with those reported in previously published results.^{136,137}

3.3.4 Electrical Characterization

All electrical measurements were recorded using Agilent 4156B semiconductor device analyzer. The drain current (I_D) vs. gate voltage (V_G) characteristics (transfer) were measured at a constant drain-source voltage (V_{DS}) of 1 V. The slope of the I_D - V_{DS} (output) characteristics in the range -0.1 V to 0.1 V at $V_G = -24\text{ V}$ (ON state) of the FET gives the ON-state conductance (G_{on}). The threshold voltages for the forward (V_{fth} , -24 V to 24 V) and reverse (V_{rth} , 24 V to -24 V) gate voltage sweeps were extracted by extrapolating the steepest portions of the I_D - V_G curve for both the gate voltage sweeps to intersect with the x-axis. The instantaneous slope of the I_D - V_G curve at a particular V_G gives the transconductance (g_m) at that V_G . g_m of the transfer curve near the threshold voltage gives the peak transconductance (g_{mp}). The difference between the threshold voltages obtained from the forward and reverse gate voltage sweeps gives the hysteresis gap (H).

For real-time bio/chemical sensing based on conductance recordings, a plot of the relative change in conductance given by $(G-G_0)/G_0$ (where G and G_0 are the steady-state conductance values after exposure to particular concentration of target

molecule and conductance after exposure to buffer only, respectively) with respect to logarithmic value of target molecule concentration was used. The drain bias was kept constant at 1 V. The average of $(G-G_0)/G_0$ obtained from at least five devices for each target molecule concentration gives the calibration curve, i.e., $(G-G_0)/G_0$ vs. target molecule concentration. To analyze the sensor performance, the sensitivity, and limit of detection (LOD) was calculated. The sensitivity in the linear region is obtained using the slope of the linear portion of $(G-G_0)/G_0$ vs. target molecule concentration in the lower concentration range. The LOD is given by $3\sigma/m$, where σ is the standard deviation of the blank measurement and m is the slope of the linear portion of the calibration curve. The correlation coefficient of determination (R^2) is obtained from a linear fit to $(G-G_0)/G_0$ vs. concentration plot.

The electrical characterization results of as-fabricated SWCNT FETs/chemiresistors were displayed by the mean ($\pm$ standard deviation) values of the transistor/chemiresistor parameters (obtained from I_D - V_G / I_D -time characteristics), i.e., G_{on} , g_{mp} , V_{th} and H .

3.4 Classification Tool

Generally, the FET/chemiresistor sensor response is interpreted in terms of the magnitude and sign of the change in output drain current, transconductance, threshold voltage, and/or hysteresis gap upon interaction with biomolecules/chemicals. Discrimination of such response data obtained from different molecular recognition processes to analyze the molecular selectivity is too complex. In this regard, data and

pattern classifications are extremely helpful in analyzing and interpreting the selectivity and discriminating capability of sensors, when dealing with such closely related sensor data.^{124,138,139} Specifically, neural networks, with their remarkable ability to extract meaning from complicated or imprecise data, act as a discrimination tool, which can detect the variations in data/pattern trends that are difficult to be comprehended by either humans or other computer techniques. A trained neural network is as an "expert" in the category of information it has been given to analyze.

Figure 3.6 (a) A typical MLP architecture. (b) Schematic diagram of ANN showing the input, hidden and output layers with 'w' and 'b' denoting the weights and bias, respectively.

In our study, we employed an artificial neural network (ANN),¹⁴⁰⁻¹⁴² a very popular tool capable of storing, acquiring, and using experiential knowledge by making use of its parallel processing units, which are connected to each other. ANN comprises several simple processing elements, or neurons, or nodes, similar to the biological neuron with the connections between nodes called synapses. The output of a node is the weighted sum of the input signals, transformed by the activation function to include the nonlinearities associated with the neurons. The process of preparing the ANN to identify the input by adjusting the weights is called learning/training.

Amongst the broad plethora of ANN models available, we used the multi-layer perceptron (MLP) architecture (Figure 3.6a) comprising a layer of input neurons, a layer of output neurons, and one or more hidden layers, employing a backpropagation learning algorithm.¹⁴¹⁻¹⁴³ A fixed-length vector defined by the user is the input unit. In the hidden unit, the thresholded weighted sum of the inputs is calculated, which represents the intermediate calculations learnt by the network (learning). The output unit is also a fixed length vector of numbers, which gives the result of the classification. The processing units are arranged in layers with each unit in one layer linked to the every other unit in the next layer, but none to the back layer, the same layer, or skipping a layer, such that the computations proceed uniformly from input to the output. Figure 3.6b shows the schematic diagram of an ANN with the input and output activation functions.

Figure 3.7 A flow chart illustrating the general steps involved in feature extraction and classification of CNT FET/chemiresistor sensor data using ANN.

Figure 3.7 describes the steps involved in classification of CNT sensor data. Typically, the raw data is obtained in the form of drain current with respect to either gate voltage or time. The raw data is accumulated before and after bio/chemical sensing from several devices and for different target molecules to constitute a dataset. Either the transistor parameters (G_{on} , g_m , V_{th} , H) obtained from the transfer curve, or, the correlation data obtained from conductance vs. time plots are designated as features and fed as input to the classifier. The required number of output classes is pre-defined, thus, enabling the clustering of closely related data into the respective class using a suitable algorithm, which is also called training. After training, once more new data is fed into the classifier, it efficiently discriminates the data. The performance of

the classifiers is estimated using accuracy, sensitivity, and specificity as described below.¹⁴¹⁻¹⁴³

Accuracy is the proportion of true results correctly classified and is computed as

$$Accuracy = \frac{True\ Positives + True\ Negatives}{Total\ number\ of\ samples} \quad (3.1)$$

Sensitivity represents the proportion of correctly identified true positives and is calculated as

$$Sensitivity = \frac{True\ Positives}{True\ Positives + False\ Negatives} \quad (3.2)$$

Finally, specificity is the proportion of correctly identified true negatives and is determined by

$$Specificity = \frac{True\ Negatives}{False\ Positives + True\ Negatives} \quad (3.3)$$

ANN-based classification allows in evaluating the discriminating ability of the sensor. A high percentage of classification accuracy, sensitivity, and specificity suggest the ease in classifying the input data/patterns, which is an indicator of greater separability between the input data/patterns of different molecular recognition processes.

Program codes were written in MATLAB R2012a (The Math Works Co. MATLAB© version 7.14) to perform MLP-based classification. For the MLP architecture, tan-sigmoid and linear functions were used as the input and output activation functions, respectively, and Levenberg Marquardt algorithm (LMA) was the back propagation algorithm adopted for the training process.^{143,144} The data used for classification was split into train (for network learning) and test data in the ratio 3:2,

and 10 validation checks were performed. Various functions in MATLAB were used to perform different steps of classification, of which, the most important ones have been listed in Table 3.1.

Table 3.1 Summary of the MATLAB functions used to perform MLP classification and the tasks performed by them.

MATLAB Functions	Tasks
<code>xlsread()</code>	Imports input data in excel document
<code>patternet()</code>	Builds the classifier according to the user requirements
<code>train()</code>	Trains the network using the given input data
<code>plotperform()</code>	Plots the performance for each training validation and test sets
<code>testX()</code>	Tests the new data against the trained network
<code>plotconfusion()</code>	Gives the overall percentages of correct and incorrect classification. It is used to calculate the sensitivity, specificity and accuracy.

Chapter 4: Effect of Pyrene Derivative Functionalization and Channel Length of CNT-Based FETs in Nucleic Acid Hybridization Detection

4.1 Introduction

The detection of hybridization of nucleic acids such as deoxyribo nucleic acid (DNA) and ribo nucleic acid (RNA) in the field of biosensing is significant in biomedical research.¹⁴⁵⁻¹⁴⁷ Hybridization involves the combination of two DNA or RNA complementary single chains to form DNA-DNA, DNA-RNA or RNA-RNA duplexes based on the concept of base pairing specificity of nucleic acids. Specifically, the nitrogenous base adenine (A) pairs with thymine (T) or uracil (U), while cytosine (C) pairs with guanine (G) through hydrogen bonding.^{148,149} For example, DNA-RNA hybrids are important in pharmacological applications in drug development of short antisense oligonucleotides for inhibition of gene expression.¹⁵⁰⁻¹⁵² Besides the structural differences between DNA and RNA, the thermodynamics, kinetics, binding affinity, and nature of the probe also contribute to the variations in the formation of DNA-DNA and DNA-RNA duplexes.¹⁵³⁻¹⁵⁶ Therefore, distinguishing these duplexes can furnish information about drug-nucleic acid related applications.¹⁵⁷

Previously, SWCNT FET-based hybridization detection studies indicated the dominance of CNT-metal electrode junction in the sensing mechanism.^{10,69,70} However, majority of these findings used short un-functionalized CNTs, which have three main concerns. Firstly, non-specific adsorption on un-functionalized SWCNTs

poses a great risk of false signals. Moreover, hybridization between single-stranded DNA (ssDNA) and its complementary target (DNA or RNA) has low probability of occurrence because probe ssDNA is adsorbed on CNT by weak van der Waals and π -stacking forces.^{158,159} Secondly, DNA-DNA and DNA-RNA cannot be discriminated by such un-functionalized SWCNTs. Finally, the presence of CNT-metal electrode junction in sensing makes distinguishing hybridization from other biological events hard to decipher during signal analysis.

Using a non-covalent approach such as a pyrene derivative linker like 1-pyrene butanoic acid succinimidyl ester (PASE),^{89,160,161} which interacts with a SWCNT through stacking between the pyrene rings, could address the first two drawbacks, thereby enhancing the selectivity of probe nucleic acid (receptor) immobilization and target hybridization (receptor-target interaction) while preserving the intrinsic CNT properties. Long SWCNT in the range of few hundred micrometers is a potential solution for the last concern. Such long channels have large coverage area, excellent normalized conductance, and extraordinary mobility at room temperature.^{11,162} The large coverage area increases the probability of hybridizations occurring on the CNT surface at a lower incubation time and makes the device response channel dominant.

In this chapter, the differences in current-voltage characteristics of long channel SWCNT-based FETs for DNA-DNA and DNA-RNA hybridization (receptor target interaction) detection were studied. Furthermore, we investigated the effect of pyrene functionalization (surface modification) on the sensing mechanism in the presence and

absence of CNT-metal junction during hybridization detection. Finally, to study the impact of channel length (device parameter), the responses of long channel pyrene-functionalized FETs were compared against devices with short and ultra-long SWCNT channels.

4.2 Pyrene Derivative Functionalization of CNT

FETs with three different lengths (6 μm , 300 μm and 1500 μm) were fabricated and used for the experiments. All the devices of a particular channel length (L) used here for testing had similar transfer characteristics. For $L=6\ \mu\text{m}$, G_{on} , g_{mp} , V_{fth} , V_{rth} and H were calculated to be $4.5\pm 1.1\times 10^{-6}\ \Omega^{-1}$, $3.1\pm 1.2\times 10^{-6}\ \Omega^{-1}$, $0\pm 2\ \text{V}$, $5\pm 2\ \text{V}$ and $6\pm 3\ \text{V}$, respectively. For $L=300\ \mu\text{m}$, G_{on} , g_{mp} , V_{fth} , V_{rth} and H were estimated to be $8.8\pm 1.4\times 10^{-8}\ \Omega^{-1}$, $6.1\pm 2.4\times 10^{-8}\ \Omega^{-1}$, $-8\pm 2\ \text{V}$, $0\pm 2\ \text{V}$ and $10\pm 2\ \text{V}$, respectively. For $L=1000\ \mu\text{m}$, G_{on} , g_{mp} , V_{fth} , V_{rth} and H were calculated to be $1.4\pm 0.4\times 10^{-8}\ \Omega^{-1}$, $9\pm 4\times 10^{-9}\ \Omega^{-1}$, $-12\pm 2\ \text{V}$, $-2\pm 2\ \text{V}$ and $15\pm 3\ \text{V}$, respectively. After the additional photolithography step for junction capping, G_{on} , g_{mp} , V_{fth} , V_{rth} and H showed certain changes for different channel lengths: -16% , -11% , $+0.5\ \text{V}$, $-0.5\ \text{V}$ and $-1\ \text{V}$ ($L=6\ \mu\text{m}$); -11% , -8% , $+1\ \text{V}$, $-1\ \text{V}$ and $-2\ \text{V}$ ($L=300\ \mu\text{m}$); and -12% , -10% , $+2\ \text{V}$, $-2\ \text{V}$ and $-3\ \text{V}$ ($L=1000\ \mu\text{m}$). (Here $-/+$ indicates decrease/increase in G_{on} , g_{mp} and H , and negative/positive shift for V_{fth} and V_{rth} after the photolithography step for junction capping).

All chemicals/reagents were purchased from Sigma Aldrich, Singapore unless stated otherwise. Figure 4.1 shows the schematic setup for hybridization detection using SWCNT FET. SWCNT FETs were incubated with 5 mM of 1-pyrenebutanoic

acid succinimidyl ester (PASE, Life technologies, Singapore) linker molecule in pure dimethylformamide (DMF) for 3 hours at room temperature, followed by washing with DMF and deionized (DI) water. 5 μ L of 10 μ M single-stranded probe DNA (probe DNA, 5'-NH₂ (CH₂)₃-CAAACACCATTGTCACACTCCA-3') dissolved in phosphate buffer saline solution (PBS, pH 7.4, Biotechnology grade, BST Scientific Ltd., Singapore) was pipetted on the devices and incubated for 16-24 hours in a humid environment. This was followed by rinsing with PBS and DI water, and blow-drying with nitrogen to remove the unbound probe DNA. Thereafter, the devices were incubated with 0.1 M ethanolamine (EA, pH 9.0) for 1 hour to quench the unreacted succinimidyl ester group on linker molecules. Similar washing procedure was adopted as stated earlier. To passivate the uncoated CNT area, the devices were incubated for 1 hour with 0.1% Tween 20 followed by the same washing procedure. For DNA-RNA hybridization, 5 μ L of 1 μ M single-stranded complementary RNA (cRNA, 5'-UGGAGUGUGACAAUGGUGUUUG-3') dissolved in RNAase free water was used as the target nucleic acid, and 5 μ L of 1 μ M single-stranded complementary DNA (cDNA, 5'- TGGAGTGTGACAATGGTGTTTG-3') dissolved in PBS was used as the target nucleic acid to detect DNA-DNA hybridization. Finally, after target incubation for about 1 hour in a humid environment, the devices were washed with RNAase free water (for RNA hybridization) and PBS (for DNA hybridization), and dried by blowing nitrogen.

Figure 4.1 A schematic setup for cDNA/cRNA detection using SWCNT FET. Here, cDNA/cRNA represents the complementary target ssDNA/ssRNA, and DNA-DNA/DNA-RNA represents the double-stranded hybrids formed by base pairing between probe DNA and cDNA/cRNA.

For control experiments, non-complementary single-stranded DNA (ncDNA, 5'-TGGTGTGTGACAGTGGTGTATG-3') was used. Several control experiments were done. Firstly, the channel-exposed devices and channel & junction-exposed devices were tested with 5 μ L of 1 μ M of ncDNA. Secondly, for testing unfunctionalized FETs (no PASE), probe DNA was directly immobilized on the CNT surface followed by passivation with Tween 20, and exposed to 5 μ L of 1 μ M of cDNA/cRNA for both channel-exposed as well as channel and junction-exposed FETs.

4.3 Mechanism of Nucleic Acid Hybridization Detection

Figures 4.2a and 4.2b show the I_D - V_{DS} curves of the functionalization steps involved in cDNA/cRNA detection for devices with $L=300$ μ m and only channel exposed to hybridization. The pyrene group of PASE interacts with CNT non-

covalently through π -stacking forces, and binds covalently to the amine group in probe DNA through its succinimidyl group. The functionalized FET showed 5-10% reduction in ON-state current and a negative shift in V_{fth} by about -3 V after probe DNA immobilization, which is a consequence of electron donation by the negatively charged probe DNA. Following the addition of EA and Tween 20, the ON-current decreased slightly more because of carrier scattering by coating of these molecules on the CNT surface.

Figure 4.2 I_D - V_{DS} curves of pyrene-functionalized long channel SWCNT FET ($L=300 \mu\text{m}$) showing the various functionalization steps for (a) cDNA and (b) cRNA detection, respectively. The gate voltage was kept at -24 V.

According to Figure 4.3a, G_{on} and g_{mp} reduced by about 36.6% and 59.1%, respectively, in the device with only channel exposed to cDNA. V_{fth} shifted by about 2 V to the left and H increased by about 4 V. The carrier scattering by DNA-DNA hybrids and the electron doping of SWCNT by cDNA resulted in the observed reduction in p-type behaviour, i.e., reduction in g_{mp} , and left shift in V_{fth} .^{9,163} The increased H is an indicator of charge trapping by DNA-DNA hybrids on CNT.⁹

Figure 4.3 I_D - V_G curves of pyrene-functionalized long channel SWCNT FET ($L=300\ \mu\text{m}$) with only channel exposed to (a) cDNA and (b) cRNA, respectively. The ‘before cDNA/cRNA’ step corresponds to the recording obtained after probe DNA, EA, and Tween 20 incubation steps. The ‘after cDNA/cRNA’ step represents the recording after incubation with cDNA/cRNA. The arrow marks indicate the direction of gate voltage sweep.

According to the transfer curve for cRNA hybridization in Figure 4.3b, G_{on} decreased by about 16.6%, g_{mp} increased by 22.9%, V_{fth} showed a positive shift of about 2 V and H reduced by about 5 V. The lower affinity of DNA-RNA hybrids on CNT causes its removal from the nanotube surface, which is the reason for enhancement in p-type behaviour, i.e., increase in g_{mp} and rightward V_{fth} shift.¹⁶⁴ Furthermore, the reduction in H is a clear indicator of the absence of charge trapping centers on the nanotube surface because of desorption of DNA-RNA duplexes.

To confirm that the observed signal was due to hybridization, we repeated the experiment using ncDNA. Clearly, from Figure 4.4a, the transfer characteristics exhibited no significant change confirming that hybridization was responsible for the observations in Figure 4.3.

Figure 4.4 I_D - V_G curves of pyrene-functionalized long channel SWCNT FET ($L=300\ \mu\text{m}$) with channel and junction exposed to (a) ncDNA and (b) cDNA/cRNA. The ‘before ncDNA’ step corresponds to the recording obtained after probe DNA, EA, and Tween 20 incubation steps. The ‘after ncDNA’ step represents the recording after incubation with ncDNA. The arrow marks indicate the direction of gate voltage sweep.

To study the influence of CNT-metal junction on the transfer characteristics, the above experiments were repeated using devices with channel and junction exposed to cDNA/cRNA. From Figure 4.4b, the I_D - V_G curves showed the same changes exhibited by devices with only channel exposed, i.e., $\Delta G_{on}/G_{on}$ (−43.8%), $\Delta g_{mp}/g_{mp}$ (−63.6%), ΔV_{fth} (−1.5 V) and ΔH (+3.5 V) after cDNA hybridization, and $\Delta G_{on}/G_{on}$ (−20.1%), $\Delta g_{mp}/g_{mp}$ (+18.9%), ΔV_{fth} (+2 V) and ΔH (−4 V) after cRNA hybridization. Thus, regardless of the presence or absence of junction during hybridization, cDNA and cRNA hybridization showed their respective change in transfer characteristics. This is contrary to the earlier studies,^{10,69,70} which indicate the dominance of Schottky barrier modulation in channel and junction-exposed devices. Since most of these reports used un-functionalized short CNTs, it is necessary to study the impact of the pyrene linker and channel length in discriminating DNA-DNA and DNA-RNA duplexes in the presence and absence of CNT-metal junction during sensing.

4.4 Effect of Functionalization

To investigate the role of pyrene, we conducted experiments on devices having only channel exposed as well as devices with channel and junction exposed in the absence of PASE functionalization on CNT as shown in Figure 4.5.

Figure 4.5 I_D - V_G curves of unfunctionalized long channel SWCNT FET ($L=300\ \mu\text{m}$) for cDNA/cRNA detection with (a) only channel exposed, and (b) channel and junction exposed. The ‘before cDNA/cRNA’ step corresponds to recording after probe DNA and Tween 20 incubation steps. The arrow marks indicate the direction of gate voltage sweep.

4.4.1 Without Junction

In the first case, un-functionalized FET with only channel exposed to either cDNA or cRNA displayed a reduction in G_{on} by about 10 %, but showed no major alterations in V_{fth} or H as seen in Figure 4.5a. The lack of change in H indicates the absence of charge trapping, which is well supported by the fact that hybridization between non-specifically adsorbed probe molecules and its complementary sequence has low probability of occurrence.^{158,159} Thus, both cDNA and cRNA produced the same response in the absence of pyrene linker.

4.4.2 With Junction

In the second case, the transfer curves of an unfunctionalized device with channel and junction exposed to either cDNA or cRNA showed an asymmetric change in I_D with a reduction in p-channel current and an increase in n-channel current, but no significant change in V_{th} and H as seen in Figure 4.5b. This asymmetric variation in I_D is caused by thinning of the tunnel barrier for the electrons because of excess accumulation of negative DNA/RNA charges at the drain due to capillary forces, which is a characteristic of Schottky barrier FETs.⁶¹ Furthermore, the lack of change in H indicates the absence of DNA-DNA or DNA-RNA charge traps on the channel region.

Overall, in devices with no pyrene functionalization, both cDNA and cRNA produced the same response. Thus, in the absence of pyrene linker, probe DNA molecules do not effectively attract the complementary target towards the channel area, which causes aggregation of the incoming target DNA/RNA molecules at the junction leading to a CNT-metal junction dominant response. In this regard, the presence of pyrene linker improves probe immobilization and probability of target binding, which results in better specificity and response to hybridization detection, and better selectivity in discriminating DNA-DNA and DNA-RNA duplexes.

The observed differences in the I - V response of FETs to DNA-DNA and DNA-RNA duplexes in the presence of pyrene linker can also be addressed based on the conformations assumed by DNA-DNA and DNA-RNA duplexes, and their interactions with PASE. Figure 4.6a shows the double-helix conformation assumed by DNA-DNA and DNA-RNA. Figures 4.6b and 4.6c show the structure of the

nucleoside with ribose/deoxyribose sugar and PASE, respectively. DNA-DNA duplex has a B-form conformation with the sugars having C2'-endo pucker with the C4'-H4' bonds directed towards the opposite minor groove wall.^{138,139} On the other hand, DNA-RNA hybrid has an A-form conformation with the deoxyribose sugar pucker adopting O4'-endo with the bond directed from the edge of the groove into the solvent. Moreover, B-form duplexes have narrow minor grooves compared to the wide and shallow minor grooves in A-form helices. These structural variations cause a difference in the duplex-PASE interaction. The van der Waals interaction forces between PASE and the wider minor groove in DNA-RNA duplex is reduced much more compared to DNA-DNA helix because of the less favorable polar interaction (dipole-dipole) between PASE and the groove. Furthermore, the interaction between the DNA-RNA duplex and butanoic acid succinimidyl ester entity is reduced substantially because the groove turns away from the butanoic acid succinimidyl ester entity. In addition, the presence of oxygen atoms at the 2'-OH positions in RNA increases steric hindrance and repulsion from the oxygen atoms in the butanoic acid succinimidyl ester moiety, which is absent in DNA-DNA hybrids. Thus, the more stable DNA-DNA hybrids are immobilized permanently resulting in the observed reduction in p-type behaviour and increase in charge traps. On the contrary, the less stable DNA-RNA hybrids are desorbed from the CNT surface resulting in improved p-type behaviour and a decrease in charge trapping behaviour.

Figure 4.6 Schematic diagram of (a) B-form (DNA-DNA) and A-form (DNA-RNA) helices. Chemical structures of (b) nucleoside with ribose/deoxy ribose sugar and (c) pyrene butanoic acid succinimidyl ester (PASE), respectively.

4.5 Effect of Channel Length

The above experiments were performed using FETs with $L=300\ \mu\text{m}$. The response to hybridization depends on the number of hybridizations occurring on the channel surface, which in turn, is dependent on L . In this regard, it is necessary to investigate the effect of L on the efficacy of pyrene-functionalized SWCNT FET to detect and distinguish DNA-DNA and DNA-RNA duplexes. For cDNA detection in only channel-exposed devices, the drop in G_{on} increased from 3.3% for $L=6\ \mu\text{m}$ to 39.1% for $L=300\ \mu\text{m}$ and declined to 20.4% for $L=1500\ \mu\text{m}$ as shown in Figure 4.7a. For DNA-RNA hybridization in only channel-exposed devices, the reduction in G_{on}

increased from 2.3% for $L=6\ \mu\text{m}$ to 14.3% for $L=300\ \mu\text{m}$ and decreased to 10.4% for $L=1500\ \mu\text{m}$ as shown in Figure 4.7b. The rise in $\Delta G_{on}/G_{on}$ from $L=6\ \mu\text{m}$ to $300\ \mu\text{m}$ is attributable to the increase in the number of hybridizations occurring on the SWCNT surface. However, for $L=1500\ \mu\text{m}$, the conductance response is lower compared to devices with $L=300\ \mu\text{m}$, which suggests that very high channel resistance could be a limiting factor in ultra-long channel.

Figure 4.7 The variation in the conductance response of channel and junction-exposed ($\Delta G_{on}/G_{on}$) devices and only channel-exposed ($\Delta G_{ch}/G_{ch}$) devices with L for (a) cDNA and (b) cRNA detection, respectively. The negative sign on the y-axis indicates the decrease in magnitude of conductance after hybridization. The solid lines are a guide to the eye.

The variation in conductance response of channel-exposed ($\Delta G_{ch}/G_{ch}$) pyrene-functionalized short channel ($L=6\ \mu\text{m}$), long channel ($L=300\ \mu\text{m}$) and ultra-long channel ($L=1500\ \mu\text{m}$) FETs is compared against channel and junction-exposed ($\Delta G_{on}/G_{on}$) devices for cDNA and cRNA detection in Figures 4.7a and 4.7b, respectively. Clearly, $\Delta G_{ch}/G_{ch} \approx \Delta G_{on}/G_{on}$ for $L=300\ \mu\text{m}$ and $1500\ \mu\text{m}$, which indicates

a channel dominant response in channel and junction-exposed devices. However, the response of devices with $L=1500\text{ }\mu\text{m}$ was lower due to high channel resistance,¹⁶⁵ which reduces the detection capability. On the other hand, $\Delta G_{on}/G_{on} \gg \Delta G_{ch}/G_{ch}$ for $L=6\text{ }\mu\text{m}$, which indicates that in addition to the change in channel resistance (ΔR_{ch}), the change in contact resistance (ΔR_c) contributes to the change in total ON-state resistance (ΔR_{on}) in channel and junction-exposed devices following hybridization. Clearly, pyrene-functionalized long channel FETs produced better response in comparison to short and ultra-long channel FETs irrespective of the presence or absence of CNT-metal junction during sensing.

The variation of other FET parameters such as g_{mp} , V_{fth} , V_{rth} and H following DNA-DNA and DNA-RNA hybridization are plotted in Figures 4.8a-c for different channel lengths. The percentage drop in g_{mp} after cDNA detection increased from 20.3% for $L=6\text{ }\mu\text{m}$ to 70.1% for $L=300\text{ }\mu\text{m}$ and reduced to 30.4% for $L=1500\text{ }\mu\text{m}$. The magnitudes of ΔV_{fth} , ΔV_{rth} and ΔH following DNA-DNA hybridization increased with channel length from -1.5 V to -3 V , 1 V to 3 V and 1.5 V to 5 V , respectively.

The number of DNA-DNA hybrids formed on the CNT surface increases with channel length, which enhances the charge transfer from DNA to CNT, and hence, the magnitude of ΔV_{th} increases with channel length. Moreover, the number of charge traps formed during hybridization increases along the length of the nanotube, thus, offering more trapping/detrapping sites leading to an increase in ΔH with L and therefore, magnitude of ΔH increased with channel length.

Figure 4.8 (a) The relative change in peak transconductance ($\Delta g_{mp}/g_{mp}$) following exposure to cDNA and cRNA, respectively. The change in threshold voltage (ΔV_{th}) and hysteresis gap (ΔH) following (b) cDNA and (c) cRNA hybridization, respectively for different L . The additional subscripts ‘f’ and ‘r’ in V_{th} represent the threshold voltages for the forward and reverse gate voltage sweep, respectively. The negative and positive sign of the threshold voltage shift indicates the leftward and rightward shift in the transfer curve. A positive ΔH indicates rise in hysteresis whereas, a negative sign indicates reduction in hysteresis. The change in all electrical parameters induced by hybridization was obtained with respect to the ‘before cDNA/cRNA’ I_D - V_G curve. The solid lines are a guide to the eye.

On the other hand, for cRNA hybridization, the percentage increase in g_{mp} increased from 5.3% for $L=6 \mu\text{m}$ to 40.3% for $L=300 \mu\text{m}$ and dropped to 25.4% for $L=1500 \mu\text{m}$. Moreover, the magnitudes of ΔV_{fth} , ΔV_{rth} , and ΔH increased with channel length from 1 V to 5 V, -1 V to -3 V and -2 V to -5 V, respectively. The number of double stranded hybrids removed from the CNT surface increases with channel length,

which enhances the charge transfer from CNT to DNA resulting in the increase in magnitude of ΔV_{th} with channel length. Desorption of more number of charge traps with channel length decreased the magnitude of ΔH .

Clearly, for all channel lengths, the transfer characteristics showed a change in transconductance, threshold voltage and hysteresis gap, which confirms the contribution of carrier scattering, charge transfer and charge trapping in detecting hybridization. These mechanisms include the effect of transfer of electrons, CNT-contact work function modulation, double stranded DNA (dsDNA) affinity on SWCNT, hopping conduction etc. on the response. Consequently, it is necessary to consider the contribution of the change in g_m , V_{th} and H caused by hybridization when explaining the effect of channel length on FET response. Therefore, we use Eqs. (2.11) and (2.12) corresponding to effective mobility (μ_{eff}) and field-effect transistor mobility (μ_{fe}) to define two parameters, which encompass the change in these electrical parameters. μ_{eff} include V_{th} and G , whereas μ_{fe} includes g_m ; therefore, a parameter defined using these two mobilities could contain all the three FET parameters. Δ represents the absolute change induced by hybridization and the terms with subscript ‘ b ’ and ‘ a ’ denote ‘before hybridization’ and ‘after hybridization’, respectively. In general, the hybridization-induced change in each of the FET parameters is given by,

$$\Delta G = G_b - G_a \quad (4.1)$$

$$\Delta V_{th} = V_{thb} - V_{tha} \quad (4.2)$$

$$\Delta g_m = g_{mb} - g_{ma} \quad (4.3)$$

Using Eqs. (4.1) and (4.2) in Eq. (2.11) gives,

$$\Delta\mu_{eff} = \mu_{effb} - \mu_{effa} = \frac{L^2(G_bV_{tha} - G_aV_{thb} - \Delta G\Delta V_G)}{C(V_{tha} - V_G)(V_{thb} - V_G)} \quad (4.4)$$

Using Eq. (4.3) in Eq. (2.12) gives,

$$\Delta\mu_{fe} = \mu_{feb} - \mu_{fea} = \frac{L^2(g_{mb} - g_{ma})}{CV_{DS}} \quad (4.5)$$

Let, K , denote the ratio of the change in intrinsic to the change in device mobility induced by hybridization, i.e., $\Delta\mu_{eff}/\Delta\mu_{fe}$. From Eqs. (4.4) and (4.5), evidently, ' K ' encompasses the change in G , g_m , V_{th} brought about by hybridization. To obtain the relation for K , it is necessary to obtain μ_{eff}/μ_{fe} . The influence of various device-attributes like contact resistance, parasitic resistance, surface effects, etc. makes the estimated field-effect mobility different from effective mobility. Mathematically, μ_{fe} could be related to the μ_{eff} by a certain device factor, φ , i.e., $\mu_{fe} = \mu_{eff}/\varphi$, where ' $1/\varphi$ ' indicates the contribution of device attributes.^{156,157} Let

$$\mu_{effb} = \varphi_b \mu_{feb} \quad (4.6)$$

$$\mu_{effa} = \varphi_a \mu_{fea} \quad (4.7)$$

where, $\Delta\varphi = \varphi_b - \varphi_a$. Dividing Eq. (4.6) by Eq. (4.7) and subtracting 1 from L.H.S and R.H.S gives,

$$\frac{\mu_{effb}}{\mu_{effa}} - 1 = \frac{\varphi_b \mu_{feb}}{\varphi_a \mu_{fea}} - 1 \quad (4.8)$$

$$\Delta\mu_{eff} = \mu_{effb} - \mu_{effa} = \varphi_b \mu_{feb} - \varphi_a \mu_{fea} \quad (4.9)$$

Similarly, we get,

$$\Delta\mu_{fe} = \mu_{feb} - \mu_{fea} = \frac{\varphi_a \mu_{effb} - \varphi_b \mu_{effa}}{\varphi_b \varphi_a} \quad (4.10)$$

To engulf the change in G , g_m and V_{th} induced by cDNA hybridization, and represent them by a single parameter, we divide Eq. (4.9) by Eq. (4.10).

$$K = \frac{\Delta\mu_{eff}}{\Delta\mu_{fe}} = \frac{(\varphi_b\mu_{feb}-\varphi_a\mu_{fea})}{(\varphi_a\mu_{effb}-\varphi_b\mu_{effa})}(\varphi_b\varphi_a) \quad (4.11)$$

From Eq. (4.11), clearly, ‘ K ’ encircles the change in the above electrical parameters and is related to the device factor (φ). Therefore, it is befitting to use $\Delta\varphi$ and K to enucleate this parabolic trend in the conductance response with channel length.

Ideally, the ratio of the intrinsic mobility to device mobility should be the same before and after hybridization, which means that the contribution of device attributes does not change during hybridization, i.e. source of mobility change is solely from the channel such that $\varphi_a=\varphi_b=\varphi \Rightarrow \Delta\varphi=0$. Using $\varphi_a=\varphi_b=\varphi$ in Eq. (4.11), we obtain, $K=\varphi$, which implies that the ratio of the mobilities is the same as the ratio of the change in the mobilities induced by hybridization, i.e., φ remains unaffected after hybridization. ‘ K ’ can aid in the analysis of the effect of gate voltage, channel length, channel number, etc. on the response of FET when multiple sensing mechanisms contribute to produce a change in G , g_m and V_{th} .

Depending on the gate bias applied, $\Delta\varphi$ and K can be obtained in the linear, near-threshold, or the subthreshold regimes.¹⁰⁹ Eqs. (2.11) and (2.12) are used for estimation of mobility in the region above threshold voltage; therefore, the succeeding analysis is limited to the linear (ON state) and near-threshold (maximum g_m) regimes. $\Delta\varphi$ vs. L and K vs. L plots for forward and reverse sweeps in the linear and near-threshold regimes for cDNA hybridization detection are displayed in Figures 4.9a-d.

Figure 4.9 $\Delta\phi$ vs. L for (a) forward and (b) reverse sweeps in the linear and near-threshold regimes. K vs. L for (c) forward and (d) reverse sweeps in the linear and near-threshold regimes. The solid lines are a guide to the eye.

$\Delta\phi$ decreased from ~ 4.50 for $L=6 \mu\text{m}$ to ~ 0.55 for $300 \mu\text{m}$, and then, increased to ~ 2.03 for $L=1500 \mu\text{m}$ in the linear regime. K exhibited similar trend and reduced from ~ 5.41 to ~ 1.82 , and then increased to ~ 3.32 for an increase in channel length from $6 \mu\text{m}$ via $300 \mu\text{m}$ to $1500 \mu\text{m}$. $\Delta\phi$ decreased from ~ 3.20 for $L=6 \mu\text{m}$ to ~ 0.25 for $L=300 \mu\text{m}$, and then, increased to ~ 1.11 for $L=1500 \mu\text{m}$ in the near-threshold regime. K values for $L=6 \mu\text{m}$, $300 \mu\text{m}$ and $1500 \mu\text{m}$ were calculated to be ~ 2.9 , ~ 1.05 , and

~ 1.7 , respectively. The magnitudes of $\Delta\varphi$ and K were slightly different for forward and reverse sweeps, but the variation trends with L in both regimes were the same.

Two points are worth noting from the above observations. Firstly, devices with $L=6\text{ }\mu\text{m}$ and $1500\text{ }\mu\text{m}$ showed higher $\Delta\varphi$ and K values in both the regimes ($\Delta\varphi > 0$ and $K \neq \varphi$) in comparison to FETs with $L=300\text{ }\mu\text{m}$ ($\Delta\varphi \rightarrow 0$ and $K \rightarrow \varphi$). Secondly, $\Delta\varphi$ and K in the linear regime was greater than the near-threshold regime. The possible explanations are illustrated as follows.

Since φ is influenced by contact resistance,¹⁶⁸ optical/acoustic phonon scattering,¹⁵⁵ and trapped charges⁵⁴ for different L and V_G , $\Delta\varphi$ deviates from the ideal case of zero, resulting in $\Delta\varphi \neq 0$, and consequently, $K \neq \varphi$. As mentioned earlier, in short channel lengths, the modulation of CNT-metal work function affects the mobility. Scattering by phonons is present at all biases and increases with L ,¹⁶⁹ which degrades the detection capability of FET. Finally, the presence of hysteresis indicates the possibility of interface defects or bulk defects,¹⁷⁰ which participates in Coulombic scattering,¹⁷¹ thereby affecting mobility.

If $\Delta\varphi_c$, $\Delta\varphi_s$ and $\Delta\varphi_h$ represent the respective contributions of contact resistance, phonon scattering, and charge traps to $\Delta\varphi$, then, upon substituting $\Delta\varphi = (\Delta\varphi_c + \Delta\varphi_s + \Delta\varphi_h)$ in Eq. (4.11) yields,

$$K = M(\varphi_b^2) + M\varphi_b\Delta\varphi_c + M\varphi_b\Delta\varphi_s + M\varphi_b\Delta\varphi_h \quad (4.12)$$

where $M = \left[\frac{(\varphi_b\mu_{fb} - \varphi_a\mu_{fa})}{(\varphi_a\mu_{eb} - \varphi_b\mu_{ea})} \right]$. With increasing L , the influence of change in contact resistance (i.e. $\Delta\varphi_c$) diminishes, and the effect of phonon scattering¹⁶⁹ (i.e. $\Delta\varphi_s$)

decreases with reduction in L . On considering $\Delta\varphi_c \gg \Delta\varphi_s$ for $L=6\ \mu\text{m}$, $\Delta\varphi_c + \Delta\varphi_s \cong 0$ for $L=300\ \mu\text{m}$ and $\Delta\varphi_c \ll \Delta\varphi_s$ for $L=1500\ \mu\text{m}$, respectively, the third, second and third, and second terms in Eq. (4.12) for the corresponding channel lengths can be neglected. As a result, devices with $L=6\ \mu\text{m}$ and $1500\ \mu\text{m}$ having an extra factor of $\Delta\varphi_c$ and $\Delta\varphi_s$, respectively (both regimes), leading to $K > \varphi$. However, for devices with $L=300\ \mu\text{m}$, $\Delta\varphi$ tends to zero (both regimes), and thereby K will approach φ , which is in agreement with the observations.

In this section, the terms with additional subscripts of “ l ” and “ t ” denote parameters extracted in the linear and near-threshold regimes, respectively. The effect of Schottky barrier declines in the linear regime (higher V_G) leading to lower contact resistance compared to the near-threshold regime (lower V_G).¹⁶⁸ Thus, a greater contribution from the contacts towards the mobility change at higher V_G results in $\varphi_{cl} > \varphi_{ct}$. In addition, the presence of phonon scattering (optical at high bias and acoustic at low bias) at all biases results in $\varphi_{cl} + \varphi_{sl} \gg \varphi_{ct} + \varphi_{st}$. In the linear regime, the contribution of φ_{hl} is neglected because the high V_G converts all injected charges in SiO_2 into holes, thereby filling all the charge traps.⁵⁶ However, in the near-threshold regime, the injected charges are not dissipated because of hysteresis causing the trapped charge induced potential to exceed the back gate bias potential, which presses the need to consider the influence of trapped charges ($\Delta\varphi_h$) in $\Delta\varphi$.⁵⁶ In accordance to earlier reports,¹⁶¹ in the near-threshold regime, Coulomb scattering by trapped charges produce lesser effect on CNT mobility than acoustic phonon scattering, i.e., $\varphi_{st} \gg \varphi_{ht}$.

Thus, a combination of all the above factors results in $\Delta\phi_l > \Delta\phi_t$, and hence $K_l > K_t$, which suggests that the near-threshold regime will produce greater response to hybridization with minimum influence of device attributes compared to the linear regime for all channel lengths. Evidently, from $\Delta\phi$ vs. L and K vs. L plots, the devices with $L=300$ μm comply with the condition of $\Delta\phi$ approaching zero compared to the other channel lengths, and hence K tends to ϕ , which is mirrored as the best response to DNA hybridization.

Based on the summary of the device response and sensing mechanism shown in Tables 4.1a and 4.1b, some of the important distinctions and improvements in this study from previously published results have been discussed below. According to the SWCNT FET-based hybridization detection studies reported by Staii. *et al.*,¹⁰ Tang. *et al.*,⁶⁹ and Byon. *et al.*,⁷⁰ the CNT-metal electrode junction interferes in hybridization detection resulting in a Schottky barrier dependent mechanism. In addition, such FETs show lack of discrimination between complementary DNA and RNA. Herein, the use of pyrene derivative functionalization resolved this issue by serving the dual purpose of improving the probe-DNA immobilization on the CNT as well as channelizing the incoming DNA/RNA target to the channel area, which resulted in channel dominant mechanisms, i.e., charge transfer, charge trapping and carrier scattering. Consequently, the pyrene functionalized CNT FETs displayed appreciable response to channel dependent mechanisms, irrespective of the presence or absence of CNT-metal junction during sensing. Furthermore, the differences in interaction between pyrene linker and

DNA/RNA resulted in the discrimination of the two targets, which is apparent from the distinct responses for DNA and RNA hybridization, as seen from the opposite directional shifts in transconductance, threshold voltage and hysteresis. According to reports by Gui. *et al.*,⁷¹ charge transfer also contributes to hybridization detection in addition to work function modulation of CNT-metal junction. Herein, the large negative shift in V_{fth} indicates electron trapping by the guanine and adenine bases.^{163,172} Similarly, large positive shift in V_{rth} is an indicator of hole trapping by the cytosine and thymine bases.^{163,172} Thus, the increase in charge traps in the channel region leads to an overall shift in V_{th} for forward and reverse sweeps, reflected as an increase in H . Thus, the response to charge transfer in pyrene functionalized devices used here emanates from the channel, which differs from those reported by Gui. *et al.*,⁷¹ where charge density modification near the CNT-metal electrode junction through electron doping causes a negative shift in the forward and reverse sweep threshold voltages. In the case of junction-covered devices, the response to hybridization was poor as reported by Meng *et. al* and Nandy *et. al.*^{158,159} Also, these reports suggest that the probability of hybridization is very low on bare CNTs. The 300 μm long-channel SWCNT FET displayed high μ_e and μ_f values of $\sim 1.04 \times 10^4 \text{ cm}^2 \text{V}^{-1} \text{s}^{-1}$ and $2.53 \times 10^3 \text{ cm}^2 \text{V}^{-1} \text{s}^{-1}$, respectively, obtained using Eqs. (2.11) and (2.13). Moreover, the use of such long SWCNTs increased the probability of hybridizations occurring on the CNT surface at a lower incubation time. Consequently, the channel response augmented to hybridization detection.

Table 4.1 Summary of the observed responses and mechanisms of SWCNT FET of three different channel lengths (a) with and (b) without the presence of CNT-metal junction for hybridization detection in the presence and absence of pyrene linker. +/- sign for I_D and H indicate increase/decrease in these parameters after hybridization. +/- sign for V_{fth} and V_{rth} indicate positive/negative shift in these parameters following hybridization.

(a)

Channel Length	Pyrene	No pyrene
Short	<p>small $-I_D$; small $-V_{fth}$, $+V_{rth}$ and $+H$</p> <p>small carrier scattering; small electron transfer in channel area; small charge trapping</p>	<p>large asymmetric change in I_D for p- and n-channel; large $-V_{fth}$ and $-V_{rth}$; no change in H</p> <p>large Schottky barrier modulation; large electron transfer in junction area; no charge trapping</p>
Long	<p>large $-I_D$; medium $-V_{fth}$, $+V_{rth}$ and $+H$</p> <p>large carrier scattering; medium electron transfer in channel area; medium charge trapping</p>	<p>small asymmetric change in I_D for p- and n-channel; no change in V_{fth}, V_{rth} and H</p> <p>small Schottky barrier modulation; no electron transfer; no charge trapping</p>
Ultralong	<p>medium $-I_D$; large $-V_{fth}$, $+V_{rth}$ and $+H$</p> <p>medium carrier scattering; large electron transfer in channel area; large charge trapping</p>	<p>small asymmetric change in I_D for p- and n-channel; no change in V_{fth}, V_{rth} and H</p> <p>small Schottky barrier modulation; no electron transfer; no charge trapping</p>

(b)

Channel Length	Pyrene	No pyrene
Short	<p>small $-I_D$; small $-V_{fth}$, $+V_{rth}$ and $+H$</p> <p>small carrier scattering; small electron transfer in channel area; small charge trapping</p>	<p>large $-I_D$; no change in V_{fth}, V_{rth} and H</p> <p>large carrier scattering; no electron transfer; no charge trapping</p>
Long	<p>large $-I_D$; medium $-V_{fth}$, $+V_{rth}$ and $+H$</p> <p>large carrier scattering; medium electron transfer in channel area; medium charge trapping</p>	<p>small $-I_D$; no change in V_{fth}, V_{rth} and H</p> <p>small carrier scattering; no electron transfer; no charge trapping</p>
Ultralong	<p>medium $-I_D$; large $-V_{fth}$, $+V_{rth}$ and $+H$</p> <p>medium carrier scattering; large electron transfer in channel area; large charge trapping</p>	<p>small $-I_D$; no change in V_{fth}, V_{rth} and H</p> <p>small carrier scattering; no electron transfer; no charge trapping</p>

4.6 Conclusions

The detection of DNA-DNA and DNA-RNA hybridization was demonstrated using pyrene modified long channel individual SWCNT based FETs. The FETs showed a reduction in p-type behaviour (reduced transconductance and negative shift in forward sweep threshold voltage) and an increase in charge trapping behaviour (increase in

hysteresis) for DNA-DNA hybridization. On the other hand, DNA-RNA hybridization resulted in an increase in p-type behaviour (increase in transconductance and positive shift in forward sweep threshold voltage) and reduction in charge trapping behaviour (decrease in hysteresis).

The drop in FET conductance and transconductance signifies carrier scattering in CNT by hybridized double stranded duplexes. The charge transfer mechanism is characterized by a negative/positive shift in the threshold voltage upon binding with the complementary target. The charge trapping mechanism is determined by the increase/decrease in hysteresis, which is proportional to the number of charge traps formed/removed after hybridization. Overall, the pyrene functionalized FETs exhibited a channel dominant response through a combination of carrier scattering, charge transfer and charge trapping mechanism. In addition, irrespective of the presence or absence of metal contact during sensing, the pyrene linker-based surface modification improved the device specificity and selectivity to hybridization detection through effective probe immobilization. Furthermore, FETs with $\sim 300\text{ }\mu\text{m}$ long SWCNT exhibited the most appreciable response to hybridization compared to few micrometres or millimetres long channel due to minimum contribution of device attributes in hybridization detection, which was supported by the variation trend in response interpreted using the new defined parameters.

Chapter 5: Effect of SsDNA Sequence on the Electrical Response of CNT-Based FETs in Dopamine Detection

5.1 Introduction

Dopamine (DA) belongs to a class of neurotransmitters with high clinical significance in different brain functions such as learning, memory formation, message transfer in the central nervous system and pathological processes of Parkinson's disease.¹⁷³ Normal SWCNT-based sensors suffer from poor sensitivity and selectivity in DA detection because of the presence of an interfering compound like uric acid (UA). Moreover, most methods rely on time consuming electrochemical methods.^{12,174,175} Hence, to overcome these drawbacks, the use of an electronic detection approach with a chemically modified nanotube surface is necessary. Surface modification influences the interaction strength between the nanotube and the target analyte, thereby improving the affinity and specificity of detection, and resulting in faster detection.^{151,176}

Single-stranded deoxyribo nucleic acid (ssDNA) decoration on SWCNT as a surface modification approach has garnered tremendous interest because of its selectivity and sensitivity towards a wide range of analytes such as ligands, hormones, proteins, enzymes, and vapour-phase odorants, besides being economical and easily available.^{10,69} SsDNA is a biopolymer capable of non-covalently binding to SWCNT surface through π - π stacking interactions, which can be contrived to attain affinity to a

range of molecular targets.¹⁷⁷ DNA nucleotide is composed of a deoxyribose sugar, a phosphate and one of the four nitrogenous bases namely, adenine (A), cytosine (C), guanine (G), or thymine (T).¹⁷⁸ Thus, ssDNA decoration serves the dual purpose of surface functionalization and receptor immobilization as it renders the CNT surface responsive and acts as a receptor by binding with the target analyte.

SsDNA-decorated SWCNT used in a FET configuration merges the excellent electronic properties of SWCNT and the molecular diversity of ssDNA to give a rapid electronic detection platform. The presence of multiple bases gives the possibility of numerous sequence combinations, which interact with CNT and DA differently, thereby influencing the FET response. Thus, ssDNA-decorated SWCNT FET creates a sensing platform, which can be tuned using selective ssDNA sequences to detect a plethora of aqueous and vapour-phase target analytes with a high level of chemical diversity.^{13,179,180} The electrical transistor parameters including conductance, transconductance, threshold voltage and hysteresis gap, which are indicators of the contributing sensing mechanisms,⁷ aid in interpreting the sequence dependent response. Therefore, the variation in transistor parameters obtained from the current–voltage characteristics due to ssDNA-DA interaction will facilitate the design of ssDNA sequences for sensitive and selective detection of a DA.

In this chapter, we investigate the effect of ssDNA decoration (surface modification) of SWCNT used in a FET system to detect DA, UA, and DA-UA solution mixture. Furthermore, we interpret the sequence dependent electrical response

of both homo and repeated ssDNA-decorated SWCNT FETs to DA, in the presence and absence of UA, based on the CNT-ssDNA (CNT-receptor) and ssDNA-DA (receptor-target) interactions. In addition, we evaluate the selectivity of ssDNA-decorated SWCNT FETs by detecting DA in the presence of UA, and classifying the different responses using an ANN-based data classification.

5.2 SsDNA Decoration of SWCNT

SWCNTs from a single CVD growth run were used for FET fabrication ($L=100\text{ }\mu\text{m}$) to avoid device variability. Selective patterning as described earlier was used to cover the CNT-metal junction. A total of 168 devices out of more than 500 fabricated devices with single CNT as channel and a current on/off ratio of >1000 were selected to ensure the semiconducting nature of the devices. G_{on} , g_{mp} , V_{fth} and H for 168 devices were calculated to be $4.52\times 10^{-7}\pm 1.32\times 10^{-7}\text{ }\Omega^{-1}$, $8.42\times 10^{-8}\pm 1.63\times 10^{-8}\text{ }\Omega^{-1}$, $4.3\pm 1.2\text{ V}$ and $11.7\pm 2.2\text{ V}$, respectively. For each ssDNA, 20 devices were used— 8 for DA, 5 for UA and 7 devices for a solution mixture of DA and UA, respectively.

Figure 5.1 Schematic diagram of ssDNA-decorated SWCNT FET for DA detection.

Eight ssDNA sequences (G_{22} , A_{22} , C_{22} , T_{22} , $(GT)_{22}$, $(GA)_{22}$, $(AC)_{22}$, $(CT)_{22}$) of the same sequence length, dopamine 3-hydroxytyrammine and uric acid were purchased from Sigma Aldrich, Singapore. Repeating base ssDNA sequences $(AT)_{22}$ and $(GC)_{22}$ were not used in this study because these sequences are known to have high self-complementarity and form aggregates, which is undesirable. All solutions were prepared using phosphate buffer saline (PBS, pH 7.4, BST Scientific, Ltd., Singapore) unless stated otherwise.

Figure 5.1 shows the schematic setup of a typical ssDNA-decorated SWCNT FET for DA sensing. For ssDNA immobilization, a 5 μ L drop of 10 μ M ssDNA was pipetted on the devices and incubated in a 100% humid environment for 1 hour. After incubation, the drop was removed by blow-drying with nitrogen. Thereafter, 5 μ L of 1 μ M of either DA, or UA, or DA-UA solution mixture (1:1) was pipetted on the devices decorated with different ssDNA sequences, and incubated for 15-20 minutes in a humid environment. This was followed by washing with PBS and DI water, and blow-drying with nitrogen gas.

5.3 Effect of Surface Modification

The typical I_D - V_G characteristics of a bare SWCNT-based FET tested with DA, UA and DA-UA solution mixture, respectively, is shown in Figure 5.2. Bare CNT devices on exposure to DA and UA showed a slight positive (about +0.8 V) and negative V_{fth} shift (about -0.6 V), respectively, with either minor or insignificant change in G_{on} (<5 %), or g_{mp} (<5 %), or H (<1 V) (Figure 5.2a). However, the bare CNT-based device

did not display any significant change in the transfer curve after exposure to DA-UA solution mixture (Figure 5.2b).

DA and UA are polar molecules carrying a positive and negative charge, respectively, in PBS at pH 7.4.¹⁸¹ The slight opposite directional shifts in the transfer curves for DA and UA occurred because of electron withdrawal from SWCNT by positively charged DA, and electron donation by negatively charged UA, respectively.^{65,182} DA and UA in a solution mixture stabilize each other through electrostatic forces due to their opposite charges resulting in electrical neutrality of the mixture, which does not produce any effect on the FET response.¹⁸¹ Moreover, the hydrophobic nature of CNT does not encourage the binding of polar molecules on the nanotube surface. Thus, the electrical neutrality of the solution mixture and hydrophobic nature of CNT together result in non-reliable and non-reproducible charge transfer between DA/UA and SWCNT. Hence, the detection of DA in the presence of UA is a challenge.

Figure 5.2 I_D - V_G curves of (a) bare SWCNT FET and (b) (GA)₂₂-decorated SWCNT FET after exposure to DA, UA and DA-UA solution mixture. The arrow marks indicate the direction of gate voltage sweep.

The FET transfer curve of (GA)₂₂-decorated device showed a reduction in G_{on} (~75.8 %), decrease in g_{mp} (~81.1 %), negative shift in V_{fth} (~6 V), and an increase in H (~8 V) after exposure to DA as shown in Figure 5.2b. Moreover, UA alone failed to produce any change in the transfer curves of the DNA-modified FET. And more importantly, DA-UA solution mixture produced the same effect on the transfer curve of (GA)₂₂-decorated FET as seen when exposed to DA alone, although with lower magnitude of change in transistor parameters, i.e., reduction in G_{on} (~67.1 %), decrease in g_{mp} (~74.2 %), negative shift in V_{fth} (~-4.8 V), and increase in H (~6 V). A comparison of Figures 5.2a and 5.2b showed that both DA and DA-UA solution mixture produced a negative V_{fth} shift in contrast to the positive V_{fth} shift shown by bare SWCNT FET exposed to DA, which suggest the interaction between ssDNA and DA.

The reduction in G_{on} and g_{mp} , leftward shift in V_{fth} and rise in H indicates the contribution of carrier scattering, charge transfer and charge trapping mechanism, respectively.⁷ Overall, three important points are worth mentioning. First, the lack of interaction between ssDNA and UA results in no response in ssDNA-decorated device to UA. Second, transfer curve of ssDNA coated FETs showed the same change in transistor parameters for DA and DA-UA mixture, which confirms that the source of signal is due to ssDNA-DA interaction. Third, the magnitude response of ssDNA-decorated FETs were much higher and significant compared to bare SWCNT FETs, even in the presence of UA, thus, underlining the positive effect of ssDNA surface

modification on the device response, and the improvement in selective DA recognition in the presence of UA.

To interpret the influence of ssDNA decoration on SWCNT on the FET response to DA, UA and DA-UA solution mixture, the nature of SWCNT-ssDNA interaction needs to be understood.^{183,184} For all the ssDNA sequences used, V_{fth} shifted towards the left by ~5 V because of electron donation by the negatively charged ssDNA, and G_{on} decreased by 15-35% compared to bare devices because of weak carrier scattering by molecular coating.¹³ No significant changes were observed in g_{mp} or H . The basis for using ssDNA-decorated SWCNT-based FETs to detect DA is illustrated as follows. According to molecular dynamics (MD) simulations,^{185,186} SWCNT-ssDNA system interacts via DNA bases and SWCNT sidewall,^{187,188} with a significant number of the bases being desorbed¹⁸⁹. Moreover, these simulations showed that the hydrophobic groups (the nitrogenous bases) of ssDNA sequence have great affinity for the hydrophobic SWCNT surface, while the hydrophilic phosphate groups of the ssDNA do not bind to the SWCNT. The negatively charged phosphate backbone of ssDNA creates a hydrophilic environment surrounding the nanotube surface, and this hydrophilicity increases with greater binding of ssDNA to the SWCNT. Thus, the presence of ssDNA on SWCNT converts the hydrophobic nanotube surface to hydrophilic and enhances the possibility of formation of a sequence dependent set of binding pockets within few nanometers of the SWCNT sidewall. Such a hydrophilic environment on the CNT surface attracts polar analytes

onto these hydration layers and solvates them, which increases their binding affinity to these pockets. In addition, the binding pockets modulate the electrostatic potential around the nanotubes as more polar molecules are adsorbed. Thus, the creation of a hydrophilic environment on the nanotube surface provides a favourable environment for ssDNA-DA binding, which is mirrored as the augmentation in device response.

5.4 Mechanism of SsDNA-DA Interaction Detection

The observed response of ssDNA-decorated device to DA, UA and DA-UA mixture based on the sign of the electrical parameters ($-\Delta G_{on}/G_{on}$, $-\Delta g_{mp}/g_{mp}$, $-\Delta V_{th}$ and $+\Delta H$) following DA exposure is explained based on the nature of interaction between ssDNA and DA.^{183,184} According to the strength of the interaction, the binding of ssDNA with DA is attributable to strong interactions such as hydrogen bonding and mutual association of the hydrophobic regions between DA and ssDNA or weak electrostatic attractions with electrostatic forces being the dominant interaction forces in the ssDNA-DA complex.¹⁹⁰ The positively charged cationic DA is drawn towards the ssDNA main chain establishing strong electrostatic interactions with the negatively charged phosphate groups of the ssDNA. The two $-OH$ groups in DA with hydrogen donor/acceptor capability compete with the positively charged region of DA for the ssDNA phosphate groups. This renders the positively charged $-NH_3^+$ of DA free to interact with the DNA bases, thereby allowing DA to participate in the solvation mechanism of DNA bases through hydrogen bonding interactions. Thus, $-NH_3^+$ group in DA is protonated during solvation by the DNA hydration layer, which resulted in

the negative signal, i.e., fall in conductance ($-\Delta G_{on}/G_{on}$).¹⁹¹ During this process, the DNA bases lose electrons to the nanotube, which alters the electrostatic environment around the nanotube, and consequently, resulted in threshold voltage shift ($-\Delta V_{th}$).⁶⁵ Moreover, the electron donation to CNT reduced the effective carrier density inside the nanotubes causing the formation of static charges, which generates carrier scattering leading to the reduction in slope of the transfer curve ($-\Delta g_{mp}/g_{mp}$).⁷ Furthermore, the ssDNA-DA system is capable of trapping charges, and the charge trap centers of the DNA base-DA adduct containing G and A bases, which have better affinity to SWCNT,¹⁹² are held in greater proximity to the nanotube surface resulting in the increased hysteresis ($+\Delta H$).

We also tested these ssDNA-decorated devices with the interferent, UA, which yielded no significant response. Anions like UA are predominantly involved in hydrogen-bond interactions with C, A and G bases.¹⁸¹ Moreover, there exists repulsion between the negatively charged phosphate backbone and UA, which screens the UA molecules from interacting with the DNA bases, and consequently, there is no response (similar to transfer curve for DA and UA mixture in Figure 5.2a). Noticeably, both DA and DA-UA mixture produced the same effect on the I - V characteristics, but with lower magnitude in the case of DA-UA, which is a consequence of the decrease in the proportion of DA molecules interacting with ssDNA on account of its attraction towards oppositely charged UA through electrostatic forces.

5.5 SsDNA Sequence Dependent Response

The sequence dependency of the binding pockets around the nanotubes results in a sequence dependent FET response. Since many combinations of the base sequence are possible, we investigate the effect of sequence alteration on the device response.

According to Figures 5.3a-d, DA interaction with ssDNA-decorated SWCNT FETs elicited a base-dependent trend in the relative change in ON conductance ($\Delta G_{on}/G_{on}$) and change in peak transconductance ($\Delta g_{mp}/g_{mp}$), shift in threshold voltage (ΔV_{th}) and change in hysteresis gap (ΔH). For homo sequences G₂₂, A₂₂, and C₂₂, following DA interaction, G_{on} dropped by about 55.2%, 29.4% and 18.4% whereas g_{mp} decreased by about 80.6%, 46.4% and 21.3%, respectively (Figures 5.3a and 5.3b). For the same order of sequences, ΔV_{fth} shifted by about -5.1 V, -3.8 V, and -1.8 V, respectively (Figure 5.3c). On the other hand, H increased by 6.9 V, 4.7 V and 3.5 V for sequences G₂₂, A₂₂, and C₂₂, respectively (Figure 5.3d). For repeated base sequences (GA)₂₂, (GT)₂₂, (AC)₂₂ and (CT)₂₂, G_{on} reduced by about 80.3%, 62.2%, 39.5% and 5.1%, and g_{mp} decreased by about 87.4%, 63.2%, 34.2% and 10.2%, respectively (Figures 5.3a and 5.3b). For the same order of sequences, ΔV_{fth} displayed a negative shift of about -6.1 V, -3.9 V, -3.1 V, and -1 V, respectively (Figure 5.3c). On the other hand, H increased by 7.4 V, 6.1 V, 4.1 V and 1.3 V, for sequences (GA)₂₂, (GT)₂₂, (AC)₂₂ and (CT)₂₂, respectively (Figure 5.3d).

Figure 5.3 Summary of the sequence dependent variation in FET electrical parameters induced by DA and solution mixture of DA and UA. (a) $\Delta G_{on}/G_{on}$, (b) $\Delta g_{mp}/g_{mp}$, (c) ΔV_{th} , and (d) ΔH . – sign on the y-axis in (a) and (b) indicates the drop in the respective parameters with respect to the ssDNA functionalized state. – and + on the y-axis in (c) and (d) indicate the left shift in V_{th} and increase in H , respectively, with respect to the ssDNA functionalized state. The additional subscript ‘f’ in V_{th} represents the threshold voltages obtained from the forward gate voltage sweep.

To confirm that the ssDNA sequences decorated on SWCNT FETs can selectively identify DA, we repeated the experiment using DA-UA solution mixture. Clearly, from Figures 5.3a-d, DA-UA mixture produced the same trend in FET response as displayed by devices exposed to DA alone, but with lower magnitude response, for reason stated earlier. Evidently, DA interaction with ssDNA-decorated

SWCNTs elicited a base-dependent trend as follows: $G_{22} > A_{22} > C_{22}$ and $(GA)_{22} > (GT)_{22} > (AC)_{22} > (CT)_{22}$ for homo- and repeated base sequences, respectively. Since devices decorated with T_{22} showed no significant change in G_{on} and g_{mp} , and about ~1 V right shift in V_{th} , which is similar to the transfer curve of bare SWCNT exposed to DA (Figure 5.2a), it has been omitted from the above trend.

The magnitude of the change in transistor electrical parameters induced by DA is determined by the strength and nature of SWCNT-ssDNA and ssDNA-DA interactions.^{183,184} The difference in magnitude of the electrical response is due to the differences in binding affinity, wrapping tendency and solvation effects for different bases.^{193, 194} The base-SWCNT binding free energies (ΔE_{bind}) for the bases found using thermodynamic integration follows the trend given below.^{192,195-197}

$$\Delta E_{bind}^G < \Delta E_{bind}^A < \Delta E_{bind}^T < \Delta E_{bind}^C \quad (5.1)$$

Since ssDNA and SWCNT interact through the bases, the total binding energy of the ssDNA sequence on the SWCNT will approximately scale with the sum of individual base binding free energies as shown,^{192,195-197}

$$\Delta E_{bind}^{ssDNA} \sim n_G \Delta E_{bind}^G + n_A \Delta E_{bind}^A + n_T \Delta E_{bind}^T + n_C \Delta E_{bind}^C \quad (5.2)$$

Here n_A , n_C , n_G , and n_T are the number of A, C, G and T in the sequence, respectively.

For homo and repeated base ssDNAs, we expect the binding affinity to follow the trends: $G_{22} > A_{22} > T_{22} > C_{22}$, and $(GA)_{22} > (GT)_{22} > (AC)_{22} > (CT)_{22}$, which is similar to our results. Thus, the strength of SWCNT-ssDNA interaction has a significant effect on the sequence dependent electronic response to DA. The presence of more number

of hydrogen donor/acceptor sites in bases G and A leads to greater response in CNT containing them compared to sequences with bases C and T.¹³⁹ In addition, another type of non-bonded interaction known as the edge-to-face NH- π interactions^{193,195} is possible between the hydrogen of amino groups of bases G and A facing the aromatic ring system of DA, which further enhances the response. Compared to other sequences, T₂₂-decorated devices showed a right shift in V_{th} , which is similar to the transfer characteristics of DA interaction with the bare nanotube surface. From earlier studies,^{194,199} it is known that ssDNA with high pyrimidine content (G and A) has very good affinity, but poor wrapping tendency to SWCNT sidewalls, i.e, wrapping tendency follows the order T>C>A>G. Consequently, major portions of the nanotube surface are left exposed following helical wrapping of T₂₂, which allows DA to directly interact with CNT surface. Even if DA interacts with T₂₂-decorated SWCNT, the electrical response is not significant because of low binding affinity between T₂₂ and SWCNT. Thus, different SWCNT-ssDNA systems exhibit different magnitude response to DA and DA-UA mixture, which is a good indicator of the sequence dependent discriminating capacity of the FETs.

Different ssDNAs display varying magnitude of change in the electrical parameters following interaction with DA, which makes it possible to distinguish the responses for each SWCNT-ssDNA system. Therefore, we used an MLP-based ANN data classification approach in MATLAB to classify the different ssDNA-DA interactions using the four electrical parameters as input. The four electrical

parameters of all the ssDNA-decorated devices (8 sequences) before and after DA introduction were designated as inputs of ANN. Eight output classes were designated, namely, G, A, T, C, GA, GT, AC and CT, respectively. Overall, 4 features from 64 ssDNA-decorated devices (8 for each ssDNA) were obtained before and after DA exposure, constituting a 128×4 matrix data set. Out of the 128×4 data set, 64×4 observations constitute the ssDNA-decorated class, and the remaining 64×4 observations belong to the DA-induced response for each of the 8 sequences, i.e., 8×4 data matrix for each sequence.

Figure 5.4 (a) Mean squared error (MSE) and (b) training state plot of the MLP classifier for a 4-input feature and 8-output class classification.

The mean squared error (MSE) and the training plot graphs of ANN-based MLP classification are shown in Figures 5.4a and 5.4b, respectively. The average classification accuracy, sensitivity and the specificity was 90.3%, 87.7%, and 98.2%, respectively. Table 5.1 summarizes the performance parameters of MLP classification for different ssDNA-DA systems. Overall, the response of different SWCNT-ssDNA

systems to DA are efficiently classified, which underlines the sequence dependent discriminating ability of the FETs.

Table 5.1 Summary of MLP-based classification of electrical responses of different ssDNA-decorated SWCNT FETs before and after interaction with DA for homo base sequences, repeated base sequences and a combination of both.

Performance parameters	Accuracy (%)	Sensitivity (%)	Specificity (%)
Inputs			
Homo bases	97.1	96.2	100
Repeated bases	95.1	94.1	100
Homo and repeated bases	90.3	87.7	98.2

5.6 Conclusions

In this chapter, it was demonstrated that ssDNA decoration on SWCNT improved the response of FET-based detection to DA, which otherwise displayed poor response. The drop in FET conductance and transconductance signifies carrier by ssDNA-DA polar interactions. The charge transfer mechanism was visible from the negative shift in the threshold voltage because of electron doping of CNTs upon binding of the nitrogenous bases in ssDNA with DA. The formation of ssDNA-DA adducts exhibited a charge trapping behavior apparent from the increase in hysteresis. Overall, the ssDNA-decorated SWCNT FETs exhibited a combination of carrier scattering, charge transfer and charge trapping mechanisms to detect DA. Moreover, such ssDNA-modified SWCNT FETs recognized DA even in the presence of UA, which underlines the improvement in molecular selectivity. The response of the FETs was sequence

dependent with G_{22} and $(GA)_{22}$ exhibiting the best response to both DA and DA-UA solution mixture. The sequence dependent response highlights the discriminating ability of the different SWCNT-ssDNA systems in recognizing different ssDNA-DA interactions, which was corroborated by discriminating the sequence dependent responses efficiently by an ANN-based data classification strategy.

Chapter 6: β -Cyclodextrin-Decorated CNT-Based Chemiresistors for Detecting Host-Guest Interactions

6.1 Introduction

Molecules such as 9-anthracenecarboxylic acid (9-ACA, polycyclic aromatic hydrocarbon derivative),¹⁴ diclofenac sodium (DCFNa, a non-steroidal anti-inflammatory drug)¹⁵ and curcumin (naturally occurring pigment in the plant *curcuma longa*)¹⁶ are important for environmental and health safety. However, SWCNTs lack response, sensitivity, and selectivity when used alone to recognize these molecules. Nevertheless, the excellent chemical stability of SWCNTs allows sidewall functionalization,^{112,200} which encourages the modification of CNT surface with receptor molecules to improve the sensitivity and selectivity of molecular detection.²⁰¹⁻²⁰³ Earlier reports employing nanostructures to determine 9-ACA,²⁰⁴ DCFNa,^{205,206} and curcumin²⁰⁷ were solely by electrochemical approaches, which exhibited poor sensitivity and high limit of detection. Moreover, the number of reports pertaining to their detection is scarce. This encourages the need to explore an electronic alternative utilizing nanostructures with suitable surface modification to detect them.

Literature confirms the formation of host-guest complexes between these molecules and β -cyclodextrin (β -CD), which differ in terms of their chemical structure, polarity, and molecular dimensions. CDs are oligosaccharides consisting of six, seven, or eight glucose units (named α -, β -, or γ -CD) having a truncated cone structure.^{208,209} The hydrophilic outer surface of CD gives it water-solubility, and the

inner hydrophobic central cavity displays high molecular selectivity and enantioselectivity by providing a congenial environment for the encapsulation of a wide range of appropriately sized and/or nonpolar part of guest molecules to form stable host-guest inclusion complexes.²⁰⁹ CDs have been used extensively as functionalization entities for SWCNTs in the field of chemical/biosensing.^{17,210,211} Thus, the combination of the exceptional electronic properties of SWCNT, molecular selectivity of CD cavity, and the electronic readout of chemiresistor setup provides a faster route to electronic detection of host-guest interaction. An important aspect of efficient electronic detection of host-guest interaction detection is the effective immobilization of the host receptor CD on the CNT surface. A non-covalent approach employing a pyrene derivative linker molecule like 3, 4, 9, 10-perylene tetracarboxylic acid (PTCA),²¹² which interacts with SWCNT through π -stacking and binds covalently to the amine terminated CD, enhances the selectivity of receptor immobilization and host-guest interaction. The number of reports showing the use of nanowire/nanotube-based FETs/chemiresistors to detect CD host-guest interactions is limited.^{18,213,214}

In this chapter, we investigate the electronic transduction mechanism of CNT chemiresistor for detecting β -CD-guest interaction (receptor-target interaction) using different targets (9-ACA, DCFNa, and curcumin). We also study the impact of surface modification on the device response by analyzing the sensor performance. Furthermore, the conductance correlation characteristics of different host-guest

systems are used to analyze the selectivity of the molecular recognition processes, which is further evaluated by an ANN-based pattern classification approach.

6.2 β -CD Decoration of CNT

The CNT networks used in this study were obtained from a single run to maintain homogeneity and uniform density. Only devices with similar density distribution were used for sensing studies. At least 5 devices were used for each sensing experiment. The bare CNT network containing devices exhibited conductance of $2.12 \pm 1.02 \times 10^{-7} \Omega^{-1}$ at 1 V.

All chemicals and reagents were purchased from Sigma Aldrich, Singapore, unless stated otherwise. The as-fabricated chemiresistors were incubated with 2 mM of 3, 4, 9, 10-perylene tetracarboxylic acid (PTCA) dissolved in pure dimethylformamide (DMF) for 3 hours at room temperature, after which, the devices were washed with DMF and de-ionized (DI) water. Subsequently, the chemiresistors were incubated for 3 hours with 1 mM of mono-(6-ethanediamine-6-deoxy)- β -cyclodextrin (NH_2 - β -CD, ATP Chems, Shanghai, China) dissolved in DMF. This was followed by washing with DMF and DI water. Figures 6.1a and 6.1b show the chemical structures of NH_2 - β -CD and PTCA, respectively. Finally, the PTCA-linked β -CD-decorated chemiresistors were exposed to increasing concentration of 9-ACA (dissolved in DMF), DCFNa (dissolved in DI) and curcumin (dissolved in DMF), respectively. Figure 6.1c shows the schematic diagram of a chemiresistor setup using SWCNT for detecting different guest molecules.

Figure 6.1 The chemical structures of (a) mono-(6-ethanediamine-6-deoxy)-β-cyclodextrin and (b) 3,4,9,10-perylene tetracarboxylic acid (PTCA). (c) A schematic setup of β-CD-decorated CNT chemiresistor for host-guest interaction detection.

6.3 Mechanism of Host-Guest Interaction Detection

The aromatic pyrenyl group of PTCA interacted with the CNT through π - π stacking interactions and the carboxylic group attached to the amine group of modified β-CD molecule (NH₂-β-CD) through covalent linkage. After PTCA functionalization and β-CD decoration steps, I_D in the ON-state typically reduced by about 10-25% ($1.78 \times 10^{-7} \pm 0.22 \times 10^{-7} \Omega^{-1}$) and 7-16%, ($1.57 \times 10^{-7} \pm 0.1 \times 10^{-7} \Omega^{-1}$) respectively, suggesting

scattering by coating of these molecules on the CNT surface as shown in Figure 6.2. The non-covalent interactions such as van der Waals forces and hydrophobic interactions are the dominant forces of interaction during complex formation.²⁰³ The van der Waals forces represent small attractive forces between neutral molecules other than chemical bonds or electrostatic interactions. Hydrophobic interactions occur between water-hating non-polar molecules. The non-polar and hydrophobic nature of the benzene ring of guest molecule and the CD cavity results in van der Waals forces and hydrophobic interactions. During host-guest interaction on the nanotube, charge transfer⁷ occurs either between CD and CNT due to variations in the charge distribution of CD, or between the polar parts of the guest molecule and CNT, which is reflected in the change in device conductance. In the succeeding sections, we elaborate the possible causes of the observed change in device conductance following host-guest interaction, and discuss the performance of the sensor.

Figure 6.2 I_D - V_{DS} characteristics following PTCA functionalization and CD decoration steps in a CNT chemiresistor.

6.3.1 Determination of 9-ACA

The variation in $(G-G_0)/G_0$ with time for increasing concentration of 9-ACA is shown in Figure 6.3a. Clearly, until 100 pM of 9-ACA, the response was insignificant, but for higher concentrations, the response increased progressively (fall in conductance indicated by the negative sign) until about 10 nM. Thereafter, $(G-G_0)/G_0$ saturated, and is considered insignificant. From the calibration curve in Figure 6.3b, the linear range of detection is found to be ~100 pM-10 nM with sensitivity, LOD and R^2 of $\sim 6.1 \times 10^{-2} \text{ nM}^{-1}$, ~95 pM and ~0.988, respectively.

Figure 6.3 (a) $(G-G_0)/G_0$ vs. time and (b) $(G-G_0)/G_0$ vs. concentration plots of PTCA linked β -CD-decorated CNT chemiresistor for increasing concentration of 9-ACA. (c) The chemical structure of 9-ACA. The arrows indicate the starting time of the introduction of 9-ACA for each concentration.

The drop in conductance with increasing concentration of 9-ACA is explained based on the formation of 1:1 complex between β -CD and 9-ACA (Figure 6.3c).¹⁸ The complex formation could rearrange the charge distribution of the CD, resulting in charge transfer between CD and SWCNTs, thereby changing the charge carrier density in the SWCNTs.⁶⁵ A second possibility is that the guest molecules bound to the β -CD cavities modify the scattering potentials of the β -CD receptors by reducing the charge mobility.⁷

6.3.2 Determination of DCFNa

From Figure 6.4a, it is seen that $(G-G_0)/G_0$ of β -CD-decorated CNT chemiresistors for increasing concentrations of DCFNa showed no significant change upto 1 nM. The linear detection range obtained from the calibration curve in Figure 6.4b is found to be ~1 nM-100 nM with sensitivity, LOD and R^2 of ~1 nM-100 nM, $\sim 2.07 \times 10^{-3} \text{ nM}^{-1}$, ~898 pM and ~0.929, respectively.

The formation of β -CD-DCFNa host-guest complex can explain the increase in $(G-G_0)/G_0$ with DCFNa concentration. According to earlier spectroscopic studies,²¹⁵ the 1:1 DCFNa- β -CD inclusion complex consists of β -CD cavity encapsulating either the phenylacetate ring or the acetate group of the DCFNa molecule (Figure 6.4c). Another possibility is the formation of a 2:1 host-guest complex with both phenyl rings of the DCFNa molecule included in the cavities of two CD receptors.²¹⁶ The simultaneous presence of 1:1 and 2:1 complexes has also been suggested by some reports.²¹⁷ A 1:1 complex has one of the benzene rings of DCFNa encapsulated within

a β -CD cavity by van der Waals forces and hydrophobic interactions while the other phenyl ring and the functional group of DCFNa are outside the β -CD cavity. The phenylacetate and dichlorophenyl groups outside the cavity are capable of electron withdrawal,^{218,219} which is reflected in the form of increased device conductance, i.e., increase in hole density. Similarly, a 2:1 host-guest complex formed by encapsulation of both benzene groups of DCFNa by two adjacent β -CD molecules causes the $-\text{NH}$ group to be left outside the CD cavity,^{217,218} which increases hole concentration in CNTs by electron withdrawal, thereby increasing the conductance.

Figure 6.4 (a) $(G-G_0)/G_0$ vs. time and (b) $(G-G_0)/G_0$ vs. concentration plots of PTCA linked β -CD-decorated CNT chemiresistor for increasing concentration of DCFNa. (c) The chemical structure of DCFNa. The arrows indicate the starting time of the introduction of DCFNa for each concentration.

6.3.3 Determination of Curcumin

Similar to DCFNa, increasing concentration of curcumin increased the conductance of CNT chemiresistors as seen in Figure 6.5a. The sensor response is estimated to be significant within ~1 nM to 100 nM from the calibration curve shown in Figure 6.5b with a sensitivity, LOD and R^2 of $\sim 5.0 \times 10^{-3} \text{ nM}^{-1}$, $\sim 978 \text{ pM}$ and ~ 0.956 , respectively.

Figure 6.5 (a) $(G-G_0)/G_0$ vs. time and (b) $(G-G_0)/G_0$ vs. concentration plots of PTCA linked β -CD-decorated CNT chemiresistor for increasing concentration of curcumin. (c) The chemical structure of curcumin. The arrows indicate the starting time of the introduction of curcumin for each concentration.

This increase in $(G-G_0)/G_0$ with curcumin concentration can be interpreted based on β -CD-curcumin complex formation. Previously, spectroscopic studies of the host-guest complex between curcumin and β -CD indicate the formation of a 1:2 curcumin- β -CD complex with each of the benzene rings of curcumin (Figure 6.5c)

included within one β -CD cavity by van der Waals forces and hydrophobic interactions, and the electron donor groups in curcumin forming hydrogen bonds within the β -CD cavity.²²⁰ Such a 2:1 complex results in the straight chain of curcumin containing the ketone functional group to be left outside the β -CD cavity. The electron withdrawing nature of the ketone group reduces the electron concentration in CNT,^{217,218} which increased the channel conductance (hole density increases).

6.4 Effect of Surface Modification

The effective immobilization of β -CD receptor on CNT surface is of paramount importance as it determines the efficient interaction of β -CD molecules with the guest molecules, necessary for the change in channel conductance. In this study, we employed PTCA linker to channelize β -CD receptors on the CNT surface for improving target detection. Therefore, to evaluate the effect of PTCA surface modification on the sensor performance, we performed similar experiments on devices decorated with β -CD molecule directly on CNT in the absence of PTCA as bridging molecule.

Figures 6.6a-c show the $(G-G_0)/G_0$ vs. time plots for the three host-guest systems using β -CD-decorated CNT chemiresistor with no PTCA. In the absence of PTCA, CDs are non-specifically adsorbed, and their probability of being displaced from the CNT surface following host-guest interaction rises on encountering guest molecules. Therefore, even upon successful formation of the host-guest complex, the chemiresistors will not be able to detect such interactions because the complexes are

displaced from the active surface. Despite the likelihood of non-specifically adsorbed CDs interacting with 9-ACA/DCFNa being low, there is an increase/decrease (DCFNa/9-ACA) in the conductance at higher concentrations (Figures 6.6a and 6.6b). With rising guest concentration, the proportion of the host-guest interactions on the CNT surface increases, which eventually causes an increase/decrease (DCFNa/9-ACA) in the conductance. On the contrary, the sensors with PTCA linkage immobilize the CDs effectively, and channelize the host-guest interactions on the CNT surface even for lower guest concentrations.

Figure 6.6 $(G-G_0)/G_0$ vs. time plots of β -CD-decorated CNT chemiresistor with no PTCA linkage for increasing concentration of (a) 9-ACA, (b) DCFNa, and (c) curcumin, respectively.

Table 6.1 Summary of the detection range, LOD, sensitivity and R^2 for β -CD-decorated CNT chemiresistors in the detection of 9-ACA and DCFNa with and without PTCA linker. Curcumin was not detected by chemiresistors without PTCA linkage, and therefore, has been neglected from the table.

Performance parameters	9-ACA		DCFNa	
	With PTCA	No PTCA	With PTCA	No PTCA
Detection Range	100 pM– 10 nM	10 nM– 100 nM	1 nM– 100 nM	100 nM– 10 μ M
Sensitivity (nM^{-1})	7.10×10^{-2} $\pm 2.11 \times 10^{-2}$	5.55×10^{-4} $\pm 1.13 \times 10^{-4}$	1.98×10^{-3} $\pm 8.15 \times 10^{-4}$	7.57×10^{-6} $\pm 3.71 \times 10^{-6}$
LOD	87.2 $\pm$ 23.5 pM	6.39 $\pm$ 3.3 nM	863 $\pm$ 105 pM	86.12 $\pm$ 25.6 nM
R^2	0.968 $\pm$ 0.03	0.855 $\pm$ 0.03	0.936 $\pm$ 0.01	0.897 $\pm$ 0.02

Table 6.1 summarizes the sensor performance with and without PTCA linkage in the detection of 9-ACA and DCFNa. Clearly, the magnitude of the conductance response at the lower detection limit of β -CD decorated CNT chemiresistors with PTCA linkage reduced from ~30% (9-ACA) and ~13% (DCFNa) to ~11% (9-ACA) and ~5% (DCFNa) in devices without PTCA. Moreover, the lower limit of the range of detection for β -CD-decorated devices with PTCA (~100 pM for DCFNa; ~1 nM for 9-ACA) was lower compared to the devices without PTCA (~10 nM for DCFNa; ~100 nM for 9-ACA). The sensitivity and correlation coefficient (R^2) values for 9-ACA detection for devices with PTCA reduced from $\sim 6.1 \times 10^{-2} \text{ nM}^{-1}$ and ~0.988 to $\sim 5.43 \times 10^{-4} \text{ nM}^{-1}$ and ~0.885, respectively, for devices without PTCA. For DCFNa detection with devices containing PTCA, the sensitivity and R^2 values reduced from

$\sim 2.10 \times 10^{-3} \text{ nM}^{-1}$ and ~ 0.930 to $7.1 \times 10^{-6} \text{ nM}^{-1}$ and ~ 0.881 , respectively, for those without PTCA. The LOD for devices with PTCA increased from $\sim 95 \text{ pM}$ for 9-ACA and $\sim 898 \text{ pM}$ for DCFNa to $\sim 6.3 \text{ nM}$ and $\sim 86.1 \text{ nM}$, respectively, for chemiresistors without PTCA. Overall, the devices with PTCA to anchor the β -CD molecules outperform the devices without them in terms of all sensor performance parameters.

Chemiresistors in curcumin detection typically exhibited detection range, sensitivity, LOD and R^2 of 1 nM - 100 nM , 4.12×10^{-3} , 844 pM and 0.943 , respectively, for PTCA containing devices. In curcumin detection, $(G-G_0)/G_0$ of β -CD-decorated CNT chemiresistors with and without PTCA linkage follow opposite trends (Figure 6.5a and Figure 6.6c), which is interpreted based on the 1:2 complex with β -CD. In devices without PTCA linker, the likelihood of encapsulation of curcumin molecules by two non-specifically adsorbed β -CD molecules is low, resulting in the formation of partial complexes, which have one benzene ring of the curcumin molecule inside the β -CD cavity, and the other phenyl ring along with the straight chain outside the cavity. These partial complexes and non-specifically adsorbed guest molecules act as scattering potentials, which suppress the device conductance with increasing concentration of curcumin. As a result, the conductance response of β -CD decorated chemiresistors (conductance decreases) without PTCA and with PTCA (conductance increases) display contrasting behaviour. From the above discussions, evidently, PTCA linkage plays an active role in improving not only the sensor response, but also the sensitivity and specificity of host-guest interaction on the SWCNT surface.

Figure 6.7 I_D vs. time plots of bare CNT chemiresistor for increasing concentrations of (a) 9-ACA, (b) DCFNa, and (c) curcumin, respectively.

To analyze the effect of the guest species on bare SWCNTs, control experiments were conducted using devices with neither PTCA nor CD. Figures 6.7a-c show the variation of I_D with time for increasing concentration of guest molecules on bare CNT-based chemiresistors. Evidently, the molecules failed to produce any significant variation in conductance even at high guest concentrations.

6.5 Selectivity Using Conductance Correlation

The selectivity of the sensor in distinguishing the different host-guest systems is an important criterion when analyzing sensor performance. Use of data analytical methods in the calculation of the correlation function may be helpful in analyzing the selectivity of a sensor. The conductance response varies in a stepwise manner with

time with increasing concentration of guest molecules until it saturates (Figures. 6.3a, 6.4a and 6.5a) due to insufficient CD receptors on the CNT surface to encapsulate the incoming guest molecules. Here, the conductance characteristics obtained after the addition of guest molecules for a particular guest concentration (common to the three guest molecules) within the linear detection range were treated as distinct data segments.

The correlation functions are pattern recognition measures that enable identification of the degree of similarity within a signal or between different signals. The correlation is between two values of the same variable at time t and $t+k$, averaged over the whole signal. It is defined in two ways– autocorrelation and two-point correlation function

6.5.1 Autocorrelation Function

The autocorrelation function is a correlation of a data set with itself. The expression used for computation of autocorrelation function is

$$R_k = \frac{\frac{1}{N} \sum_{t=k}^{N-(k+1)} (G(t) - G') (G(t+k) - G')}{\frac{1}{N} \sum_{t=k}^{N-1} (G(t) - G')^2} \quad (6.1)$$

where $G(t)$ is the normalized conductance at time t as defined earlier, and $G' = \frac{1}{N} \sum_{t=0}^{N-1} (G(t))$ is the mean of the conductance over the time interval $0 \leq t \leq (N-1)$. N is the total number of observations and $k=0, 1, 2, 3, \dots$ is the time lag.^{221,222}

R_k gives information about the consistency of a signal obtained from a single device over a certain period by analyzing different data segments. R_k value closer to 1 is an indicator of high consistency. The use of R_k for conductance characteristics can

furnish information about the variation in signal within the linear range of detection for a specific molecular detection. The slope of the $\log R_k$ vs. time plot is an indicator of the sensitivity of detection.

Figure 6.8 Plots of (a) R_k vs. k and (b) $\log R_k$ vs. k upto 10 s for the three host-guest systems (9-ACA, DCFNa and curcumin) at a guest concentration of 1 nM for a β -CD-decorated CNT chemiresistor with PTCA linkage. R_k vs. k plots for different guest concentrations within the linear detection range for (c) β -CD-9-ACA, (e) β -CD-DCFNa and (g) β -CD-curcumin host-guest systems, respectively. Plots of $\log R_k$ vs. k upto 10 s for (d) β -CD-9-ACA, (f) β -CD-DCFNa and (h) β -CD-curcumin host-guest systems, respectively, for different guest concentrations within the linear detection range.

From Figure 6.8a, it is seen that the variation of R_k with time calculated using Eq. (6.1) for each of the three host-guest systems is different, which indicates that the autocorrelation function of the β -CD decorated CNT sensor gives distinct patterns for each host-guest system. The $\log R_k$ vs. k curve in Figure 6.8b shows different slopes for each host-guest system indicating that the autocorrelation function distinguished the guest molecules with different sensitivities, which highlights the discriminating ability of the sensor due to the differences in the host-guest complex formation. However, for a particular host-guest system and within the linear detection range, the slopes were similar for different guest concentration (Figures 6.8c, 6.8e, 6.8g, and Figures. 6.8d, 6.8f, and 6.8h), which suggests that for a specific host-guest system, the

correlation functions are independent of the concentration within the linear detection range, thus, justifying the use of correlation functions for sensor selectivity evaluation.

6.5.2 Two-Point Correlation Function

The two-point correlation function, $A(t)$, for the conductance is re-defined from earlier works^{221,222} related to gas sensing to suit liquid phase sensing as given below,

$$A(t) = \frac{1}{n} \sum_{i=1}^n G_i(t) G_i(t + \delta t) - \left(\frac{1}{n} \sum_{i=1}^n G_i(t) \right)^2 \quad (6.2)$$

$G_i(t)$ is the normalized conductance for the i^{th} data segment for a particular guest concentration, $\delta t=1$ s represents the sampling interval and n is the total number of data segments available for a particular guest concentration of a specific host-guest system. $A(t)$ makes use of cumulative data segments obtained from many devices over a period to analyze the consistency across signals. It gives the extent of variability of the signal within the linear range of detection obtained from different devices for a specific molecular detection.

The two-point conductance correlation function in Eq. (6.2) was estimated using the experimental data of normalized conductance variation with time for different concentrations. Figure 6.9a shows the results of variation in $A(t)$ with time for each host-guest system at a guest concentration of 1 nM. Clearly, $A(t)$ pattern differs for each host-guest system, which indicates the selective recognition of different guest molecule by the same sensor. On the other hand, the $A(t)$ pattern for different concentrations within the linear detection range of a particular host-guest system is similar as seen in Figures 6.9b-d. These results further corroborate the

aforementioned fact that the correlation function for a specific host-guest system is independent of the concentration within the linear detection range, but varies with different host-guest interactions, which highlights the sensitivity and selectivity of the chemiresistive sensor.

Figure 6.9 (a) $A(t)$ vs. time graphs for different host-guest systems (9-ACA, DCFNa and curcumin) at guest concentration of 1 nM for a β -CD-decorated CNT chemiresistor with PTCA linkage. Plots of $A(t)$ vs. time for (b) β -CD-9-ACA, (c) β -CD-DCFNa and (d) β -CD-curcumin host-guest systems, respectively, for different guest concentrations within the linear detection range.

Table 6.2 shows the range of values of the $A(t)$ for each guest molecule in its linear detection range. Overall, the distinct correlation function of different host-guest systems shows the sensor selectivity in recognizing different guest species.

Table 6.2 Range of values of the two-point correlation function, $A(t)$, for 9-ACA, DCFNa and curcumin detection in their respective linear detection range.

Concentration	100 pM	1 nM	10 nM	100 nM
Guest molecule				
9-ACA ($\times 10^{-3}$)	−0.89 to 1.14	−0.82 to 1.37	−1.18 to 0.91	—
DCFNa ($\times 10^{-4}$)	—	−2.16 to 1.96	−3.13 to 2.87	−3.80 to 4.04
Curcumin ($\times 10^{-4}$)	—	− 1.06 to 5.39	−0.68 to 3.76	−0.94 to 4.37

In order to evaluate the extent of the distinction between the different host-guest correlation functions, we employ an MLP-based ANN classification approach with the correlation functions as input. The data patterns of the autocorrelation and two-point correlation function obtained from at least from 5 devices corresponding to each host-guest system were fed as inputs to a MLP-based ANN classifier in MATLAB. A total of 1500 sample points each of R_k and $A(t)$ were used as inputs.

Figure 6.10 (a) The mean squared error (MSE) and (b) training plot of MLP-based classification. The classification method used the correlation functions (R_k and $A(t)$) obtained at a guest molecule concentration of 1 nM as input patterns for classifying the conductance response into three host-guest system classes, i.e., 9-ACA, DCFNa and curcumin.

The mean squared error (MSE) and the corresponding training plot for MLP-based classification are shown in Figures 6.10a and 6.10b, respectively. The classification yielded average classification accuracy, sensitivity, and specificity of ~91.83%, ~90.13%, and ~85.39%, respectively. These results highlight the distinction between the different host-guest correlation patterns, which affirms the excellent selectivity of the sensor.

6.6 Conclusions

In this chapter, we demonstrated the electronic detection of host-guest interaction between host β -CD and guest molecules such as 9-ACA, DCFNa, and curcumin using CNT chemiresistor. The drop in conductance characterized 9-ACA detection whereas, DCFNa and curcumin showed an increase in conductance in β -CD-decorated CNT chemiresistors. The sensors exhibited good linear detection range, sensitivity, and LOD. The use of PTCA linker considerably improved the sensor performance as well as the specificity of host-guest interaction. The selectivity of molecular recognition was demonstrated by the distinct conductance correlation patterns for each host-guest system for a particular guest concentration within the detection range, and similar correlation patterns for a specific host-guest system for different guest concentration within the detection range, which was corroborated by an ANN-based pattern classification approach. Thus, for effective β -CD receptor immobilization and detection of host-guest interaction occurring on CNT in a chemiresistor setup, surface modification is essential. Moreover, conductance correlation pattern of different host-

guest complexes serve as excellent templates for evaluating the selectivity of molecular recognition.

Chapter 7: Conclusions and Future Work

7.1 Conclusions

CNT-based FETs and chemiresistors have a significant role in the development of electronic sensors for detection of molecular recognition of various bio/chemical target analytes. The increment of sensor sensitivity and selectivity, better specificity, faster response and understanding the sensing mechanism are imperative requisites for efficient electronic sensing. To meet these requisites, better design of transducer surface and device structure is necessary, which enables in attaining a sustainable, stable, and reliable transduction output. Electronic molecular recognition of different bio/chemical analytes involves different transduction mechanisms, which are dependent on CNT-receptor and receptor-target interactions. Moreover, CNT surface modification and device structure influence this interaction, which consequently determines the sensing mechanism. Limits in understanding of the sensing mechanism, and the effect of surface modification and device structure on the transduction mechanism are hurdles in realizing CNT-based FET/chemiresistor as bio/chemical sensors.

Herein, individual and network SWCNTs were successfully grown using CVD under optimized conditions and fabricated into FETs/chemiresistors with varying channel lengths and network densities. Using the fabricated devices, we studied the sensing mechanisms and addressed the influence of surface modification and/or device structure on the transduction response to molecular recognition of different

bio/chemical species. From the different studies, we categorize the conclusions based on the sensing mechanism, the effect of surface modification on sensing, and the effect of device structure on sensing, and list the following important conclusions and contributions.

i) Sensing Mechanism

The CNT FET sensing mechanisms reported in this thesis involved a channel dominant response, which included a combination of carrier scattering, charge transfer and charge trapping. These were discriminated and interpreted based on the sign and magnitude shifts of the various transistor parameters (G_{on} , g_{mp} , V_{fth} , V_{rth} and H). For example, a significant drop in conductance and transconductance signifies scattering potential generated by the target molecules on the CNTs. A shift in the threshold voltage to the more negative (positive) values is a characteristic of electron donation (withdrawal) to CNTs. The charge trapping behavior is detected from the increase in hysteresis gap following target detection because of the increase in charge trapping centers formed on the CNT. In a chemiresistor configuration, the decrease (increase) in channel conductance suggested electron transfer (withdrawal) to CNTs. Based on these mechanisms, the various results pertaining to sensing mechanism for each chapter have been summarized as follows.

- ❖ The hybridization of nucleic acids relies on hydrogen bonding between complementary base pairs (receptor-target interaction). SWCNT FETs showed a reduction in p-type behaviour and an increase in charge trapping for DNA-

DNA hybridization whereas DNA-RNA hybridization caused an increase in p-type behaviour and reduction in charge trapping behaviour. Thus, SWCNT FETs electronically detected DNA-DNA and DNA-RNA hybridization through a combination of charge transfer, carrier scattering and charge trapping mechanism.

- ❖ ssDNA-DA interacts through electrostatic forces. The drop in conductance and transconductance, left shift in threshold voltage and increase in hysteresis gap characterized the electrical response. Thus, ssDNA-decorated devices responded to DA based on a combination of carrier scattering, charge transfer and charge trapping mechanism. The sequence dependent response for homo and repeated base sequences followed the trend: G>A>C and GA>GT>AC>CT, respectively.
- ❖ CNT chemiresistors electronically detected the host-guest complex formation of 9-ACA, DCFNa, and curcumin with β -CD. The chemiresistors showed a reduction in conductance for 9-ACA, and an increase in device conductance for DCFNa and curcumin, with increasing guest molecule concentration.

ii) *Effect of Surface Modification*

- ❖ CNT surface modification using a pyrene derivative improved the response and specificity of the SWCNT FET in hybridization detection. In the presence of pyrene modification, the transfer characteristics of DNA-DNA and DNA-RNA

hybridization were distinguishable, irrespective of the presence of CNT-metal contact junction during sensing.

- ❖ Surface modification of SWCNT using ssDNA improved the response of SWCNT FET to DA, which otherwise showed poor response. In addition, the ssDNA decoration helped in identifying DA even in the presence of an interferent such as UA, which shows the improvement in selectivity of molecular recognition.
- ❖ The use of PTCA linkage for β -CD immobilization on CNT chemiresistors considerably improved the response, sensitivity, and specificity of host-guest interaction between β -CD and 9-ACA, DCFNa and curcumin molecules. The different binding affinities of the complexes on CNTs yielded distinct conductance correlation patterns, thereby highlighting the selectivity of molecular recognition.

iii) *Effect of Device Structure*

- ❖ A study on the effect of channel length (device parameter) for hybridization detection revealed that long SWCNT-based FETs showed better response compared to short or ultralong channels.

Overall, the molecular recognition of different bio/chemical species based on different receptor-target interactions such as hydrogen bonding, electrostatic forces, electron transfer, and complex formation were detected electronically using CNT-based FETs/chemiresistors. The dominant electronic transduction mechanisms of FET

included charge transfer, carrier scattering and charge trapping while chemiresistors exhibited an increase/decrease in conductance following molecular recognition. The presence of surface modification plays a key role in improving sensor sensitivity, specificity, and selectivity of molecular recognition detection. Moreover, optimization of device parameters aids in the design of device structures for enhancing sensor sensitivity and minimizing variability across devices, which is essential for better molecular recognition. Finally, multi-parameter FET data and conductance correlation patterns act as benchmarks for evaluating the selectivity of molecular recognition in FETs and chemiresistors, for offline and real time detection, respectively.

7.2 Future Work

Based on the conclusions, we recommend the following future work aimed at different aspects:

- i) Use alternate CNT functionalization approaches to study the impact on the electronic sensing mechanism and device response.
- ii) Analyze the effect of varying the concentration of surface functionalization/receptor entities and/or target analyte on the CNT FET/chemiresistor device response to molecular recognition.
- iii) Study the effect of other device structure parameters such as channel number, thickness of dielectric, type of substrate (e.g. quartz), CNT diameter etc., on the sensing output.

- iv) Use multi-parameter FET data/conductance correlation patterns of CNT-based FET/chemiresistor for analyzing the selectivity of molecular recognition of other analytes like vapor/gas.

List of Publications

Salila Vijayalal Mohan, H. K.; An, J.; Zheng, L., Electrical Field Dependent Mobility Analysis of Ultralong Individual Single Walled Carbon Nanotube Field-Effect Transistor. *Journal of Nanoelectronics and Optoelectronics* **2013**, 8 (2), 202-207.

Salila Vijayalal Mohan, H. K.; An, J.; Zheng, L., Identification of Mobility Changes Induced by Deoxyribo Nucleic Acid in the Inversion Regions of Ultralong Single Walled Carbon Nanotube Field-Effect Transistor Using Support Vector Machine and Multi-Layer Perceptron. *International Journal of Nanotechnology* **2014**, 11(1), 207-221.

An, J.; Zhan, Z.; **Salila Vijayalal Mohan, H. K.;** Zheng, L., Growth Condition Mediated Catalyst Effects on the Density and Length of Horizontally Aligned Single-Walled Carbon Nanotube Arrays. *Chemical Engineering Journal* **2014**, 237 (0), 16-22.

Salila Vijayalal Mohan, H. K.; An, J.; Liao, K.; Wong C.H, Zheng, L., Detection and Classification of Host-Guest Interactions Using β -Cyclodextrin-Decorated Carbon Nanotube-Based Chemiresistors, *Current Applied Physics* **2014**, 14 (12), 1649-1658.

Salila Vijayalal Mohan, H. K.; An, J.; Zheng, L., Sequence Dependent Electrical Response of Ss-DNA-Decorated Carbon Nanotube Field-Effect Transistors to Dopamine, *Beilstein Journal of Nanotechnology* **2014**, 5, 2081-2091.

Salila Vijayalal Mohan, H. K.; An, J.; Zhang, Y., Wong C.H, Zheng, L., Effect of Channel Length on the Electrical Response Of Carbon Nanotube Field-Effect Transistors To Deoxyribonucleic Acid Hybridization, *Beilstein Journal of Nanotechnology* **2014**, 5, 2113-2121

Salila Vijayalal Mohan, H. K.; Varghese Hansen, R.; Zheng, L., Polyaniline/Carbon Nanotube Composite Based Chemiresistors for Dopamine Sensing, 6th *International Symposium on Microchemistry and Microsystems*, Singapore, 30 July-1 August, 2014.

Salila Vijayalal Mohan, H. K.; An, J.; Zheng, L., Mobility Analysis in the Strong Inversion and Near-threshold Region of Millimetre Long Individual Single Walled Carbon Nanotube Field-effect Transistor, 7th *International Conference on Materials for Advanced Technologies (ICMAT)*, Singapore, 30 June-5 July 2013.

Salila Vijayalal Mohan, H. K.; An, J.; Zheng, L, DNA Oligomer Sequence Specific Electrical Response of Ultralong Parallel CNTFET to Dopamine. *Proceedings of the 4th International Conference on Integrity Reliability and Failure (IRF)*, Funchal, Portugal, 23-27 June 2013; pp301-302.

Salila Vijayalal Mohan, H. K.; An, J.; Zheng, L., A Neural Network Approach to Classify Inversion Regions of High Mobility Ultralong Channel Single Walled Carbon Nanotube Field-Effect Transistors for Sensing Applications, *Proceedings of the IEEE 5th International Nanoelectronics Conference (INEC)*, Singapore, 2-4 January 2013; pp 85-88.

References

1. Avouris, P.; Chen, Z.; Perebeinos, V., Carbon-Based Electronics. *Nature Nanotechnology* **2007**, 2 (10), 605-615.
2. Jariwala, D.; Sangwan, V.; Lauhon, L.; Marks, T.; Hersam, M., Carbon Nanomaterials for Electronics, Optoelectronics, Photovoltaics, and Sensing. *Chemical Society Reviews* **2013**, 42 (7), 2824-2860.
3. Shim, M.; Shi Kam, N. W.; Chen, R. J.; Li, Y.; Dai, H., Functionalization of Carbon Nanotubes for Biocompatibility and Biomolecular Recognition. *Nano Letters* **2002**, 2 (4), 285-288.
4. Hu, P.; Zhang, J.; Li, L.; Wang, Z.; O'Neill, W.; Estrela, P., Carbon Nanostructure-Based Field-Effect Transistors for Label-Free Chemical/Biological Sensors. *Sensors* **2010**, 10 (5), 5133-5159.
5. Compton, R. G.; Wildgoose, G. G.; Wong, E. L. S., Carbon Nanotube-Based Sensors and Biosensors. In *Biosensing Using Nanomaterials*, (ed A. Merkoçi), John Wiley & Sons, Inc., Hoboken, NJ, USA, **2009**; pp 1-37.
6. Michele, P.; Giorgio, S.; Wojtek, W.; Yongxiang, L., Nanomaterials for Chemical Sensing Technologies. *Journal of Sensors* **2009**, 2009, 2pp.
7. Heller, I.; Janssens, A. M.; Mannik, J.; Minot, E. D.; Lemay, S. G.; Dekker, C., Identifying the Mechanism of Biosensing with Carbon Nanotube Transistors. *Nano Letters* **2007**, 8 (2), 591-595.

8. Tey, J. N.; Wijaya, I. P. M.; Wei, J.; Rodriguez, I.; Mhaisalkar, S. G., Nanotubes-/Nanowires-Based, Microfluidic-Integrated Transistors for Detecting Biomolecules. *Microfluidics and Nanofluidics* **2010**, *9* (6), 1185-1214.
9. Martínez, M. T.; Tseng, Y.-C.; Ormategui, N.; Loinaz, I.; Eritja, R.; Bokor, J., Label-Free DNA Biosensors Based on Functionalized Carbon Nanotube Field Effect Transistors. *Nano Letters* **2009**, *9* (2), 530-536.
10. Staii, C.; Johnson, A. T.; Chen, M.; Gelperin, A., DNA-Decorated Carbon Nanotubes for Chemical Sensing. *Nano Letters* **2005**, *5* (9), 1774-1778.
11. Dürkop, T.; Getty, S. A.; Cobas, E.; Fuhrer, M. S., Extraordinary Mobility in Semiconducting Carbon Nanotubes. *Nano Letters* **2004**, *4* (1), 35-39.
12. Zhao, J.; Zhang, W.; Sherrell, P.; Razal, J.; Huang, X.-F.; Minett, A.; Chen, J., Carbon Nanotube Nanoweb-Bioelectrode for Highly Selective Dopamine Sensing. *ACS Applied Materials & Interfaces* **2012**, *4* (1), 44-48.
13. Khamis, S. M.; Jones, R. A.; Johnson, A. T. C.; Preti, G.; Kwak, J.; Gelperin, A., DNA-Decorated Carbon Nanotube-Based FETs as Ultrasensitive Chemical Sensors: Discrimination of Homologues, Structural Isomers, and Optical Isomers. *AIP Advances* **2012**, *2* (2), 022110-1-02210-11.
14. Shen, X.; Cui, Y.; Pang, Y.; Qian, H., Graphene Oxide Nanoribbon and Polyhedral Oligomeric Silsesquioxane Assembled Composite Frameworks for Pre-Concentrating and Electrochemical Sensing of 1-Hydroxypyrene. *Electrochimica Acta* **2012**, *59* (0), 91-99.

15. Iliescu, T.; Baia, M.; Miclăuș, V., A Raman Spectroscopic Study of the Diclofenac Sodium-Beta-Cyclodextrin Interaction. *European Journal of Pharmaceutical Sciences* **2004**, 22 (5), 487-495.
16. Maheshwari, R. K.; Singh, A. K.; Gaddipati, J.; Srimal, R. C., Multiple Biological Activities of Curcumin: A Short Review. *Life Sciences* **2006**, 78 (18), 2081-2087.
17. Ogoshi, T.; Harada, A., Chemical Sensors Based on Cyclodextrin Derivatives. *Sensors* **2008**, 8 (8), 4961-4982.
18. Yan-Li, Z.; Liangbing, H.; Stoddart, J. F.; George, G., Pyrenecyclodextrin-Decorated Single-Walled Carbon Nanotube Field-Effect Transistors as Chemical Sensors. *Advanced Materials* **2008**, 20 (10), 1910-1915.
19. Zhao, Y.-L.; Stoddart, J. F., Noncovalent Functionalization of Single-Walled Carbon Nanotubes. *Accounts of Chemical Research* **2009**, 42 (8), 1161-1171.
20. Rosales, L.; Gonzalez, J., Transport Properties of Two Finite Armchair Graphene Nanoribbons. *Nanoscale Research Letters* **2013**, 8 (1), 1-6.
21. Reilly, R. M., Carbon Nanotubes: Potential Benefits and Risks of Nanotechnology in Nuclear Medicine. *Journal of Nuclear Medicine* **2007**, 48 (7), 1039-1042.
22. Lyshevski, M. A. Carbon Nanotubes Analysis, Classification and Characterization. *Proceedings of the 4th IEEE Conference on Nanotechnology*, NY, USA, **2004**; pp 527-529.

23. Shi, Z.; Lian, Y.; Zhou, X.; Gu, Z.; Zhang, Y.; Iijima, S.; Zhou, L.; Yue, K. T.; Zhang, S., Mass-Production of Single-Wall Carbon Nanotubes by Arc Discharge Method. *Carbon* **1999**, *37* (9), 1449-1453.
24. Vasily, N. L.; Sergey, M. P.; Elena, D. O.; Sergey, I. K.; Alexey, F. B., Single-Shot and Single-Spot Measurement of Laser Ablation Threshold for Carbon Nanotubes. *Journal of Physics D: Applied Physics* **2013**, *46* (5), 052002 (5pp).
25. Brukh, R.; Mitra, S., Mechanism of Carbon Nanotube Growth by CVD. *Chemical Physics Letters* **2006**, *424* (1–3), 126-132.
26. Das Sarma, S.; Adam, S.; Hwang, E. H.; Rossi, E., Electronic Transport in Two-Dimensional Graphene. *Reviews of Modern Physics* **2011**, *83* (2), 407-470.
27. McEuen, P. L.; Fuhrer, M. S.; Park, H., Single-Walled Carbon Nanotube Electronics. *IEEE Transactions on Nanotechnology* **2002**, *1* (1), 78-85.
28. Liu, K.; Burghard, M.; Roth, S.; Bernier, P., Conductance Spikes in Single-Walled Carbon Nanotube Field-Effect Transistor. *Applied Physics Letters* **1999**, *75* (16), 2494-2496.
29. Feigel, I. M.; Vedala, H.; Star, A., Biosensors Based on One-Dimensional Nanostructures. *Journal of Materials Chemistry* **2011**, *21* (25), 8940-8954.
30. Palaniappan, A.; Goh, W. H.; Tey, J. N.; Wijaya, I. P. M.; Mochhala, S. M.; Liedberg, B.; Mhaisalkar, S. G., Aligned Carbon Nanotubes on Quartz Substrate for Liquid Gated Biosensing. *Biosensors and Bioelectronics* **2010**, *25* (8), 1989-1993.

31. Kaul, A. B.; Wong, E. W.; Epp, L.; Hunt, B. D., Electromechanical Carbon Nanotube Switches for High-Frequency Applications. *Nano Letters* **2006**, 6 (5), 942-947.
32. Acquaviva, D.; Arun, A.; Esconjauregui, S.; Bouvet, D.; Robertson, J.; Smajda, R.; Magrez, A.; Forro, L.; Ionescu, A. M., Capacitive Nanoelectromechanical Switch Based on Suspended Carbon Nanotube Array. *Applied Physics Letters* **2010**, 97 (23), 233508-1-233508-3.
33. Stampfer, C.; Helbling, T.; Obergfell, D.; Schöberle, B.; Tripp, M. K.; Jungen, A.; Roth, S.; Bright, V. M.; Hierold, C., Fabrication of Single-Walled Carbon-Nanotube-Based Pressure Sensors. *Nano Letters* **2006**, 6 (2), 233-237.
34. Burg, B. R.; Helbling, T.; Hierold, C.; Poulikakos, D., Piezoresistive Pressure Sensors with Parallel Integration of Individual Single-Walled Carbon Nanotubes. *Journal of Applied Physics* **2011**, 109 (6), 064310-1-064310-6.
35. Moore, E. W.; Lee, S.; Hickman, S. A.; Harrell, L. E.; Marohn, J. A., Evading Surface and Detector Frequency Noise in Harmonic Oscillator Measurements of Force Gradients. *Applied Physics Letters* **2010**, 97 (4), 044105-1-044105-3.
36. Sandberg, R.; Boisen, A.; Svendsen, W., Characterization System for Resonant Micro- and Nanocantilevers. *Review of Scientific Instruments* **2005**, 76 (12), 125101-1-125101-6.
37. Lu, M.; Jang, M.-W.; Campbell, S. A.; Cui, T., Aligned Dense Single-Walled Carbon Nanotube Beams and Cantilevers for Nanoelectromechanical Systems

Applications. *Journal of Vacuum Science & Technology B: Microelectronics and Nanometer Structures* **2010**, 28 (3), 522-526.

38. Gouttenoire, V.; Barois, T.; Perisanu, S.; Leclercq, J.-L.; Purcell, S. T.; Vincent, P.; Ayari, A., Digital and FM Demodulation of a Doubly Clamped Single-Walled Carbon-Nanotube Oscillator: Towards a Nanotube Cell Phone. *Small* **2010**, 6 (9), 1060-1065.

39. Heller, D. A.; Baik, S.; Eurell, T. E.; Strano, M. S., Single-Walled Carbon Nanotube Spectroscopy in Live Cells: Towards Long-Term Labels and Optical Sensors. *Advanced Materials* **2005**, 17 (23), 2793-2799.

40. Penza, M.; Cassano, G.; Aversa, P.; Cusano, A.; Cutolo, A.; Giordano, M.; Nicolais, L., Carbon Nanotube Acoustic and Optical Sensors for Volatile Organic Compound Detection. *Nanotechnology* **2005**, 16 (11), 2536-2547.

41. Sadeghi, S., Plasmonic Meta-Resonance Nanosensors: Ultra-Sensitive Tunable Optical Sensors Based on Nanoparticle Molecules. *IEEE Transactions on Nanotechnology* **2011**, 10 (3), 566-571.

42. Zhou, L.; Wang, J.-P.; Gai, L.; Li, D.-J.; Li, Y.-B., An Amperometric Sensor Based on Ionic Liquid and Carbon Nanotube Modified Composite Electrode for the Determination of Nitrite in Milk. *Sensors and Actuators B: Chemical* **2013**, 181 (0), 65-70.

43. Afkhami, A.; Bagheri, H.; Shirzadmehr, A.; Khoshsafar, H.; Hashemi, P., A Potentiometric Sensor for Cd²⁺ Based on Carbon Nanotube Paste Electrode

Constructed from Room Temperature Ionic Liquid, Ionophore and Silica Nanoparticles. *Electroanalysis* **2012**, 24 (11), 2176-2185.

44. Randviir, E. P.; Metters, J. P.; Stainton, J.; Banks, C. E., Electrochemical Impedance Spectroscopy versus Cyclic Voltammetry for the Electroanalytical Sensing of Capsaicin Utilising Screen Printed Carbon Nanotube Electrodes. *Analyst* **2013**, 138 (10), 2970-2981.

45. Chunglok, W.; Wuragil, D. K.; Oaew, S.; Somasundrum, M.; Surareungchai, W., Immunoassay Based on Carbon Nanotubes-Enhanced ELISA for Salmonella Enterica Serovar Typhimurium. *Biosensors and Bioelectronics* **2011**, 26 (8), 3584-3589.

46. Arora, N., MOSFET DC Model. In *MOSFET Models for VLSI Circuit Simulation*, Springer Vienna, **1993**; pp 230-324.

47. Yue-Hua, D.; Jun-Ning, C.; Dao-Ming, K.; Jia, E. S. Effective Mobility in Nano-Scaled n-MOSFETs, *Proceedings of the 5th International Power Electronics and Motion Control Conference*, Shanghai, China, **2006**; pp 1-5.

48. Jimenez-Cadena, G.; Riu, J.; Rius, F. X., Gas Sensors Based on Nanostructured Materials. *Analyst* **2007**, 132 (11), 1083-1099.

49. Dayeh, S. A.; Yu, E. T.; Wang, D., Transport Coefficients of InAs Nanowires as a Function of Diameter. *Small* **2009**, 5 (1), 77-81.

50. Jiang, X.; Xiong, Q.; Nam, S.; Qian, F.; Li, Y.; Lieber, C. M., InAs/InP Radial Nanowire Heterostructures as High Electron Mobility Devices. *Nano Letters* **2007**, 7 (10), 3214-3218.

51. Scheffler, M.; Nadj-Perge, S.; Kouwenhoven, L. P.; Borgstrom, M. T.; Bakkers, E. P. A. M., Diameter-Dependent Conductance of InAs Nanowires. *Journal of Applied Physics* **2009**, *106* (12), 124303-1-124303-4.
52. Ford, A. C.; Ho, J. C.; Chueh, Y.-L.; Tseng, Y.-C.; Fan, Z.; Guo, J.; Bokor, J.; Javey, A., Diameter-Dependent Electron Mobility of InAs Nanowires. *Nano Letters* **2008**, *9* (1), 360-365.
53. Li, H.; Zhang, Q.; Li, J., Carbon-Nanotube-Based Single-Electron/Hole Transistors. *Applied Physics Letters* **2006**, *88* (1), 013508-1-013508-3.
54. Ong, H. G.; Cheah, J. W.; Zou, X.; Li, B.; Cao, X. H.; Tantang, H.; Li, L. J.; Zhang, H.; Han, G. C.; Wang, J., Origin of Hysteresis in the Transfer Characteristic of Carbon Nanotube Field Effect Transistor. *Journal of Physics D: Applied Physics* **2011**, *44* (28), 285301 (5pp).
55. Khanal, D. R.; Levander, A. X.; Yu, K. M.; Liliental-Weber, Z.; Walukiewicz, W.; Grandal, J.; Sanchez-Garcia, M. A.; Calleja, E.; Wu, J., Decoupling Single Nanowire Mobilities Limited by Surface Scattering and Bulk Impurity Scattering. *Journal of Applied Physics* **2011**, *110* (3), 033705-1-033705-7.
56. Reese, C.; Bao, Z., Overestimation of the Field-Effect Mobility via Transconductance Measurements and the Origin of the Output/Transfer Characteristic Discrepancy in Organic Field-Effect Transistors. *Journal of Applied Physics* **2009**, *105* (2), 024506-1-024506-8.

57. Fuhrer, M. S.; Kim, B. M.; Dürkop, T.; Brintlinger, T., High-Mobility Nanotube Transistor Memory. *Nano Letters* **2002**, 2 (7), 755-759.
58. Krompiewski, S., Modeling a Schottky-Barrier Carbon Nanotube Field-Effect Transistor with Ferromagnetic Contacts. *Nanotechnology* **2007**, 18 (48), 485708 (4pp).
59. Suehiro, J.; Imakiire, H.; Hidaka, S.-i.; Ding, W.; Zhou, G.; Imasaka, K.; Hara, M., Schottky-Type Response of Carbon Nanotube NO₂ Gas Sensor Fabricated onto Aluminum Electrodes by Dielectrophoresis. *Sensors and Actuators B: Chemical* **2006**, 114 (2), 943-949.
60. Zhu, W.; Kaxiras, E., Schottky Barrier Formation at a Carbon Nanotube-Metal Junction. *Applied Physics Letters* **2006**, 89 (24), 243107-1-243107-3.
61. Javey, A.; Guo, J.; Wang, Q.; Lundstrom, M.; Dai, H., Ballistic Carbon Nanotube Field-Effect Transistors. *Nature* **2003**, 424 (6949), 654-657.
62. Zheng, L. X.; O'Connell, M. J.; Doorn, S. K.; Liao, X. Z.; Zhao, Y. H.; Akhadow, E. A.; Hoffbauer, M. A.; Roop, B. J.; Jia, Q. X.; Dye, R. C.; Peterson, D. E.; Huang, S. M.; Liu, J.; Zhu, Y. T., Ultralong Single-Wall Carbon Nanotubes. *Nature Materials* **2004**, 3 (10), 673-676.
63. Boussaad, S.; Tao, N. J.; Zhang, R.; Hopson, T.; Nagahara, L. A., In Situ Detection of Cytochrome C Adsorption with Single Walled Carbon Nanotube Device. *Chemical Communications* **2003**, (13), 1502-1503.
64. Bradley, K.; Davis, A.; Gabriel, J.-C. P.; Grüner, G., Integration of Cell Membranes and Nanotube Transistors. *Nano Letters* **2005**, 5 (5), 841-845.

65. Bradley, K.; Briman, M.; Star, A.; Grüner, G., Charge Transfer from Adsorbed Proteins. *Nano Letters* **2004**, *4* (2), 253-256.
66. Hu, P.; Fasoli, A.; Park, J.; Choi, Y.; Estrela, P.; Maeng, S. L.; Milne, W. I.; Ferrari, A. C., Self-Assembled Nanotube Field-Effect Transistors for Label-Free Protein Biosensors. *Journal of Applied Physics* **2008**, *104* (7), 074310-1-074310-5.
67. Chen, R. J.; Bangsaruntip, S.; Drouvalakis, K. A.; Wong Shi Kam, N.; Shim, M.; Li, Y.; Kim, W.; Utz, P. J.; Dai, H., Noncovalent Functionalization of Carbon Nanotubes for Highly Specific Electronic Biosensors. *Proceedings of the National Academy of Sciences* **2003**, *100* (9), 4984-4989.
68. Heller, I.; Kong, J.; Williams, K. A.; Dekker, C.; Lemay, S. G., Electrochemistry at Single-Walled Carbon Nanotubes: The Role of Band Structure and Quantum Capacitance. *Journal of the American Chemical Society* **2006**, *128* (22), 7353-7359.
69. Tang, X.; Bansaruntip, S.; Nakayama, N.; Yenilmez, E.; Chang, Y.-l.; Wang, Q., Carbon Nanotube DNA Sensor and Sensing Mechanism. *Nano Letters* **2006**, *6* (8), 1632-1636.
70. Byon, H. R.; Choi, H. C., Network Single-Walled Carbon Nanotube-Field Effect Transistors (SWNT-FETs) with Increased Schottky Contact Area for Highly Sensitive Biosensor Applications. *Journal of the American Chemical Society* **2006**, *128* (7), 2188-2189.
71. Gui, E. L.; Li, L.-J.; Zhang, K.; Xu, Y.; Dong, X.; Ho, X.; Lee, P. S.; Kasim, J.; Shen, Z. X.; Rogers, J. A.; Mhaisalkar, DNA Sensing by Field-Effect Transistors

Based on Networks of Carbon Nanotubes. *Journal of the American Chemical Society* **2007**, *129* (46), 14427-14432.

72. Chen, R. J.; Choi, H. C.; Bangsaruntip, S.; Yenilmez, E.; Tang, X.; Wang, Q.; Chang, Y.-L.; Dai, H., An Investigation of the Mechanisms of Electronic Sensing of Protein Adsorption on Carbon Nanotube Devices. *Journal of the American Chemical Society* **2004**, *126* (5), 1563-1568.

73. Star, A.; Gabriel, J.-C. P.; Bradley, K.; Grüner, G., Electronic Detection of Specific Protein Binding Using Nanotube FET Devices. *Nano Letters* **2003**, *3* (4), 459-463.

74. Fu, D.; Okimoto, H.; Lee, C.; Takenobu, T.; Iwasa, Y.; Kataura, H.; Li, L.-J., Ultrasensitive Detection of DNA Molecules with High On/Off Single-Walled Carbon Nanotube Network. *Advanced Materials* **2010**, *22* (43), 4867-4871.

75. Maehashi, K.; Katsura, T.; Kerman, K.; Takamura, Y.; Matsumoto, K.; Tamiya, E., Label-Free Protein Biosensor Based on Aptamer-Modified Carbon Nanotube Field-Effect Transistors. *Analytical Chemistry* **2006**, *79* (2), 782-787.

76. Mahendra Wijaya, I. P.; Nie, T. J.; Gandhi, S.; Boro, R.; Palaniappan, A.; Hau, G. W.; Rodriguez, I.; Suri, C. R.; Mhaisalkar, S. G., Femtomolar Detection of 2,4-Dichlorophenoxyacetic Acid Herbicides via Competitive Immunoassays Using Microfluidic Based Carbon Nanotube Liquid Gated Transistor. *Lab on a Chip* **2010**, *10* (5), 634-638.

77. Pacios, M.; Martin-Fernandez, I.; Borrise, X.; del Valle, M.; Bartroli, J.; Lora-Tamayo, E.; Godignon, P.; Perez-Murano, F.; Esplandiu, M. J., Real Time Protein Recognition in a Liquid-Gated Carbon Nanotube Field-Effect Transistor Modified with Aptamers. *Nanoscale* **2012**, *4* (19), 5917-5923.
78. Lange, U.; Mirsky, V. M., Chemiresistors Based on Conducting Polymers: A Review on Measurement Techniques. *Analytica Chimica Acta* **2011**, *687* (2), 105-113.
79. An, J.; Zhan, Z.; Hari Krishna, S. V.; Zheng, L., Growth Condition Mediated Catalyst Effects on the Density and Length of Horizontally Aligned Single-Walled Carbon Nanotube Arrays. *Chemical Engineering Journal* **2014**, *237* (0), 16-22.
80. Cho, S.; Kwon, O. S.; You, S. A.; Jang, J., Shape-Controlled Polyaniline Chemiresistors for High-Performance DMMP Sensors: Effect Of Morphologies and Charge-Transport Properties. *Journal of Materials Chemistry A* **2013**, *1* (18), 5679-5688.
81. Frazier, K. M.; Swager, T. M., Robust Cyclohexanone Selective Chemiresistors Based on Single-Walled Carbon Nanotubes. *Analytical Chemistry* **2013**, *85* (15), 7154-7158.
82. Wu, H.-C.; Chang, X.; Liu, L.; Zhao, F.; Zhao, Y., Chemistry of Carbon Nanotubes in Biomedical Applications. *Journal of Materials Chemistry* **2010**, *20* (6), 1036-1052.

83. Georgakilas, V.; Kordatos, K.; Prato, M.; Guldi, D. M.; Holzinger, M.; Hirsch, A., Organic Functionalization of Carbon Nanotubes. *Journal of the American Chemical Society* **2002**, *124* (5), 760-761.
84. Chen, Y.; Haddon, R. C.; Fang, S.; Rao, A. M.; Eklund, P. C.; Lee, W. H.; Dickey, E. C.; Grulke, E. A.; Pendergrass, J. C.; Chavan, A.; Haley, B. E.; Smalley, R. E., Chemical Attachment of Organic Functional Groups to Single-walled Carbon Nanotube Material. *Journal of Materials Research* **1998**, *13* (9), 2423-2431.
85. Holzinger, M.; Vostrowsky, O.; Hirsch, A.; Hennrich, F.; Kappes, M.; Weiss, R.; Jellen, F., Sidewall Functionalization of Carbon Nanotubes. *Angewandte Chemie International Edition* **2001**, *40* (21), 4002-4005.
86. Hamon, M. A.; Hui, H.; Bhowmik, P.; Itkis, H. M. E.; Haddon, R. C., Ester-Functionalized Soluble Single-Walled Carbon Nanotubes. *Applied Physics A* **2002**, *74* (3), 333-338.
87. Hiura, H.; Ebbesen, T. W.; Tanigaki, K., Opening and Purification of Carbon Nanotubes in High Yields. *Advanced Materials* **1995**, *7* (3), 275-276.
88. Mickelson, E. T.; Huffman, C. B.; Rinzler, A. G.; Smalley, R. E.; Hauge, R. H.; Margrave, J. L., Fluorination of Single-Wall Carbon Nanotubes. *Chemical Physics Letters* **1998**, *296* (1-2), 188-194.
89. Britz, D. A.; Khlobystov, A. N., Noncovalent Interactions of Molecules with Single Walled Carbon Nanotubes. *Chemical Society Reviews* **2006**, *35* (7), 637-659.

90. Star, A.; Stoddart, J. F.; Steuerman, D.; Diehl, M.; Boukai, A.; Wong, E. W.; Yang, X.; Chung, S.-W.; Choi, H.; Heath, J. R., Preparation and Properties of Polymer-Wrapped Single-Walled Carbon Nanotubes. *Angewandte Chemie International Edition* **2001**, *40* (9), 1721-1725.
91. Park, H.-J.; Kim, J.; Seo, Y.; Shim, J.; Sung, M.-Y.; Kwak, S., Wear Behaviour of In Situ Polymerized Carbon Nanotube/Ultra High Molecular Weight Polyethylene Composites. *Macromolecular Research* **2013**, *21* (9), 965-970.
92. Jafariesfad, N.; Ramazani, S. A. A.; Azinfar, B., Property Investigation of Polypropylene/Multiwall Carbon Nanotube Nanocomposites Prepared via In Situ Polymerization. *Polymer International* **2014**, *63* (4), 689–694.
93. Backes, C.; Hirsch, A., Noncovalent Functionalization of Carbon Nanotubes. In *Chemistry of Nanocarbons*, John Wiley & Sons, Ltd: (eds Akasaka, T; Wudl, F.; Nagase, S), Chichester, UK, **2010**; pp 1-48.
94. Tu, X.; Manohar, S.; Jagota, A.; Zheng, M., DNA Sequence Motifs for Structure-Specific Recognition and Separation of Carbon Nanotubes. *Nature* **2009**, *460* (7252), 250-253.
95. Chen, R. J.; Zhang, Y.; Wang, D.; Dai, H., Noncovalent Sidewall Functionalization of Single-Walled Carbon Nanotubes for Protein Immobilization. *Journal of the American Chemical Society* **2001**, *123* (16), 3838-3839.

96. Dugas, V.; Elaissari, A.; Chevalier, Y., Surface Sensitization Techniques and Recognition Receptors Immobilization on Biosensors and Microarrays. In *Recognition Receptors in Biosensors*, Zourob, M., Ed. Springer New York: **2010**; pp 47-134.
97. Carot, M. L.; Torresi, R. M.; Garcia, C. D.; Esplandiu, M. J.; Giacomelli, C. E., Electrostatic and Hydrophobic Interactions Involved in CNT Biofunctionalization with Short ss-DNA. *The Journal of Physical Chemistry C* **2010**, *114* (10), 4459-4465.
98. Athira, C. R.; Shilpa, S.; Parvathy, C. M.; Nithya, S.; Vinothaa, V.; Subashini, S. P.; Varun Gopal, K.; Parimalam, B.; Namboori, P. K. K., Computational Characterization of CNT-Papain Interactions for Developing a Biosensor. In *Computer Networks and Information Technologies*, Das, V.; Stephen, J.; Chaba, Y., Eds. Springer Berlin Heidelberg, **2011**, *142*; pp 553-556.
99. Szente, L.; Szemán, J., Cyclodextrins in Analytical Chemistry: Host–Guest Type Molecular Recognition. *Analytical Chemistry* **2013**, *85* (17), 8024-8030.
100. Gao, Z.; Agarwal, A.; Trigg, A. D.; Singh, N.; Fang, C.; Tung, C.-H.; Fan, Y.; Buddharaju, K. D.; Kong, J., Silicon Nanowire Arrays for Label-Free Detection of DNA. *Analytical Chemistry* **2007**, *79* (9), 3291-3297.
101. Patolsky, F.; Zheng, G.; Hayden, O.; Lakadamyali, M.; Zhuang, X.; Lieber, C. M., Electrical Detection of Single Viruses. *Proceedings of the National Academy of Sciences* **2004**, *101* (39), 14017-14022.

102. Goh, R. G. S.; Bell, J. M.; Motta, N.; Ho, P. K. H.; Wacławik, E. R., P-Channel, N-Channel and Ambipolar Field-Effect Transistors Based on Functionalized Carbon Nanotube Networks. *Superlattices and Microstructures* **2009**, *46* (1–2), 347-356.
103. Nair, P. R.; Alam, M. A., Design Considerations of Silicon Nanowire Biosensors. *IEEE Transactions on Electron Devices* **2007**, *54* (12), 3400-3408.
104. Sheehan, P. E.; Whitman, L. J., Detection Limits for Nanoscale Biosensors. *Nano Letters* **2005**, *5* (4), 803-807
105. Lee, C. W.; Dong, X.; Goh, S. H.; Wang, J.; Wei, J.; Li, L.-J., Illumination-Enhanced Hysteresis of Transistors Based on Carbon Nanotube Networks. *The Journal of Physical Chemistry C* **2009**, *113* (12), 4745-4747.
106. Hu, L.; Hecht, D. S.; Grüner, G., Percolation in Transparent and Conducting Carbon Nanotube Networks. *Nano Letters* **2004**, *4* (12), 2513-2517.
107. Bisri, S. Z.; Gao, J.; Derenskyi, V.; Gomulya, W.; Iezhokin, I.; Gordiichuk, P.; Herrmann, A.; Loi, M. A., High Performance Ambipolar Field-Effect Transistor of Random Network Carbon Nanotubes. *Advanced Materials* **2012**, *24* (46), 6147-6152.
108. Sangwan, V. K.; Behnam, A.; Ballarotto, V. W.; Fuhrer, M. S.; Ural, A.; Williams, E. D., Optimizing Transistor Performance of Percolating Carbon Nanotube Networks. *Applied Physics Letters* **2010**, *97* (4), 043111-043113.
109. Gao, X. P. A.; Zheng, G.; Lieber, C. M., Subthreshold Regime has the Optimal Sensitivity for Nanowire FET Biosensors. *Nano Letters* **2009**, *10* (2), 547-552.

110. Snow, E. S.; Novak, J. P.; Campbell, P. M.; Park, D., Random Networks of Carbon Nanotubes as an Electronic Material. *Applied Physics Letters* **2003**, 82 (13), 2145-2147.
111. Engel, M.; Small, J. P.; Steiner, M.; Freitag, M.; Green, A. A.; Hersam, M. C.; Avouris, P., Thin Film Nanotube Transistors Based on Self-Assembled, Aligned, Semiconducting Carbon Nanotube Arrays. *ACS Nano* **2008**, 2 (12), 2445-2452.
112. LeMieux, M. C.; Roberts, M.; Barman, S.; Jin, Y. W.; Kim, J. M.; Bao, Z., Self-Sorted, Aligned Nanotube Networks for Thin-Film Transistors. *Science* **2008**, 321 (5885), 101-104.
113. Kong, J.; Dai, H., Full and Modulated Chemical Gating of Individual Carbon Nanotubes by Organic Amine Compounds. *The Journal of Physical Chemistry B* **2001**, 105 (15), 2890-2893.
114. Heller, I.; Männik, J.; Lemay, S. G.; Dekker, C., Optimizing the Signal-to-Noise Ratio for Biosensing with Carbon Nanotube Transistors. *Nano Letters* **2008**, 9 (1), 377-382.
115. Das, B. K.; Tlili, C.; Badhulika, S.; Cella, L. N.; Chen, W.; Mulchandani, A., Single-Walled Carbon Nanotubes Chemiresistor Aptasensors for Small Molecules: Picomolar Level Detection of Adenosine Triphosphate. *Chemical Communications* **2011**, 47 (13), 3793-3795.

116. Wang, F.; Gu, H.; Swager, T. M., Carbon Nanotube/Polythiophene Chemiresistive Sensors for Chemical Warfare Agents. *Journal of the American Chemical Society* **2008**, *130* (16), 5392-5393.
117. Ma, X.; Sim, S. J., Ultrasensitive Detection of the Reduced Form of Nicotinamide Adenine Dinucleotide Based on Carbon Nanotube Field Effect Transistor. *Analyst* **2012**, *137* (14), 3328-3334.
118. Besteman, K.; Lee, J.-O.; Wiertz, F. G. M.; Heering, H. A.; Dekker, C., Enzyme-Coated Carbon Nanotubes as Single-Molecule Biosensors. *Nano Letters* **2003**, *3* (6), 727-730.
119. Liu, N.; Cai, X.; Lei, Y.; Zhang, Q.; Chan-Park, M. B.; Li, C.; Chen, W.; Mulchandani, A., Single-Walled Carbon Nanotube Based Real-Time Organophosphate Detector. *Electroanalysis* **2007**, *19* (5), 616-619.
120. Huang, Y.; Chen, P., Nanoelectronic Biosensing of Dynamic Cellular Activities Based on Nanostructured Materials. *Advanced Materials* **2010**, *22* (25), 2818-2823.
121. Huang, Y.; Sudibya, H. G.; Fu, D.; Xue, R.; Dong, X.; Li, L.-J.; Chen, P., Label-Free Detection of ATP Release from Living Astrocytes with High Temporal Resolution Using Carbon Nanotube Network. *Biosensors and Bioelectronics* **2009**, *24* (8), 2716-2720.
122. Stefansson, S.; Kwon, H. H.; Ahn, S. N., Targeting Antibodies to Carbon Nanotube Field Effect Transistors by Pyrene Hydrazide Modification of Heavy Chain Carbohydrates. *Journal of Nanotechnology* **2012**, *2012*, 8pp.

123. Martínez, M.; Tseng, Y.-C.; Salvador, J.; Marco, M.; Ormategui, N.; Loinaz, I.; Bokor, J., Electronic Anabolic Steroid Recognition with Carbon Nanotube Field-Effect Transistors. *ACS Nano* **2010**, *4* (3), 1473-1480.
124. Chatterjee, S.; Castro, M.; Feller, J. F., An E-Nose Made of Carbon Nanotube Based Quantum Resistive Sensors for the Detection of Eighteen Polar/Nonpolar VOC Biomarkers of Lung Cancer. *Journal of Materials Chemistry B* **2013**, *1* (36), 4563-4575.
125. Kong, L.; Wang, J.; Luo, T.; Meng, F.; Chen, X.; Li, M.; Liu, J., Novel Pyrenehexafluoroisopropanol Derivative-Decorated Single-Walled Carbon Nanotubes for Detection of Nerve Agents by Strong Hydrogen-Bonding Interaction. *Analyst* **2010**, *135* (2), 368-374.
126. Kim, T. H.; Lee, B. Y.; Jaworski, J.; Yokoyama, K.; Chung, W.-J.; Wang, E.; Hong, S.; Majumdar, A.; Lee, S.-W., Selective and Sensitive TNT Sensors Using Biomimetic Polydiacetylene-Coated CNT-FETs. *ACS Nano* **2011**, *5* (4), 2824-2830.
127. Huang, Y.; Palkar, P. V.; Li, L.-J.; Zhang, H.; Chen, P., Integrating Carbon Nanotubes and Lipid Bilayer for Biosensing. *Biosensors and Bioelectronics* **2010**, *25* (7), 1834-1837.
128. Timmermans, M.; Estrada, D.; Nasibulin, A.; Wood, J.; Behnam, A.; Sun, D.-m.; Ohno, Y.; Lyding, J.; Hassanien, A.; Pop, E.; Kauppinen, E., Effect of carbon nanotube network morphology on thin film transistor performance. *Nano Research* **2012**, *5* (5), 307-319.

129. Behnam, A.; Sangwan, V. K.; Zhong, X.; Lian, F.; Estrada, D.; Jariwala, D.; Hoag, A. J.; Lauhon, L. J.; Marks, T. J.; Hersam, M. C.; Pop, E., High-Field Transport and Thermal Reliability of Sorted Carbon Nanotube Network Devices. *ACS Nano* **2012**, 7 (1), 482-490.
130. Choi, W. J.; Park, D.-W.; Park, S.; Jeong, D. W.; Yang, C.-S.; Kim, B. S.; Kim, J.-J.; Lee, J.-O., High-Performance Carbon Nanotube Network Transistors Fabricated Using a Hole Punching Technique. *Journal of Materials Chemistry C* **2013**, 1 (26), 4087-4093
131. Zhang, Y.; Zheng, L., Towards Chirality-Pure Carbon Nanotubes. *Nanoscale* **2010**, 2 (10), 1919-1929.
132. Zheng, L.; Satishkumar, B. C.; Gao, P.; Zhang, Q., Kinetics Studies of Ultralong Single-Walled Carbon Nanotubes. *The Journal of Physical Chemistry C* **2009**, 113 (25), 10896-10900.
133. Jorio, A.; Pimenta, M. A.; Filho, A. G. S.; Saito, R.; Dresselhaus, G.; Dresselhaus, M. S., Characterizing Carbon Nanotube Samples with Resonance Raman Scattering. *New Journal of Physics* **2003**, 5 (1), 139.1-139.17.
134. Meyer, J. C.; Paillet, M.; Michel, T.; Moréac, A.; Neumann, A.; Duesberg, G. S.; Roth, S.; Sauvajol, J.-L., Raman Modes of Index-Identified Freestanding Single-Walled Carbon Nanotubes. *Physical Review Letters* **2005**, 95 (21), 217401-1-217401-1-4.

135. Jorio, A.; Souza Filho, A. G.; Dresselhaus, G.; Dresselhaus, M. S.; Swan, A. K.; Ünlü, M. S.; Goldberg, B. B.; Pimenta, M. A.; Hafner, J. H.; Lieber, C. M.; Saito, R., G-band resonant Raman study of 62 isolated single-wall carbon nanotubes. *Physical Review B* **2002**, *65* (15), 15541-1-15541-9.
136. Lafi, L.; Cossement, D.; Chahine, R., Raman Spectroscopy and Nitrogen Vapour Adsorption for the Study of Structural Changes during Purification of Single-Wall Carbon Nanotubes. *Carbon* **2005**, *43* (7), 1347-1357.
137. Chu, H.; Wang, J.; Ding, L.; Yuan, D.; Zhang, Y.; Liu, J.; Li, Y., Decoration of Gold Nanoparticles on Surface-Grown Single-Walled Carbon Nanotubes for Detection of Every Nanotube by Surface-Enhanced Raman Spectroscopy. *Journal of the American Chemical Society* **2009**, *131* (40), 14310-14316
138. Chatterjee, S.; Castro, M.; Feller, J. F., An E-Nose Made of Carbon Nanotube Based Quantum Resistive Sensors for the Detection of Eighteen Polar/Nonpolar VOC Biomarkers of Lung Cancer. *Journal of Materials Chemistry B* **2013**, *1* (36), 4563-4575.
139. Zhang, X.; Yang, B.; Liu, W.; Zhang, J., Detection of Partial Discharge in SF₆ Decomposition Gas Based on Modified Carbon Nanotubes Sensors. *Procedia Engineering* **2012**, *29* (0), 4107-4111.
140. Gardner, M. W.; Dorling, S. R., Artificial Neural Networks (The Multilayer Perceptron)—A Review of Applications in the Atmospheric Sciences. *Atmospheric Environment* **1998**, *32* (14–15), 2627-2636.

141. Benrekia, F.; Attari, M.; Bouhedda, M., Gas Sensors Characterization and Multilayer Perceptron (MLP) Hardware Implementation for Gas Identification Using a Field Programmable Gate Array (FPGA). *Sensors* **2013**, *13* (3), 2967-2985.
142. de Sousa, H. C.; Carvalho, A. C. P. L. F.; Riul, A., Jr.; Mattoso, L. H. C. Using MLP Networks to Classify Red Wines and Water Readings of an Electronic Tongue. *Proceedings of the VII Brazilian Symposium on Neural Networks*, Pernambuco, Brazil, **2002**; pp 13-18.
143. Krishna, S. V. H.; An, J. N.; Zheng, L. X., Identification of Mobility Changes Induced by Deoxyribo Nucleic Acid in the Inversion Regions of Ultralong Single Walled Carbon Nanotube Field–Effect Transistor Using Support Vector Machine and Multi–Layer Perceptron. *International Journal of Nanotechnology* **2014**, *11* (1), 207-221.
144. Hari Krishna, S. V.; Jianing, A.; Lianxi, Z. A Neural Network Approach to Classify Inversion Regions of High Mobility Ultralong Channel Single Walled Carbon Nanotube Field-Effect Transistors for Sensing Applications, *Proceedings of the IEEE 5th International Nanoelectronics Conference (INEC)*, Singapore, **2013**; pp 85-88.
145. Dubuffet, A.; Smith, J.; Solter, L.; Perotti, M.; Braig, H.; Dunn, A., Specific Detection and Localization of Microsporidian Parasites in Invertebrate Hosts by Using In Situ Hybridization. *Applied and Environmental Microbiology* **2013**, *79* (1), 385-388.

146. Li, H.; LaBean, T. H.; Leong, K. W., Nucleic Acid-Based Nanoengineering: Novel Structures for Biomedical Applications. *Interface Focus* **2011**, *1* (5), 702-724.
147. Metaferia, B.; Wei, J. S.; Song, Y. K.; Evangelista, J.; Aschenbach, K.; Johansson, P.; Wen, X.; Chen, Q.; Lee, A.; Hempel, H.; Gheeya, J. S.; Getty, S.; Gomez, R.; Khan, J., Development of Peptide Nucleic Acid Probes for Detection of the *HER2* Oncogene. *PloS One* **2013**, *8* (4), e58870-1- e58870-7.
148. Blackburn, G.M; Gait, M.J., J. D. Loakes, J.D., Williams, D. M., Chapter 2 DNA and RNA Structure. In *Nucleic Acids in Chemistry and Biology* (3), The Royal Society of Chemistry, Cambridge, UK, **2006**; pp 13-76.
149. Blackburn, G.M; Gait, M.J., J. D. Loakes, J.D., Williams, D. M., Chapter 7 RNA Structure and Function. In *Nucleic Acids in Chemistry and Biology* (3), The Royal Society of Chemistry, Cambridge, UK: 2006; pp 253-293.
150. Caruthers, M., The Chemical Synthesis of DNA/RNA: Our Gift to Science. *The Journal of Biological Chemistry* **2013**, *288* (2), 1420-1427.
151. Wheelhouse, R. T.; Garbett, N. C.; Buurma, N. J.; Chaires, J. B., Probing the Molecular Recognition of a DNA·RNA Hybrid Duplex. *Angewandte Chemie International Edition* **2010**, *122* (18), 3207-3210.
152. Zheng, K. W.; Xiao, S.; Liu, J. Q.; Zhang, J. Y.; Hao, Y. H.; Tan, Z., Co-Transcriptional Formation of DNA:RNA Hybrid G-Quadruplex and Potential Function as Constitutional Cis Element for Transcription Control. *Nucleic Acids Research* **2013**, *41* (10), 5533-5541.

153. Barone, F.; Cellai, L.; Matzeu, M.; Mazzei, F.; Pedone, F., DNA, RNA and Hybrid RNA–DNA Oligomers of Identical Sequence: Structural and Dynamic Differences. *Biophysical Chemistry* **2000**, *86* (1), 37-47.
154. Rauzan, B.; McMichael, E.; Cave, R.; Sevcik, L.; Ostrosky, K.; Whitman, E.; Stegemann, R.; Sinclair, A.; Serra, M.; Deckert, A., Kinetics and Thermodynamics of DNA, RNA, and Hybrid Duplex Formation. *Biochemistry* **2013**, *52* (5), 765-772.
155. Graugnard, E.; Cox, A.; Lee, J.; Jorcyk, C.; Yurke, B.; Hughes, W., Kinetics of DNA and RNA Hybridization in Serum and Serum-SDS. *IEEE Transactions on Nanotechnology* **2010**, *9* (5), 603-609.
156. Lang, B.; Schwarz, F., Thermodynamic Dependence of DNA/DNA and DNA/RNA Hybridization Reactions on Temperature and Ionic Strength. *Biophysical Chemistry* **2007**, *131* (1-3), 96-104.
157. Kim, J.; Baek, J.; Kim, H.; Lee, K.; Lee, S., Integration of Enzyme Immobilized Single-Walled Carbon Nanotubes Massinto the Microfluidic Platform and its Application for the Glucose-Detection. *Sensors and Actuators A: Physical* **2006**, *128* (1), 7-13.
158. Meng, S.; Kaxiras, E., Interaction of DNA with CNTs: Properties and Prospects for Electronic Sequencing. In *Biosensing Using Nanomaterials*, (ed A. Merkoçi), John Wiley & Sons, Inc., Hoboken, NJ, USA, **2009**; pp 67-96.
159. Nandy, B.; Santosh, M.; Maiti, P., Interaction of Nucleic Acids with Carbon Nanotubes and Dendrimers. *Journal of Biosciences* **2012**, *37* (3), 457-474.

160. Balasubramanian, K.; Lee, E. J. H.; Weitz, R. T.; Burghard, M.; Kern, K., Carbon Nanotube Transistors—Chemical Functionalization and Device Characterization. *Physica Status Solidi (a)* **2008**, 205 (3), 633-646.
161. Chung, C. L.; Nguyen, K.; Lonnais, S.; Streiff, S.; Campidelli, S.; Goux-Capes, L.; Bourgoïn, J. P.; Filoramo, A., DNA Linked to Single Wall Carbon Nanotubes: Covalent versus Non-Covalent Approach. *AIP Conference Proceedings* **2008**, 1062 (1), 129-139.
162. Liu, Z.; Jiao, L.; Yao, Y.; Xian, X.; Zhang, J., Aligned, Ultralong Single-Walled Carbon Nanotubes: From Synthesis, Sorting, to Electronic Devices. *Advanced Materials* **2010**, 22 (21), 2285-2310.
163. Giese, B., Long-Distance Electron Transfer Through DNA. *Annual Review of Biochemistry* **2002**, 71 (1), 51-70.
164. Dastagir, T.; Forzani, E.; Zhang, R.; Amlani, I.; Nagahara, L.; Tsui, R.; Tao, N., Electrical Detection of Hepatitis C Virus RNA on Single Wall Carbon Nanotube-Field Effect Transistors. *The Analyst* **2007**, 132 (8), 738-740.
165. Guo, J.; Lundstrom, M., Role of Phonon Scattering in Carbon Nanotube Field-Effect Transistors. *Applied Physics Letters* **2005**, 86 (19), 193103-1-193103-3.
166. Servati, P.; Nathan, A.; Amaratunga, G. A. J., Generalized Transport-Band Field-Effect Mobility in Disordered Organic and Inorganic Semiconductors. *Physical Review B* **2006**, 74 (24), 245210-1-245210-7.

167. Krishna, S. V. H.; An, J.; Zheng, L., Electrical Field Dependent Mobility Analysis of Ultralong Individual Single Walled Carbon Nanotube Field-Effect Transistor. *Journal of Nanoelectronics and Optoelectronics* **2013**, 8 (2), 202-207.
168. Jo, G.; Maeng, J.; Kim, T.-W.; Hong, W.-K.; Choi, B.-S.; Lee, T., Channel-Length and Gate-Bias Dependence of Contact Resistance and Mobility for In₂O₃ Nanowire Field Effect Transistors. *Journal of Applied Physics* **2007**, 102 (8), 084508-1-084508-1-7.
169. Hamieh, S. D.; Desgreys, P.; Naviner, J. F., Scattering Effects on the Performance of Carbon Nanotube Field Effect Transistor in a Compact Model. *European Physical Journal B* **2010**, 73 (2), 223-227.
170. Jin, S. H.; Islam, A. E.; Kim, T.-i.; Kim, J.-h.; Alam, M. A.; Rogers, J. A., Sources of Hysteresis in Carbon Nanotube Field-Effect Transistors and their Elimination via Methylsiloxane Encapsulants and Optimized Growth Procedures. *Advanced Functional Materials* **2012**, 22 (11), 2276-2284.
171. David, E.; Sumit, D.; Albert, L.; Eric, P., Reduction of Hysteresis for Carbon Nanotube Mobility Measurements Using Pulsed Characterization. *Nanotechnology* **2010**, 21 (8), 085702 (7pp).
172. Kan, Y.; Schuster, G. B., Long-Range Guanine Damage in Single-Stranded DNA: Charge Transport through a Duplex Bridge and in a Single-Stranded Overhang. *Journal of the American Chemical Society* **1999**, 121 (47), 10857-10864.

173. Fabregat, G.; Córdova-Mateo, E.; Armelin, E.; Bertran, O.; Alemán, C., Ultrathin Films of Polypyrrole Derivatives for Dopamine Detection. *The Journal of Physical Chemistry C* **2011**, *115* (30), 14933-14941.
174. Sansuk, S.; Bitziou, E.; Joseph, M.; Covington, J.; Boutelle, M.; Unwin, P.; Macpherson, J., Ultrasensitive Detection of Dopamine Using a Carbon Nanotube Network Microfluidic Flow Electrode. *Analytical Chemistry* **2013**, *85* (1), 163-169.
175. Wang, L.; Qin, X.; Liu, S.; Luo, Y.; Asiri, A. M.; Al-Youbi, A. O.; Sun, X., Single-Stranded DNA-Mediated Immobilization of Graphene on a Gold Electrode for Sensitive and Selective Determination of Dopamine. *ChemPlusChem* **2012**, *77* (1), 19-22.
176. Balasubramanian, K., Label-Free Indicator-Free Nucleic Acid Biosensors Using Carbon Nanotubes. *Engineering in Life Sciences* **2012**, *12* (2), 121-130.
177. Enyashin, A. N.; Gemming, S.; Seifert, G., DNA-Wrapped Carbon Nanotubes. *Nanotechnology* **2007**, *18* (24), 245702 (10pp).
178. Kricka, L. J., Nucleic Acid Detection Technologies — Labels, Strategies, and Formats. *Clinical Chemistry* **1999**, *45* (4), 453-458.
179. Liu, Y.; Chen, M.; Wang, M. L.; Dokmeci, M. R., RNA Functionalized Singled-Walled Carbon Nanotube Devices for Chemical Sensing. *Applied Physics Letters* **2013**, *103* (10), 103103-1-103103-4.
180. Chen, C.-L.; Yang, C.-F.; Agarwal, V.; Kim, T.; Sonkusale, S.; Busnaina, A.; Chen, M.; Dokmeci, M., DNA-Decorated Carbon-Nanotube-Based Chemical Sensors

on Complementary Metal Oxide Semiconductor Circuitry. *Nanotechnology* **2010**, *21* (9), 95504 (8pp).

181. Ali, S. R.; Ma, Y.; Parajuli, R. R.; Balogun, Y.; Lai, W. Y. C.; He, H., A Nonoxidative Sensor Based on a Self-Doped Polyaniline/Carbon Nanotube Composite for Sensitive and Selective Detection of the Neurotransmitter Dopamine. *Analytical Chemistry* **2007**, *79* (6), 25.

182. Peng, N.; Zhang, Q.; Chow, C. L.; Tan, O. K.; Marzari, N., Sensing Mechanisms for Carbon Nanotube Based NH₃ Gas Detection. *Nano Letters* **2009**, *9* (4), 1626-1630.

183. Roxbury, D.; Jagota, A.; Mittal, J., Structural Characteristics of Oligomeric DNA Strands Adsorbed onto Single-Walled Carbon Nanotubes. *The Journal of Physical Chemistry. B* **2013**, *117* (1), 132-140.

184. Manohar, S.; Tang, T.; Jagota, A., Structure of Homopolymer DNA-CNT Hybrids†. *The Journal of Physical Chemistry C* **2007**, *111* (48), 17835-17845.

185. Johnson, R.; Johnson, A.; Klein, M., Probing the Structure of DNA-Carbon Nanotube Hybrids with Molecular Dynamics. *Nano Letters* **2008**, *8* (1), 69-75.

186. Cheatham, T., Simulation and Modeling of Nucleic Acid Structure, Dynamics and Interactions. *Current Opinion in Structural Biology* **2004**, *14* (3), 360-367.

187. Johnson, R.; Johnson, A.; Klein, M., The Nature of DNA-Base-Carbon-Nanotube Interactions. *Small* **2010**, *6* (1), 31-34.

188. Meng, S.; Maragakis, P.; Papaloukas, C.; Kaxiras, E., DNA Nucleoside Interaction and Identification with Carbon Nanotubes. *Nano Letters* **2007**, 7 (1), 45-50.
189. Johnson, R.; Kohlmeyer, A.; Johnson, A.; Klein, M., Free Energy Landscape of a DNA-Carbon Nanotube Hybrid Using Replica Exchange Molecular Dynamics. *Nano Letters* **2009**, 9 (2), 537-541.
190. Liu, J.; Wang, Z.-H.; Luo, G.-A.; Li, Q.-W.; Sun, H.-W., The Interaction of DNA with Dopamine by Spectroscopic and Electrochemical Methods. *Analytical Sciences* **2002**, 18 (7), 751-755.
191. Kybert, N.; Lerner, M.; Yodh, J.; Preti, G.; Johnson, A., Differentiation of Complex Vapor Mixtures Using Versatile DNA-Carbon Nanotube Chemical Sensor Arrays. *ACS Nano* **2013**, 7 (3), 2800-2807.
192. Fernando, A.; Mary, E. H.; Jene, A. G.; Daniel, B., Base Dependent DNA–Carbon Nanotube Interactions: Activation Enthalpies and Assembly–Disassembly Control. *Nanotechnology* **2009**, 20 (39), 395101 (9pp).
193. Dixit, S.; Mezei, M.; Beveridge, D., Studies of Base Pair Sequence Effects on DNA Solvation Based on All-Atom Molecular Dynamics Simulations. *Journal of Biosciences* **2012**, 37 (3), 399-421.
194. Furse, K. E.; Corcelli, S. A., Molecular Dynamics Simulations of DNA Solvation Dynamics. *The Journal of Physical Chemistry Letters* **2010**, 1 (12), 1813-1820.

195. Gowtham, S.; Scheicher, R.; Pandey, R.; Karna, S.; Ahuja, R., First-Principles Study of Physisorption of Nucleic Acid Bases on Small-Diameter Carbon Nanotubes. *Nanotechnology* **2008**, *19* (12), 125701 (6pp).
196. Neihshal, S.; Periyasamy, G.; Samanta, P.; Pati, S., Understanding the Binding Mechanism of Various Chiral SWCNTs and SsDNA: A Computational Study. *The Journal of Physical Chemistry. B* **2012**, *116* (51), 14754-14759.
197. Khamis, S. M.; Johnson, R. R.; Luo, Z.; Charlie Johnson, A. T., Homo-DNA Functionalized Carbon Nanotube Chemical Sensors. *Journal of Physics and Chemistry of Solids* **2010**, *71* (4), 476-479.
198. Várnai, P.; Zakrzewska, K., DNA and its Counterions: A Molecular Dynamics Study. *Nucleic Acids Research* **2004**, *32* (14), 4269-4280.
199. Karachevtsev, M.; Karachevtsev, V., Peculiarities of Homooligonucleotides Wrapping Around Carbon Nanotubes: Molecular Dynamics Modeling. *The Journal Of Physical Chemistry. B* **2011**, *115* (29), 9271-9279.
200. Wei, L.; Shi, D.; Ye, P.; Dai, Z.; Chen, H.; Chen, C.; Wang, J.; Zhang, L.; Xu, D.; Wang, Z.; Zhang, Y., Hole Doping and Surface Functionalization of Single-Walled Carbon Nanotube Chemiresistive Sensors for Ultrasensitive and Highly Selective Organophosphor Vapor Detection. *Nanotechnology* **2011**, *22* (42), 425501 (7pp).
201. Shirsat, M.; Sarkar, T.; Kakoullis, J.; Myung, N.; Konnanath, B.; Spanias, A.; Mulchandani, A., Porphyrins-Functionalized Single-Walled Carbon Nanotubes

Chemiresistive Sensor Arrays for VOCs. *The Journal of Physical Chemistry. C, Nanomaterials and Interfaces* **2012**, *116* (5), 3845-3850.

202. Das, B.; Tlili, C.; Badhulika, S.; Cella, L.; Chen, W.; Mulchandani, A., Single-Walled Carbon Nanotubes Chemiresistor Aptasensors for Small Molecules: Picomolar Level Detection of Adenosine Triphosphate. *Chemical Communications* **2011**, *47* (13), 3793-3795.

203. Zhu, G.; Zhang, X.; Gai, P.; Zhang, X.; Chen, J., β -Cyclodextrin Non-Covalently Functionalized Single-Walled Carbon Nanotubes Bridged by 3,4,9,10-Perylene Tetracarboxylic Acid for Ultrasensitive Electrochemical Sensing of 9-Anthracenecarboxylic Acid. *Nanoscale* **2012**, *4* (18), 5703-5709.

204. Daneshgar, P.; Norouzi, P.; Ganjali, M.; Dinarvand, R.; Moosavi-Movahedi, A., Determination of Diclofenac on a Dysprosium Nanowire-Modified Carbon Paste Electrode Accomplished in a Flow Injection System by Advanced Filtering. *Sensors* **2009**, *9* (10), 7903-7918.

205. Goyal, R. N.; Chatterjee, S.; Rana, A. R. S., The Effect of Modifying an Edge-Plane Pyrolytic Graphite Electrode with Single-Wall Carbon Nanotubes on its Use for Sensing Diclofenac. *Carbon* **2010**, *48* (14), 4136-4144.

206. Marcolino, V.; Zanin, G.; Durrant, L.; Benassi, M. D. T.; Matioli, G., Interaction of Curcumin and Bixin with β -Cyclodextrin: Complexation Methods, Stability, and Applications in Food. *Journal of Agricultural and Food Chemistry* **2011**, *59* (7), 3348-3357.

207. Harada, A.; Takashima, Y.; Yamaguchi, H., Cyclodextrin-Based Supramolecular Polymers. *Chemical Society Reviews* **2009**, 38 (4), 875-882.
208. Chen, Y.; Zhang, Y.-M.; Liu, Y., Multidimensional Nanoarchitectures Based on Cyclodextrins. *Chemical Communications* **2010**, 46 (31), 5622-5633.
209. Abbaspour, A.; Noori, A., A Cyclodextrin Host-Guest Recognition Approach to an Electrochemical Sensor for Simultaneous Quantification of Serotonin and Dopamine. *Biosensors & Bioelectronics* **2011**, 26 (12), 4674-4680.
210. Yang, L.; Xu, Y.; Wang, X.; Zhu, J.; Zhang, R.; He, P.; Fang, Y., The Application of β -Cyclodextrin Derivative Functionalized Aligned Carbon Nanotubes for Electrochemically DNA Sensing via Host-Guest Recognition. *Analytica Chimica Acta* **2011**, 689 (1), 39-46.
211. Ludden, M.; Péter, M.; Reinhoudt, D.; Huskens, J., Attachment of Streptavidin to Beta-Cyclodextrin Molecular Printboards via Orthogonal Host-Guest and Protein-Ligand Interactions. *Small* **2006**, 2 (10), 1192-1202.
212. Duan, X.; Rajan, N. K.; Routenberg, D. A.; Huskens, J.; Reed, M. A., Regenerative Electronic Biosensors Using Supramolecular Approaches. *ACS Nano* **2013**, 7 (5), 4014-4021.
213. Kong, L.; Wang, J.; Meng, F.; Chen, X.; Jin, Z.; Li, M.; Liu, J.; Huang, X.-J., Novel Hybridized SWCNT-PCD: Synthesis and Host-Guest Inclusion for Electrical Sensing Recognition of Persistent Organic Pollutants. *Journal of Materials Chemistry* **2011**, 21 (30), 11109-11115.

214. Wenzel, T. J.; Pham, N. H., Artificial Receptor Compounds for Chiral Recognition. In *Artificial Receptors for Chemical Sensors*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, **2010**; pp 191-248.
215. Cwiertnia, B.; Hladon, T.; Stobiecki, M., Stability of Diclofenac Sodium in the Inclusion Complex with β -Cyclodextrin in the Solid State. *Journal of Pharmacy and Pharmacology* **1999**, *51* (11), 1213-1218.
216. Pose-Vilarnovo, B.; Santana-Penin, L.; Echezarreta-Lopez, M.; Perez-Marcos, M.; Vila-Jato, J.; Torres-Labandeira, J., Interaction of Diclofenac Sodium with Hand Hydroxypropyl-Cyclodextrin in Solution. *STP Pharma Sciences* **1999**, *9* (3), 231-236.
217. Astilean, S.; Ionescu, C.; Cristea, G.; Farcas, S. I.; Bratu, I.; Vitoc, R., NMR Spectroscopy of Inclusion Complex of Sodium Diclofenac with B-Cyclodextrin in Aqueous Solution. *Biospectroscopy* **1997**, *3* (3), 233-239.
218. Ting, Z.; Syed, M.; Nosang, V. M.; Marc, A. D., Recent Progress in Carbon Nanotube-Based Gas Sensors. *Nanotechnology* **2008**, *19* (33), 332001 (14 pp).
219. Voggu, R.; Rout, C. S.; Franklin, A. D.; Fisher, T. S.; Rao, C. N. R., Extraordinary Sensitivity of the Electronic Structure and Properties of Single-Walled Carbon Nanotubes to Molecular Charge-Transfer. *The Journal of Physical Chemistry C* **2008**, *112* (34), 13053-13056.
220. Tang, B.; Ma, L.; Wang, H.-y.; Zhang, G.-y., Study on the Supramolecular Interaction of Curcumin and Beta-Cyclodextrin by Spectrophotometry and its

Analytical Application. *Journal of Agricultural and Food Chemistry* **2002**, 50 (6), 1355-1361.

221. Poonam, P.; Deo, N., Effect of Gas Flow on Electronic Transport in a DNA-Decorated Carbon Nanotube. *Nanotechnology* **2011**, 22 (20), 205201 (8pp).

222. Poonam, P.; Deo, N., Current Correlation Functions for Chemical Sensors Based on DNA Decorated Carbon Nanotube. *Sensors and Actuators B: Chemical* **2008**, 135 (1), 327-335.