INTEGRATION OF SUBSTRATE-GATE COUPLED P-TYPE ANATASE TiO_2 FOR FIELD-EFFECT TRANSISTOR BASED BIOSENSORS

By

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LIST OF ABBREVIATIONS

3-D	Three dimension
AFM	Atomic force microscopy
AI	Avian- influenza
AMI	Acute Myocardial Infarction
APTES	3-Aminopropyltriethoxysilane
BOE	Buffered oxide etch
BOX	Buried oxide
BSA	Bovine serum albumin
CMOS	Complementary metal-oxide semiconductor technology
cTnI	Cardiac troponin I
cTnT	Cardiac troponin T
CVD	Chemical Vapor deposition
DMFET	Dielectric-modulated field-effect transistor
EDX	Energy dispersive X-ray spectroscopy
ELISA	Enzyme-linked immunosorbent assay
FET	Field-effect transistor
FTIR	Fourier transform infrared spectroscopy
GA	Glutaraldehyde
GNP	Gold nanoparticles
HPM	High power microscope
ICP-RIE	Inductively couple plasma reactive-ion-etching

IDE	Interdigitated Electrode
IP	Isoelectric point
LOD	Limit of detection
MEA	Monoethanolamine
NW	Nanowire
PANI	polyaniline
PBS	Phosphate bufferred saline
PR	Positive photoresist
PVD	Physical vapor deposition
RCA	Radio Corporation of America
RMS	Root mean square
SEM	Scanning electron microscopy
Si	Silicon
SiNW	Silicon nanowire
SiO_2	Silicon oxide
SOI	Silicon-on-insulator
Sol-gel	Solution gel
SPE	Screen printed electrode
TiO_2	Titanium dioxide
TTIP	Titanium (IV) isopropoxide
XPS	X-ray photoelectron spectroscopy
XRD	X-ray diffraction

LIST OF SYMBOLS

A	Ampere
Al	Aluminum
Ar	Argon
C_2H_6O	Ethanol
CF_4	Tetrafluoromethane
H	Hydrogen
H+	Hydrogen ion
H_2O	Water
H_2O_2	Hydrogen peroxide
HCL	Hydrochloric acid
I_d	Drain current
λ_d	Debye length
NH_4OH	Ammonium hydroxide
O	Oxygen
Ra	Average roughness
SF_6	sulphur hexafluoride
Ti	Titanium
V	Voltage
V_{bg}	Substrate-gate voltage
V_d	Drain voltage
V_{ds}	Drain to source voltage

V_g	Gate voltage

Integrasi Gandingan Get-Substrat Bersama TiO_2 Anatase Jenis-p Untuk Biopenderiaan Berasaskan Gandingan Kesan Transistor

ABSTRAK

Istilah “biopenderiaan” ialah singkatan kepada “biologi penderiaan”. Secara umumnya, biopenderiaan boleh didefinisikan sebagai peranti analisis, yang menukar respon biokimia kepada signal elektrik yang boleh diukur. Peranti tersebut terdiri daripada transduser dan reseptor biologi. Permukaan transduser perlu diolah dengan reseptor biologi seperti antibody, enzim atau asid nukleik. Reseptor biologi berfungsi sebagai pasangan jitu molekul “DNA” atau antigen dan mengubah interaksi tersebut kepada signal elektronik. Kaedah ini mampu menjadikan biopenderiaan lebih sensitif, kadar respon yang baik dan pengesanan tanpa label. Dalam kajian ini, gabungan peranti integrasi get-substrat gandingan kesan transistor (FET) bersama jenis-p *anatase* TiO_2 sebagai bahan pemindaharuh dibentangkan untuk mengesan penanda-bio *cardiac troponin I*. Ekperimen dimula dengan fabrikasi get-substrat FET biopenderiaan menggunakan jenis-p silicon atas penebat (SOI) wafer. Process fotolitografi bersama tiga topeng berbeza digunakan untuk; 1) membuka saluran sebesar 10 μm diantara saliran dan sumber, 2) untuk mendedahkan kawasan untuk elektrod get-substrat dan 3) Al dienapkan sebagai lapisan hubungan untuk saliran, sumber dan get-substrat. Kemudian, TiO_2 yang digunakan sebagai bahan pemindaharuh dienap diatas saluran menggunakan teknik sol-gel, mewujudkan lapisan nipis diatas permukaan. Beberapa jenis pencirian telah dilakukan seperti morfologi permukaan (AFM, SEM), jenis hablur bahan (XRD), jenis ikatan kimia (XPS), dan ciri-ciri elektrikal (SPA). Lapisan nipis TiO_2 mempunyai ciri-ciri struktur *anatase* jenis-p disebabkan kecacatan kekurangan titanium, dengan 65 nm purata saiz ira. Peranti yang telah dilapisi TiO_2 menunjukan aliran elektrik diantara saliran dan sumber, dan boleh dimodulasi dengan pincangan get-substrat. Selepas itu, tambahan ikatan kimia menggunakan APTES dan glutaraldehyde dilakukan diatas lapisan nipis TiO_2 sebelum proses interaksi antibody-antigen, pencirian dilakukan menggunakan XPS dan FTIR. Ia menunjukkan perubahan puncak elemen kimia pada setiap proses, membuktikan ikatan kimia tentu wujud. Untuk membuktikan fungsi dan prestasi pengesanan biomolekul, peranti tersebut digunakan untuk mengesan penanda bio *troponin* jantung (cTnI). cTnI adalah penanda bio terulung untuk pengenalan penyakit jantung. Peranti tersebut digunapakai dengan memberi pincangan dari -3 V sehingga 0 V (bersama langkah 0.1 V) dan pincangan langkah get-substrat dari -3 V to 3 V. Perubahan yang jelas terjadi terutamanya pada peningkatan aliran elektrik dan penunjukan LOD= 0.238 ng/ml pada V_{bg}= -3 V. Ini memberi pengesahan bahawa pengunaan peranti integrasi get-substrat gandingan kesan transistor memberi keupayaan untuk meningkatkan sensitiviti. Sebagai penutup, kelebihan pincangan get-substrat yang mampu memodulasikan aliran elektrik merantasi saluran peranti memberi satu peluang untuk menambahbaik mutu penguatan isyarat dari pengesanan biomolekul di masa hadapan.

Integration of Substrate-gate Coupled p-type Anatase TiO_2 For Field-Effect Transistor Based Biosensors

ABSTRACT

The term “biosensor” is a short form for “biological sensor”. A biosensor is generally defined as an analytical device, which converts the biochemical responses into quantifiable electronic signal. The device is made up of a transducer and biological receptor. The transducer surface needs to be functionalized with biological receptors such as an antibody, an enzyme or a nucleic acid. The biological receptor is employed to identify the specific target (i.e. DNA or antigen) molecule and the transducer to transform the specific interaction of the biomolecule into electronic signal. This method allows high sensitivity, rapid response and label-free detection. In this work, the integration of substrate-gate coupling of field-effect transistor (FET) based sensor with p-type anatase TiO_2 as a transducer material for detection of cardiac troponin I biomarker is presented. The work is initiated with fabrication of substrate-gated FET based biosensor on p-type silicon-on-insulator (SOI) wafer. Photolithography process with three different masks are used; 1) to create 10 µm channel in between the source and drain area, 2) to expose substrate-gate electrode through the top-silicon and buried oxide (SiO_2) layer, and 3) Al metal contact deposition for source, drain and substrate gate electrodes. Next, TiO_2 that acts as a transducer material is deposited on top of the channel by using sol-gel technique, creating a thin film TiO_2 on the surface. Several characterization methods have been used to determine the TiO_2 properties such as surface morphology (AFM, SEM), material crystallinity (XRD), surface functionalization (FTIR, XPS), and electrical characteristics (SPA). The deposited TiO_2 thin film possess p-type anatase structure due to titanium vacant defect, with average grain size of 65 nm. The fabricated device with TiO_2 thin film (before functionalization and detection of biomolecule), shows that there is electrical flow with the presence of TiO_2 connecting between source and drain, and it can be modulated with substrate-gate bias. Subsequently, the TiO_2 surface is functionalized with APTES and Glutaraldehyde prior to be subjected into antibody-antigen interaction, characterized by using XPS and FTIR. It shows, the changes or the presence of peaks at each surface functionalization proved that the chemical bonding have occurred. To demonstrate the functionality and performance of for biomolecule detection, the device is demonstrated to detection of cardiac troponin biomarker (cTnI) with concentration from 1ng/ml until 10 µg/ml. cTnI is a gold standard for diagnosis of cardiovascular disease. With the presence of substrate-gate biasing (V_{bg} = - 3 V), the device demonstrated significant amplification signal with LOD of 0.238 ng/ml can be achieved. This bring to a confirmation that the p-type anatase TiO_2 offers excellent interaction with cTnI biomolecule. Coupled with substrate-gated FET, enhance sensitivity of bio-sensing can be achieved due modulation of electrical conductivity along the channel.

CHAPTER 1

BACKGROUND

1.1 Introduction

Recognition of substances that are not visible to the naked eye, such as biomolecules, indeed requires a support from sensing devices that have sufficient sensitivity (X. Zhang, Guo, & Cui, 2009). Among different types of sensors that have been generated (e.g., optical, electrical, acoustic, and electrochemical), integrated electrical devices are of particular interest due to advantages including small sizes, ease of handling, capability of using small sample volumes, and low cost.

Biosensors attract considerable amount of attention for its vital role in medical application. The electrical-based biosensor promote better flexibility for detecting various type of biomolecule that cannot be seen by human eyes such as DNA (Nuzaihan M.N. et al., 2016), enzymes (A. Liu, Lang, Liang, & Shi, 2016), protein (Fathil et al., 2016), etc. Development of semiconducting device with very small in size, highly-sensitive and instant response detection is essential. Silicon are well-known in various electronic application due to its excellent electrical flexibility and low-cost. Silicon can change its electron-holes concentration by doping process which is good for selectivity of the device. Most of the bio-sensor applied silicon as the main material to develop high performance bio-sensor. There are several types of bio-sensors are well-known due to its performance i.e interdigitated electrode (IDE), screen printed electrode, resistance-based nanowire and field-effect transistor (FET).

FET-based sensor is one type of such integrated devices, which has been used to detect biomolecules with transducing materials (e.g., silicon and polyaniline nanowires, graphene, etc). When combined with surface modifications, these sensors can exhibit label-free and tuneable electrical conduction properties for nano-biomedical approaches as shown in Fig. 1.1. The most charming feature of the devices is to directly transduce events of biomolecules specific binding into useful electrical signals such as resistance (Peng et al., 2015), impedance (Abiri et al., 2015) and capacitance (Qureshi, Pandey, Chouhan, Gurbuz, & Niazi, 2015). FET-based sensors have the structure of a common three-electrode transistor, i.e., a source, drain and gate. Source and drain electrodes are bridged by a semiconductor channel and used as the sensing component of the device, while gate electrodes modulate the channel. Miniaturization and compatibility with complementary metal-oxide semiconductor technology (CMOS) are interesting advantages and have attracted the attention of researchers for various applications, including sensing biomolecules. A wealth of research is available discussing a fabrication technique of FET (C. Zhang et al., 2016). FET with dual gate approach has been demonstrated for enhancing the performance of the device (J. Y. Kim et al., 2012).

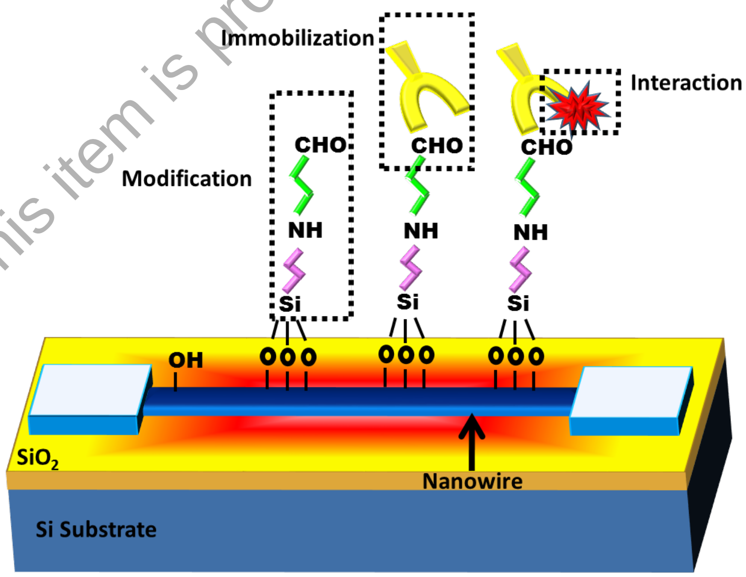

Figure 1.1: FET based biosensor for detection of specific biomolecule.

Titanium dioxide (TiO_2), also known as titanium (IV) oxide or titania, is the naturally occurring oxide of titanium. TiO_2 occurs in nature as well-known minerals rutile, anatase and brookite, and additionally as two high pressure forms, a monoclinic baddeleyite-like form and an orthorhombic like form. TiO_2 is a multifaceted compound. It's the stuff that makes toothpaste white and paint opaque. TiO_2 is also a potent photocatalyst that can break down almost any organic compound when exposed to sunlight, and a number of companies are seeking to capitalize on TiO_2 reactivity by developing a wide range of environmentally beneficial products, including self-cleaning fabrics, auto body finishes, and ceramic tiles. TiO_2 nanoparticle already shows its potential in biotechnology application. In the field of nanomedicine, intravenous injection can deliver TiO_2 nanoparticulate carriers directly into the human body. Upon intravenous exposure, TiO_2 nano-particles can induce pathological lesions of the liver, spleen, kidneys, and brain. TiO_2 thin film two-dimensional nanostructure show great potential in bio-sensing application. TiO_2 is well known due to its chemical resistance, physical endurance, and good electrical characteristic as it possess semiconductor characteristic with wide bandgap (3.2 eV for anatase and 3.0 eV for rutile) (P.Vlazan et al., 2015).

1.2 Research Backround

1.2.1 Problem statement

Acute Myocardial Infarction (AMI) is a life-threatening symptom when blood flowing in an abnormal way than it should to any part of the heart. When blood flow is not enough due to thrombosis within the coronary artery, cardiovascular muscle will receive less oxygen, causing blood clot and damaging the organ. As the symptom occurred, cardiac troponin I and T (cTnI and cTnT) were released inside the bloodstream. cTnI and cTnI then become a main selection as a modern biomarker for AMI detection.

Several characterization method to determine the concentration of the target analyte such as enzyme-linked immunosorbent assay (ELISA), western-blot, dot-blot and gel-shift method. These methods can be categorized as qualitative measurement and it comes with certain limitation. To overcome those limitation, electrical-based biosensors is the most effective way to detect the level of heart disease inside the human body via *in-vitro* method. This method allow high sensitivity, rapid response and label-free detection. TiO_2 nanoparticle as a device transducer element. It provides a low cost, high surface area, semiconductor characteristic and excellent electrochemical interaction. The device embedded with TiO_2 brings great promise for bio-sensing applications due to their compatibility with specific biomaterial and its significant effect towards the electrical characteristic of the device.

Sensor development has been reliant on the structure and design shape of the device to improve their sensitivity. Thus the device development towards ultra-sensitive detection become more difficult. The current findings explored a unique crystalline TiO_2 nanoparticles in terms of electrochemical reaction and its transducing ability. Miniaturized of transducing elements is crucial and important not only in engineering scope but also in biological field. With current technologies, process to miniature a device has become easier. However, decreasing the scale causes the cost, labour and complexity to increase. Addition of electrical biasing onto the device also become one of the main alternative to boost the sensitivity of the detection. The idea and concept was taken from the FET devices that can modulate its electrical conductivity from drain to source by variate its gate voltage.

1.2.2 Research Objectives

General Research Objective

The objective of this project is to fabricate FET based bio-sensor with integration of substrate gate TiO_2 as transducer, bridging between source and drain. The completed bio-sensors will be characterized in terms of physical, chemical and electrical. These objectives are accomplished with the following specific objectives.

Specific Research Objective

- To fabricate FET devices with integration of substrate-gate coupling and deposition of TiO_2 between the channels by utilizing thin body SOI substrate for bio-sensing.
- To characterized the architecture design and structure of the device and physical and crystallinity of the TiO_2 thin film and utilized the effect of substrate-gate biasing in terms of electrical mobility of TiO_2 thin film.
- To functionalized the surface of TiO_2 thin film for specific cTnI antibody-antigen interaction.
- To test the ability of the device in term of differentiating electrical properties of each surface functionalization with the effect of different substrate-gate biasing for enhancing the device sensitivity.

1.2.3 Research Scope

The development of substrate-gated FET for detection of cTnI antigen are divided into five parts. The research work begins by fabricating the substrate-gated FET based biosensor. Three types of mask are used for device designation with chrome mask utilization as its base for better resolution. Factory standard SOI types of wafer is used to segregate substrate-gate contact area and sensing area. Conventional photolithography process is applied to pattern the source, drain and substrate-gate structure and contact.

Second, fundamental theory on the operation of biosensors operate within certain condition is discussed in detail. Furthermore, several types of nano-material and FET based biosensors in terms of its characteristic, fabrication technique and application are discussed thoroughly. Sol-gel method is used to deposit the TiO_2 nanoparticle onto the device. TiO_2 is suspended within ethanol solution with acetic acid to stabilize the sol-gel solution. Then the solution is deposited by drop onto the device and spin coat to attain thin film structure. The TiO_2 thin film then characterized in terms of crystallinity, physical and electrical properties.

Third, Fabrication of FET based biosensor is discussed including the technique of depositing patterned TiO_2 thin film on top of the FET devices. The effect of substrate-gate biasing towards the FET based biosensor conductivity is presented. Electrical comparison of bare, as deposited TiO_2 thin film, annealed TiO_2 thin film, and each step of surface functionalization characteristic with substrate-gated biasing effect is discussed. Substrate-gate biasing is applied and study its effect towards the device conductivity and channel modulation. Optimization of substrate-gate biasing is conducted for gaining maximum current flow without destroying its characteristic.

Fourth, surface functionalization of TiO_2 thin film by using two types of linker (e.g APTES and GA) for allowing cardiac troponin antibody to bind as a probe in purpose for capturing the complementary antigen, creating antigen-antibody interaction that modulate the electrical behavior of the device. The device structure is presented by using high power microscope (HPM) and scanning electron microscopy (SEM). Then the TiO_2 nano-particle deposited by sol-gel process is observed by three types of instrument i.e. atomic force microscopy (AFM), SEM, HPM and surface profilometer. After that the crystallinity of TiO_2 nanoparticle and functional group of surface modification is discussed. X-ray diffraction (XRD) and energy dispersive X-ray spectroscopy (EDX) is used to determine the existence of TiO_2 nanostructure and its crystal type, the surface modification of TiO_2 thin for the binding of cTnI protein is characterized by using fourier transform infrared spectroscopy (FTIR) and X-ray photoelectron spectroscopy (XPS). Finally, four types of electrical characterization method are conducted i.e. source to drain biasing, substrate-gate biasing, electrical properties of TiO_2 thin film and each layer of surface functionalization, and the effect of substrate-gate biasing towards the detection of cTnI protein.

1.2.4 Thesis Organization

The thesis is divided into five different chapters and each chapter is organized with several subheading. For chapter 1, introduction, problem statement, general and specific objective and research scope is presented briefly.

Chapter two is present as the literature review of the TiO_2 FET based biosensor. The details of every aspect that related with the development of the biosensor will be expalined in here for better understanding.

Chapter three explains in detail about the methodology of this research. This chapter is divided into several section: First, deposition of TiO_2 thin film by sol-gel method, TiO_2 thin film is characterized in terms of structural stability, physical and electrical characteristic, with and without substrate-gate biasing.

Chapter four comprises of all the results obtained by different characterization method. All the results is arranged according to the research process flow for better understanding. The importance of development of this chapter is to prove that the concept of substrate-gate functionality in terms of sensitivity and stability of the detection of cTnI. Lastly, chapter five is presents about the conclusion and recommendation for future works.