



**INTEGRATION OF SUBSTRATE-GATE COUPLED
P-TYPE ANATASE TiO₂ FOR FIELD-EFFECT
TRANSISTOR BASED BIOSENSORS**

By

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A thesis submitted in fulfillment of the requirements for the degree of
Master of Science in Nanoelectronic Engineering

**INSTITUTE OF NANO ELECTRONIC ENGINEERING
UNIVERSITI MALAYSIA PERLIS**

2017

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Academic Session : 2016/2017

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ACKNOWLEDGEMENT

The road to realization of this journey has never been easy, as I always thought that pursuing Master is only for academic purposes. Grateful to Allah, this two years journey is a road of responsibility, excitement, and experience that full with uncertain matters that reshaped my life to become a stronger, better and matured person. It never been an easy task and it never was, but the support from people around me, lift me up, allow me to strive for this triumph. There is no excuses for me not to acknowledge the person that voluntarily walk this winding road together, as an appreciation and memories.

There is no such expression nor interpretation of word that would describe the unconditional love and sacrifice that my mother Che Halimah binti Ahmad, and my father Rahmat bin Idris have given to me. Both of them work hard day and night raising us until there is nothing for them, just to make sure everything is enough for us. Nevertheless, they still able to inherit their time for us, even for a few minutes every single day. Make us believe that parents will do everything just only for the sake of their children. It is a painful to watch the face of disappointment from them due to the failure to excel since primary school until my degree. They take hold of my hand, put a faith in me to let me believe that success will come one day. Eventually, now I am climbing up towards success, just to bring cheerful moment for them. I hope I can see one of the greatest smile from them both, and the reason behind that smile is me.

For my supervisor Ir. Dr. Mohd Khairuddin bin Md Arshad, at first, I am just an average student with mediocre result and lack of confidence. I am afraid that I cannot fulfil all the tasks that been entrusted to me, yet he sees me with from a different angle. He keeps his faith and support me entirely with technical guidance and advices, even when I am lost in track. He teaches me that hard work can beat almost everything and prove that even the weakest can excel by heartfelt guidance. The effort that been pour into me by him had made me work harder and push myself beyond my limit. He surely a man with knowledge with excellent technical capabilities. His way of refining me surely be remain beneficial for myself and people around me.

I would like to show my utmost appreciation for my co-supervisor, Dr Ruslinda binti Abdul Rahim. Without the faith and opportunity that been given to me, I would never have a chance to pursue my study. Nevertheless, gaining knowledge from this highly technical person is assuredly one the main reason that I can excel in my research.

My greatest gratitude goes to my friend and mentor, Mr. Mohd Faris bin Mohd Fathil. We have been this through altogether, from scratch until we achieved something that we can be proud of. With his advices, wisdom and willingness to help others, it surely became a major reason why I am still able to stand up. He was always ready to meet the next challenges even if they were bigger than he was. He proved that any problem can be solved, even if it seems to be impossible as long as we keep trying because failure is just another way of learning. Thank you so much for making me believe that.

For the INEE staff, Mr. Jasni bin Ismail, Dr. Mohd Nuzaihan bin Mohd Nor, Dr Gopi Subash Gopinath, Mr. Aizat, Mrs. Mira, Mrs. Ninie, Mrs. Eli, Mrs. Ija, Mr. Isa Mr. Fais and Mr. Azroy. With all the faith that was given to me, I am capable to learn and use all the equipment inside the lab and able to manage myself in terms of administration work. Thank you for all the guidance that has been thought to me.

With the support from my close friends, this long journey would never be this cheerful. A deepest thankfulness for my comrade that stand together with me, whether it is truly related or not in terms of my field of work. We learn together as for our family and ourselves for the greater good. Initially, I would like to acknowledge my housemate, Lee Hon Cheun, Suhaimi, Noriman, Shafiq Hafly and Mohd Ashraf. May our moment together will be not forgotten and may be in our heart forever. Next is for my colleague that been together with me in INEE, our memories are full of happiness, sharing and lessons. It is been an honour to know each of you, we all grown up together learning from our own mistake. We stand up together, knowing that we not perfect, but we perfecting each other. True friend is the person who knows all about you, and still with you.

As for my closest friend, Robiaatul Adawiyah binti Ahmad Legiman. I want to take this opportunity to show appreciation on behalf of her strength for this entire time that full of impediment. Through thick or thin, she still accepts me at my strongest yet support me at my weakest. All the difficulties that we face make us believe that to reach something beautiful is easier to said than done. We are grown up learning about responsibilities, just for taking care the one we love. May our journey in the future are full of serenity and comfort.

This acknowledgement has never been completed without crediting my sibling i.e. Arnizah binti Rahmat, Adzhmir bin Rahmat, Ahmad Jefri bin Rahmat and Ahmad Rizal bin Rahmat. Not to be forgotten, my sibling-in-law i.e Hannim, Norizan and Ameran We share our moment, hardship and proudness together. I can never reach this far in my live without the help and support from them. Thank you for becoming my protector until now. May this bonding will remain until the end, as the greatest gift from our parent was each other's.

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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 buffered 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 ₂ H ₆ O	Ethanol
CF ₄	Tetrafluoromethane
H	Hydrogen
H ⁺	Hydrogen ion
H ₂ O	Water
H ₂ O ₂	Hydrogen peroxide
HCL	Hydrochloric acid
I _d	Drain current
λ_d	Debye length
NH ₄ OH	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

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Integrasi Gandingan Get-Substrat Bersama TiO₂ 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* TiO₂ 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 saluran dan sumber, 2) untuk mendedahkan kawasan untuk elektrod get-substrat dan 3) Al diapakan sebagai lapisan hubungan untuk saluran, sumber dan get-substrat. Kemudian, TiO₂ yang digunakan sebagai bahan pemindaharuh diapakan 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 elektrik (SPA). Lapisan nipis TiO₂ mempunyai ciri-ciri struktur *anatase* jenis-p disebabkan kecacatan kekurangan titanium, dengan 65 nm purata saiz ira. Peranti yang telah dilapisi TiO₂ menunjukkan aliran elektrik diantara saluran dan sumber, dan boleh dimodulasi dengan pincangan get-substrat. Selepas itu, tambahan ikatan kimia menggunakan APTES dan glutaraldehyde dilakukan diatas lapisan nipis TiO₂ 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 penggunaan 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 TiO₂ 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 TiO₂ 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 (SiO₂) layer, and 3) Al metal contact deposition for source, drain and substrate gate electrodes. Next, TiO₂ that acts as a transducer material is deposited on top of the channel by using sol-gel technique, creating a thin film TiO₂ on the surface. Several characterization methods have been used to determine the TiO₂ properties such as surface morphology (AFM, SEM), material crystallinity (XRD), surface functionalization (FTIR, XPS), and electrical characteristics (SPA). The deposited TiO₂ thin film possess p-type anatase structure due to titanium vacant defect, with average grain size of 65 nm. The fabricated device with TiO₂ thin film (before functionalization and detection of biomolecule), shows that there is electrical flow with the presence of TiO₂ connecting between source and drain, and it can be modulated with substrate-gate bias. Subsequently, the TiO₂ 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 TiO₂ 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).

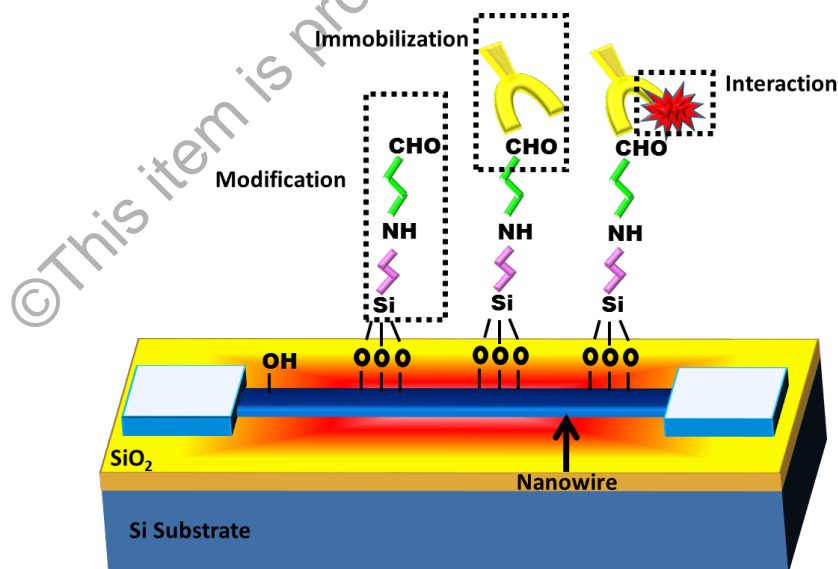


Figure 1.1: FET based biosensor for detection of specific biomolecule.

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 Background

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. TiO₂ nanoparticle as a device transducer element. It provides a low cost, high surface area, semiconductor characteristic and excellent electrochemical interaction. The device embedded with TiO₂ 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 TiO₂ 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 TiO₂ nanoparticle onto the device. TiO₂ 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 TiO₂ 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 TiO₂ 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 TiO₂ thin film, annealed TiO₂ 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 TiO₂ 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 TiO₂ 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 TiO₂ 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 TiO₂ nanostructure and its crystal type, the surface modification of TiO₂ 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 TiO₂ 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 TiO₂ 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 TiO₂ thin film by sol-gel method, TiO₂ 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.

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