PERFORMANCE ANALYSIS OF ISFET BIOSENSOR WITH DIFFERENT STRUCTURES

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DEDICATION

This project report is dedicated to my family, who have supported and encourage me unconditionally throughout the process. They have thought me the value of hard work and unceasingly support me to strive towards success

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ABSTRACT

Ion-sensitive field-effect transistor (ISFET) biosensor has gained popularity in clinical research field for biomolecules detection due to its high detection sensitivity, mass-production capability, and low manufacturing cost. Proteins are needed by all living cells for structural and functional purposes. However, some proteins such as Bovine Serum Albumin (BSA) can cause allergic reactions in human body. Besides, instability of Liposome may result in medication leaks that could harm cells. The first objective of this project is to study the effect of different proteins on the performance of different structures of ISFET biosensor. There are several limitations of ISFET biosensor such as lack of good solid-state electrodes, parasitic sensitivity to temperature and light and time dependent instability of sensor parameters. Enhancement on ISFET structures could be a good approach to improve the ISFET performance. The second objective of this research is to compare the performance of ISFET biosensors of different nanoelectronics structure in terms of settling time, sensitivity, and selectivity. In this project, an open-source software, nanohub BioSensorLab was used to simulate the settling time, sensitivity, and selectivity of the biosensors. The target proteins are Liposome and Bovine serum albumin (BSA) while the bioreceptor is collagen. Different structures of ISFET biosensor were simulated and analysed, which are planar ISFET, cylindrical nanowire, nanosphere and double-gate FET biosensors. In this research, the impact of proteins' diffusion coefficient, structures of biosensor and analyte concentration towards the settling time was analysed. Next, the sensitivity relied on the structures of biosensor. Therefore, the analysis carried out independently for different structures of biosensor. Selectivity is determined by the size of receptor molecules and parasitic molecules, concentration of target molecules and parasitic molecules. From the simulation results, the settling time decreased when analyte concentration and protein diffusion coefficient increased. In addition, the settling time increased from planar and double-gate, cylindrical nanowire to nanosphere biosensor. To obtain high sensitivity in planar ISFET biosensor, the width and the electrolyte concentration are increased while the oxide thickness and the length are decreased. For cylindrical nanowire biosensor, increasing the radius, oxide thickness and reducing the buffer ion concentration can improve the sensitivity. To obtain high sensitivity in double-gate FET, the width, back oxide thickness, and silicon body thickness need to increase while the length and top oxide thickness need to decrease. The selectivity is the same regardless of the ISFET structures. High selectivity can be obtained by increasing the size of receptor and parasitic molecules, concentration of target molecules, and decreasing the concentration of parasitic molecules. Diffusion coefficient of proteins have no impact towards the sensitivity and selectivity of ISFET biosensors.

ABSTRAK

Biosensor transistor kesan medan sensitif ion (ISFET) telah mendapat populariti dalam bidang penyelidikan klinikal untuk pengesanan biomolekul kerana kepekaan pengesanan yang tinggi, keupayaan pengeluaran besar-besaran dan kos pembuatan yang rendah. Protein diperlukan oleh semua sel hidup untuk tujuan struktur dan fungsi. Walau bagaimanapun, beberapa protein seperti Bovine Serum Albumin (BSA) boleh menyebabkan tindak balas alahan dalam tubuh manusia. Selain itu, ketidakstabilan Liposom boleh mengakibatkan kebocoran ubat yang boleh membahayakan sel. Objektif pertama projek ini adalah untuk mengkaji kesan protein yang berbeza terhadap prestasi struktur biosensor ISFET yang berbeza. Terdapat beberapa batasan biosensor ISFET seperti kekurangan elektrod keadaan pepejal yang baik, kepekaan parasit terhadap suhu dan cahaya serta ketidakstabilan parameter sensor yang bergantung kepada masa. Peningkatan pada struktur ISFET boleh menjadi pendekatan yang baik untuk meningkatkan prestasi ISFET. Objektif kedua penyelidikan ini adalah untuk membandingkan prestasi biosensor ISFET struktur nanoelektronik yang berbeza dari segi masa penyelesaian, kepekaan, dan selektiviti. Dalam projek ini, perisian sumber terbuka, nanohub BioSensorLab akan digunakan untuk mensimulasikan masa penyelesaian, kepekaan dan selektiviti biosensor. Protein sasaran ialah Liposom dan Bovine Serum Albumin (BSA) manakala bioreseptor ialah kolagen. Struktur berbeza biosensor ISFET telah disimulasikan dan dianalisis, iaitu ISFET planar, cylindrical nanowire, nanosphere dan biosensor FET double-gate. Dalam penyelidikan ini, kesan pekali resapan protein, struktur biosensor dan kepekatan analit terhadap masa mendap akan dianalisis. Seterusnya, sensitiviti bergantung pada struktur biosensor. Oleh itu, analisis dijalankan secara bebas untuk struktur biosensor yang berbeza. Selektif ditentukan oleh saiz molekul reseptor dan molekul parasit, kepekatan molekul sasaran dan molekul parasit. Daripada keputusan simulasi, masa mendap berkurangan apabila kepekatan analit dan pekali resapan protein meningkat. Di samping itu, masa mendap meningkat daripada planar dan double-gate, cylindrical nanowire kepada biosensor nanosphere. Untuk mendapatkan kepekaan tinggi dalam biosensor ISFET planar, lebar dan kepekatan elektrolit ditingkatkan manakala ketebalan dan panjang oksida dikurangkan. Untuk biosensor cylindrical nanowire, tingkatkan jejari, ketebalan oksida dan kurangkan kepekatan ion penimbal untuk meningkatkan sensitiviti. Seterusnya, untuk mendapatkan sensitiviti tinggi dalam double-gate FET, lebar, ketebalan oksida belakang dan ketebalan badan silikon perlu meningkat manakala ketebalan panjang dan oksida atas perlu berkurangan. Selektiviti adalah sama tanpa mengira struktur ISFET. Selektif yang tinggi boleh diperolehi dengan meningkatkan saiz molekul reseptor dan parasit, kepekatan molekul sasaran, dan mengurangkan kepekatan molekul parasit. Pekali resapan protein tidak mempunyai kesan terhadap sensitiviti dan selektiviti biosensor ISFET.

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LIST OF ABBREVIATIONS

β	-	Sensitivity Parameter
ψ_o	-	Electrostatic Potential
φ_f	-	Potential Difference Between the Fermi levels of Doped and Intrinsic Silicon
φ_{si}	-	Silicon Work Function
1-D	-	One-Dimension
2-D	-	Two-Dimension
3-D	-	Three-Dimension
Ag	-	Silver
AgCl	-	Silver Chloride
Al_2O_3	-	Aluminium Oxide
APTES	-	3-Aminopropyltriethoxysilane
Au	-	Gold
BSA	-	Bovine Serum Albumin
CAD	-	Coronary Artery Disease
C_{box}	-	Bottom Oxide Capacitance
cDNA	-	Complementary DNA
CorDNA	-	Cordyceps sinensis's DNA
COVID-19	-	Coronavirus Disease
C_{ox}	-	Oxide Capacitance
cTnI	-	Cardiac Troponins I
C_{tox}	-	Top Oxide Capacitance
DG	-	Dual-gate Mode
DGFET	-	Double-gate Field Effect Transistor
DIBL	-	Drain-induced Barrier Lowering
DNA	-	Deoxyribonucleic Acid
ENFET	-	Enzyme Field-effect transistor
E_{ref}	-	Reference Electrode Potential
GOD	-	Glucose Oxidase
GP-A	-	Ground Plane A

GP-B	-	Ground Plane B
HbA1c	-	Glycohemoglobin
HBV	-	Hepatitis B Virus
Ids	-	Drain Source Current
ISFET	-	Ion-sensitive Field-effect Transistor
k	-	Dielectric Constant
K_m	-	GOD Michaelis Constant
MATLAB	-	MATrix LABoratory
MOSFET	-	Metal Oxide Semiconductor Field-effect Transistor
MoS_2	-	Molybdenum Disulphide
NaCl	-	Sodium Chloride
n_{enz}	-	Enzymatic units per volume
NPBE	-	Nonlinear Poisson-Boltzman Equation
NR-ISFET	-	Dual-gate Nanoribbon-based Ion-sensitive Field Effect Transistor
pH	-	Potential of Hydrogen
PNA	-	Peptic Nucleic Acid
q	-	Charges
Q_B	-	Depletion Charges
Q_F	-	Sensor Surface Charges
Q_{ox}	-	Oxide Charges
Q_{ss}	-	Interface state charges
SG	-	Single Solution-gate Mode
Si_3N_4	-	Silicon Nitride
SiO_2	-	Silicon Dioxide
SMU	-	Source Measure Unit
SNR	-	Signal to Noise Ratio
SOI	-	Silicon-On-Insulator
SS	-	Subthreshold Swing
ssDNA	-	Untagged Single-stranded DNAs
std-GP	-	Standard Ground Plane Structure
Ta_2O_5	-	Tantalum (V) oxide
T_{BOX}	-	Back Oxide Thickness

T_{TOX}	-	Top Oxide Thickness
V_{BG}	-	Bottom Gate Bias
V_{FG}	-	Fluid Gate Bias
V_{th}	-	Threshold Voltage
UTBB	-	Ultra-Thin Body and Buried Oxide
Vfg	-	Forward Gate Voltage
WSe_2	-	Tungsten Diselenide
χ^{sol}	-	Surface Dipole of Target Solution

CHAPTER 1

INTRODUCTION

1.1 Problem Background

In recent years, biosensor has gained popularity in clinical treatment, pharmacy, biomedical and healthcare sectors due to its ability to ensure public safety while delivering health services to patients [1]. There are many types of deadly diseases in the world, including those that are fast-acting and those that progress slowly. For example, coronary artery disease (CAD), one of the heart diseases that caused 8.8 million deaths in year 2015 [2]. CAD is a slowly progressed disease that caused by various factors, for example high blood pressure, high cholesterol, and diabetes [2]. Besides, the recent outbreak disease in year 2020 has become our world's top 1 enemy and changed our lives radically. As of 20 January 2022, COVID-19 has infected more than 340 million people worldwide and caused over 5.6 million deaths as shown in Figure 1.1 [3]. Furthermore, proteins are needed by all living cells for structural and functional purpose. However, excessive intake or misuse of proteins can have negative impact towards human body. For example, accumulation of saturation fat and cholesterol in kidney or liver [4].

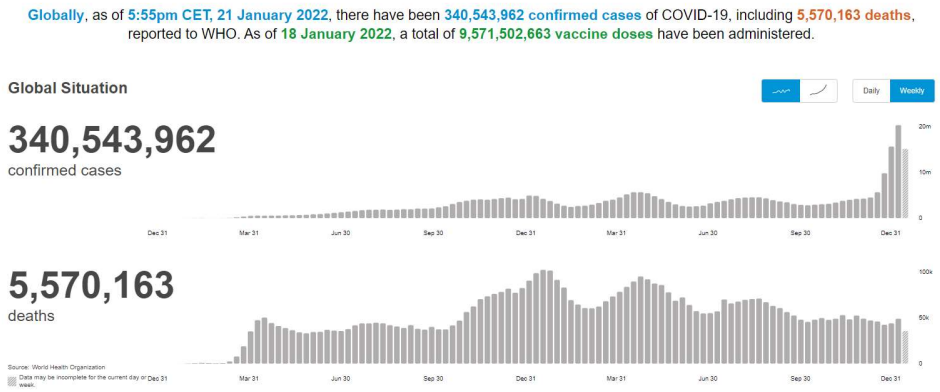

Figure 1.1 Confirmed cases and death counts of COVID-19 [3]

Biosensor can be used in detection of DNA, proteins, enzymes, and cells, which can aid in clinical diagnosis of diseases. It can be a considerable solution to help monitor the biological events in human body by providing screening infectious to early detection. Improved biosensors technology qualities allow the ability to detect disease and track the body's response to care [1]. It is critical to detect and diagnose infections, to prevent the virus from spreading to all body cells. Early therapy may increase the chances of a successful recovery. Hence, an efficient and effective biosensor should be a technology worth investing in.

1.2 Problem Statement

Protein is a chain of amino acids that plays an important part in the human body. Protein is crucial for the regulation of body tissues and organs, the repair of body cells, and the growth and development of human body, particularly in children and teenagers [5]. However, misuse of proteins can have harmful effects towards human body. For example, Liposome is used in medical field for drug delivery purpose due to its ability to encapsulate hydrophobic or hydrophilic drugs. However, the degradation of Liposome will result in the formation of undesired degradants, which will have harmful effects on cells or tissues. Besides, the instability of liposomes will cause drug leakage [6]. Furthermore, Bovine Serum Albumin (BSA) is a protein from cows, which being widely used as the protein concentration standard in various lab experiments. However, BSA can cause allergic reactions in human body [7]. Therefore, biosensor can be used to detect proteins to avoid the formation of dangerous effects towards human body.

Ion-sensitive field-effect transistor (ISFET) is a popular biosensor technology. However, there are several limitations of ISFET, such as lack of good solid-state electrodes, parasitic sensitivity to temperature and light, and time dependent instability of sensor parameters. Adoption of fluorescent labelling and parallel optical detection techniques were expensive and time-consuming ways of improving the ISFET performance [8]. To achieve fast detection of biomolecules with low concentration,

enhancement towards the structure of ISFET biosensor, such as increasing the surface to volume ratio could be a better approach.

1.3 Research Objectives

The objectives of the research are:

(a) To study the effect of different proteins on the performance of different structures of ISFET biosensor.

(b) To compare the performance of ISFET biosensors of different nanoelectronics structure in terms of settling time, sensitivity, and selectivity.

1.4 Project Scope

The scopes of this project are:

(a) The simulation tool used in this project is nanoHUB BioSensorLab.

(b) Liposome and Bovine Serum Albumin (BSA) are the proteins that will be used as the target analyte molecules for simulation and analysis.

(c) The bioreceptor is collagen.

(d) Different structures of ISFET biosensor include planar ISFET biosensor, cylindrical nanowire biosensor, nanosphere biosensor and double-gate FET biosensor will be simulated and analysed.

(e) The performance of different structures of ISFET biosensor on the proteins' detection can be evaluated based on settling time, sensitivity, and selectivity.

1.5 Project Contribution

The project contributions are:

(a) Help undergraduate or postgraduate students to build up their interest and understanding towards ISFET Biosensors.

(b) Inspire researchers to develop a more efficient ISFET biosensor in future by considering different structures of ISFET.

1.6 Thesis Outline

Gantt chart is used for proper planning and scheduling in completing this project. Table 1.1 is the Gantt chart planning for this project.

Table 1.1 Gantt Chart

Tasks	Oct-21	Nov-21	Dec-21	Jan-22	Feb-22	Mar-22	Apr-22	May-22	Jun-22	Jul-22
Problem formulation and literature review										
Submit synopsys										
Understanding how Nanohub BioSensor Lab works										
Obtain all the simulation results from Biosensor Lab for Planar and Cylindrical Nanowire Biosensor										
Project I presentation										
Proposal submission										
Obtain all the simulation results from Biosensor Lab for Nanosphere and Double-gate FET Biosensor										
Documenting and Thesis writing										
Project II presentation										
Report Submission										

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