DEVELOPMENT AND FABRICATION OF ION-SENSITIVE FIELD EFFECT TRANSISTOR (ISFET) FOR PH DETECTION, DNA IMMOBILIZATION AND HYBRIDIZATION

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Development and Fabrication of Ion-Sensitive Field Effect Transistor (ISFET) for pH Detection, DNA Immobilization and Hybridization

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LIST OF ABBREVIATIONS

pH	A measure of the acidity or alkalinity of a solution
ISFET	Ion-sensitive field-effect transistor
MOSFET	Metal oxide semiconductor field-effect transistor
BIOFET	Biologically sensitive field-effect transistors
GenFET	DNA-modified FET
DNA-FET	DNA-modified FET
ssDNA	Single stranded deoxyribonucleic acid
CMOS	Complementary metal–oxide–semiconductor
DNA	Deoxyribonucleic acid
PBS	Phosphate Buffer Solution
AutoCAD	Automated computer-aided design
HPM	High power microscope
AFM	Atomic force microscopy
EDAX	Energy dispersive x-ray spectroscopy
XRD	X-ray diffractometer
IV	Current voltage characteristic
I_D	Drain current
V_D	Drain voltage
μ_n	Electron mobility of the channel
b	Width of gate
L	Length of gate

C_o	Oxide capacitance per unit area
V_T	Threshold voltage
V_g	Gate voltage
V_{DSAT}	Saturation voltage
Φ_M	work function between gate metal
Φ_{Si}	work function between silicon
Q_{OX}	accumulated charge in the oxide
Q_{SS}	accumulated charge in oxide-silicon interface
Q_B	depletion charge in the silicon
E_{ref}	constant potential of the reference electrode
Ψ	chemical input parameter
χ^{sol}	surface dipole potential of the solvent
H^+	hydrogen ions
SiO_2	silicon dioxide
Al_2O_3	aluminium(III) oxide
Ta_2O_5	tantalum pentoxide
In_2O_3	indium(III) oxide
Si_3N_4	silicon nitride
HF	Hydrofluoric acid
H_2SO_4	Sulfuric acid
N	Nitrogen
CVD	Chemical vapor deposition
Na+	Sodium ions

K+	Potassium ions
LOCOS	Local oxidation of silicon
NH	Amine group
UV	Ultraviolet
SCE	saturated calomel electrode
Ag/AgCl	silver-silver chloride
Hg	Mercury
Cl	Chloride
IC	Integrated circuit
MOS	Metal–oxide–semiconductor
OH	Hydroxide
Ca^{2+}	Calcium ion
EnFET	enzyme-modified FET
ImmunoFET	immunologically modified FET
CPFET	cell-potential FET
IUPAC	International Union of Pure and Applied Chemistry
RNA	ribonucleic acid
dsDNA	double-stranded deoxyribonucleic acid
A	Adenine
G	Guanine
T	Thymine
C	Cytosine
VFB	flat-band voltage

N2	Nitrogen gas molecule
NH3	Ammonia
SSMCC	sulfo-succinimidyl 4-(*N*-maleimidomethyl) cyclohexane- 1-carboxylate
SNP	single nucleotide polymorphism
PR	Photoresist
Si	Silicon
RCA1	Wafer cleaning solution
RCA2	Wafer cleaning solution
DI	Deionized
DC	Direct Current
BOE	Buffered Oxide Etch
NaOH	Sodium hydroxide
APTES	3-aminopropyltriethoxysilane
R_s	Sheet resistance
HCl	Hydrochloric acid
H_2	Hydrogen gas molecule
3D	3 dimensional
A-OH=SiOH	Silanol group
BH= SiNH2	Amine group
S	Sensitivity
V_{th}	Threshold voltage

LIST OF SYMBOLS

mV	milivolt
°C	Degree celcius
%	Percentage
in.	inches
min	minute
Torr	Gas pressure measurement unit
W	Power measurement unit
nm	Nanometer
µM	Micro molar
g	gram
ml	mililiter
M	mole
µL	Microliter
Ω/sq	Ohm per square
Å	Angstrom
nm^2	Nanometer square
% V/V	Percentage of volume over volume

Pembangunan dan Fabrikasi Ion Sensitif Transistor (ISFET) Bagi Pengesanan pH, Immobilisasi dan Hibridisasi DNA

ABSTRAK

Fabrikasi ion sensitive transistor (ISFET) untuk pengesanan pH, immobilisasi dan hibridisasi DNA telah dilaporkan. Operasi ISFET adalah berdasarkan penyerapan cas pada permukaan membrane yang berinteraksi dengan larutan. Tesis ini menerangkan reka bentuk, fabrikasi dan pencirian ISFET untuk pengesanan pH, immobilisasi dan hibridisasi DNA. Empat photomasks telah digunakan dalam proses fabrikasi untuk menghasilkan ISFET. Peranti ISFET yang telah dihasilkan terlebih dahulu dibawa untuk pencirian morfologi diikuti dengan pencirian elektrik. Untuk analisis ISFET dalam larutan kajian, elektrod Ag / AgCl telah digunakan sebagai elektrod rujukan dan direndam dalam larutan pH yang berbeza. Keputusan yang dihasilkan oleh system pengukuran LabTracer 2.0 telah menunjukkan bahawa ciri IV peranti ISFET memberikan tindak balas linear. Larutan pH yang bersifat asid mengandungi ion H^+ berupaya menarik lebih banyak elektron ke dalam saluran pengaliran untuk merendahkan rintangan dan memberikan nilai arus yang lebih tinggi. Larutan alkali pula menolak electron jauh daripada saluran pengaliran sekaligus meningkatkan rintangan dan oleh itu, nilai arus adalah lebih rendah. Apabila diuji dengan larutan fosfat (PBS), graf menunjukkan trend arus menjunam apabila kepekatan PBS yang diuji semakin berkurangan. Adalah didapati bahawa peranti ISFET yang telah diuji mempunyai sensitiviti 43.13 mV/pH. Peranti ISFET telah menjalani proses DNA selepas pencirian elektrik dengan pH dan PBS. Immobilisasi dan hibridisasi DNA telah dikesan melalui nilai arus yang semakin menurun. Sebelum proses immobilisasi DNA dilakukan ke atas ISFET, permukaan silikon nitrat telah diubahsuai dengan tindak balas kimia untuk membolehkan membran ISFET untuk bergabung dengan probe DNA. Ia juga didapati bahawa penurunan kepekatan sasaran DNA dalam proses hibridisasi telah menyumbang kepada penurunan arus yang dikesan. Sebagai kesimpulan, ISFET silikon nitrat adalah peranti fleksibel yang boleh digunakan untuk mengesan pH dan juga untuk immobilisasi dan hibridisasi DNA.

Development and Fabrication of Ion Sensitive Field Effect Transistor (ISFET) for pH Detection, DNA Immobilization and Hybridization

ABSTRACT

The fabrication of ion sensitive field-effect transistor (ISFET) using silicon nitride (Si_3N_4) as the sensing membrane is reported. The operation of ISFET is based on the surface charge adsorption of the membrane-solution interface. This thesis describes the design, fabrication and characterization of ISFET for pH detection, DNA immobilization and hybridization. Four photomasks were utilized in the fabrication process to create the ISFET device. The fabricated ISFET device was first brought to morphological characterization before proceeding with the electrical characterization. For the analysis of ISFET in test solution, the Ag/AgCl electrode was used as the reference electrode immersed in different values pH buffer. The results were generated by LabTracer 2.0 measurement system which shows that IV characteristic of ISFET devices gives linear response. The acidic pH buffers contains H^+ ions which attract more electron into the conduction channel lowering the channel resistance giving higher value of current flow. While the alkaline pH buffers contains OH^- ions which pushed away the electrons from the conduction channel generating more positive holes increasing the channel resistance, thus giving a lower value of current flow. When tested with phosphate buffer solution (PBS), the curves show a decreasing trend of drain current with decreasing concentration of the PBS. It was found that the device has a sensitivity of 43.13 mV/pH. The ISFET device has undergo DNA processes after the electrical characterization with pH and PBS. The DNA immobilization and hybridization processes were detected through a drop in the drain current of the device. Prior to DNA immobilization, the silicon nitride surface was chemically modified to enable the ISFET sensing membrane for DNA probes coupling. It was also observed that with decreasing concentration of DNA complimentary targets in the hybridization process has contributed to the decreasing drain current detected. As a conclusion, the silicon nitride ISFET is a flexible device which can be used to detect pH as well as to perform DNA immobilization and hybridization.

CHAPTER 1

BACKGROUND

1.1 Introduction

In daily life, the pH plays an important role in human activities. The pH appears whenever other substances are diluted with water, specifically called a solution. The pH refers to the measure of the amount of hydrogen ions present in a solution. Solutions with pH lower than 7 are categorized as acidic while solutions with pH higher than 7 are said to be alkaline. The measurement of pH in a solution can be performed by a few methods. However, conservative ways of measuring pH is not very convenient which leads to the invention of a new device. The ISFET was invented by Bergveld in 1970 and was the first miniaturized silicon based chemical sensor. His work has shown that by omitting the metal gate from a MOSFET and leaving the oxide layer beneath to be exposed to a solution, the characteristics of the device are then affected by the ionic activities of the solution (Bergveld, 1970). This device gives plenty of advantages such as small size and weight, high reliability, fast response and low cost mass production. Moreover, it's possible field of applications varies from medicine, biotechnology, food industries, environmental monitoring and many more.

A BIOFET can be constructed from an ISFET by modifications made to the gate material as the ISFET allows the integration with biological element. These devices utilize the charge effect to transduce the recognizing phenomena of the DNA target probes bind with its complementary. In this project, the Genetic Field-Effect Transistor (GenFET) or better known as DNA-FET was fabricated. This device was made possible by immobilizing well defined sequences of single strand DNA (ssDNA) onto a transducer, which converts the specific recognition process of two DNA single strands through the hybridization event into measurable signal (Schöning & Poghossian, 2002). In this research, devices are produced to perform both pH measuring and DNA immobilization and hybridization process.

1.2 Problem Statement

There are some traditional pH measuring methods in the market such as the litmus papers and glass pH electrodes. These measuring methods are simple and giving considerably quick measurement results. However, they do have their disadvantages. Litmus papers rely on color indication which is not convenient for people with color blind difficulties. Moreover, litmus papers are not reusable after each use. Litmus papers also cannot be used for continuous monitoring of a process as it can be attacked by process solutions which can interfere the color change (Atkins & Paula, 1978). On the other hand, glass pH electrodes too are bulky and fragile. It also faces the risk of breaking and it is avoided in food industries. Glass pH electrodes cannot operate at temperature higher than 60 ℃ (Vonau & Guth, 2006). It requires frequent maintenance and high setup cost. Unlike the other pH measuring methods, ISFET is reusable, fast response, small in size and light in weight.

The material on the gate of an ISFET is a very important factor that determines the pH sensitivity of the device itself. The material of the gate must be able to detect specific ions of the sample test solutions, avoid hydration and prevent ion migration to the semiconductor layer (Cane, Gracia, & Merlos, 1997). Many researchers have been working on inorganic oxides as silicon dioxide has been identified as inadequate to function as pH sensing membrane. They have been experimenting with inorganic oxides in their works (Matsuo *et al*., 1981; Akiyama *et al*., 1982; Chan *et al*., 1987; Wong *et al*., 1989; Gimmel *et al*., 1989; Vlasov *et al*., 1990). Of the materials investigated, silicon nitride was found to be suitable as pH sensitive membrane with acceptable results (Matsuo *et al*., 1981). Therefore, silicon nitride is the good choice for ISFET considering it is also a material easily found in CMOS process foundries.

Considering both factors above, it has brought to the idea of fabricating a device that is able to perform both pH measurement and DNA detection. Current devices fabricated are normally made for single specific function. For this purpose, the silicon nitride has been chosen as the gate material as it allows DNA probes immobilization too, providing that some chemical modifications are made to its surface.

1.3 Research Objectives

The aim of this research is to design, fabricate and characterize ISFET based biosensor for DNA immobilization and hybridization process. The characterization will involve both surface morphological and electrical analysis to investigate the device working mechanism and also its sensitivity.

However, the specific objectives of this research are:

i. To study the ISFET device fabrication process using the revolutionized self-aligned method for MOSFET.

ii. To understand the working principles of ISFET and the mechanism of DNA immobilization and hybridization

iii. To evaluate the ISFET electrical characteristics using the IV system by testing with pH buffer solutions and phosphate buffer solution (PBS).

iv. To study the DNA immobilization and hybridization processes on ISFET silicon nitride gate.

v. To evaluate the ISFET device before and after DNA immobilization and hybridization.

1.4 Research Scopes

This research is embarked based on the following scopes:

i. To design four masks which include the source-drain mask, gate mask, contact mask and metallization mask. These masks will be designed by using AutoCAD tool and then printed on transparency sheets as the precision of the measurement is not the main concern of this project.

ii. To fabricate the ISFET device as the basic structure for DNA immobilization process. The device will be fabricated using the revolutionized self-aligned process for MOSFET.

iii. To characterize the optical and physical characteristic of silicon nitride gate by using high power microscope (HPM), atomic force microscopy (AFM), energy dispersive x-ray spectroscopy (EDAX), and x-ray diffractometer (XRD).

iv. To perform electrical characterization on ISFET using the IV curve technique with pH buffer solutions and phosphate buffer solution (PBS).

v. To perform surface modification, DNA immobilization and hybridization on the silicon nitride gate surface.

vi. To inspect the effect of DNA complimentary target concentration on ISFET.

1.5 Thesis Organization

This thesis consists of 5 chapters. Chapter 1 gives a general idea of the research to readers through the introduction, problem statement, objectives, significance of the project and project scopes.

Chapter 2 is the literature review which explains the fundamental theories of the working principles, device structure, device sensing layer properties and potential applications.

Chapter 3 describes the mask designs and mask dimensions, the ISFET fabrication processes, surface modification on silicon nitride using chemical solutions as well as DNA immobilization and hybridization procedures.

Chapter 4 contains the results obtained and data analysis of the research. The data obtained were tabulated and plotted into graphs for analysis. Discussion and explanation based on the results are presented in this chapter.

Last but not least, Chapter 5 summarizes the thesis findings based on the objectives that are set for this research and also some recommendation for future works to improvise the current device performance.