LOW POWER CMOS POTENTIOMETRIC CIRCUIT DESIGN FOR LABEL-FREE DNA DETECTION

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DEDICATION

To my beloved family and friends

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ABSTRACT

DNA detector is one of the main way to use in order to detect diseases, preventing crime and so on. The DNA detecting process is limited due to the bulky and expensive existing DNA detector machine. As the demand of the small, portable and inexpensive biosensor for point-of-care testing aid and medical diagnostic, the research and development of biosensor are increasing exponentially every year. The aim of this work is to develop an on-chip Complementary Metal Oxide Semiconductor (CMOS) biosensor circuit based on the charge-modulated field effect transistor (CMFET) for a label-free deoxyribonucleic acid (DNA) detection. This project focusing on low voltage and low power design potentiometric DNA detection circuit. Overall of detection circuit consists of two main circuits which are self-cascode source drain follower and two-stage differential amplifier. The proposed detection circuit is designed and simulates using 0.13 µm Silterra CMOS fabrication with 1.2 V supply. The power consumption of the improved source-drain follower circuit is 1.36 µW and with gain of 0.998 dB. The two-stage differential amplifier achives a voltage gain of 56.02 dB and high common mode rejection ration (CMRR) of 90 dB.

ABSTRAK

Pengesan DNA adalah salah satu cara utama untuk digunakan untuk mengesan penyakit, menghalang jenayah dan sebagainya. Proses pengesanan DNA terhad kerana mesin pengesan DNA yang besar dan mahal. Memandangkan permintaan biosensor yang kecil, mudah alih dan murah untuk bantuan pengujian point-of-care dan diagnostik perubatan, penyelidikan dan pembangunan biosensor semakin meningkat secara eksponen setiap tahun. Matlamat kerja ini adalah untuk membangunkan litar biosensor Logam Oksida Semikonduktor (CMOS) pada cip muatan berasaskan muatan transistor kesan medan (CMFET) untuk pengesanan asid deoxyribonucleic bebas DNA (DNA). Projek ini memberi tumpuan kepada voltan rendah dan reka bentuk kuasa rendah litar pengesanan DNA potentiometrik. Keseluruhan litar pengesanan terdiri daripada dua litar utama yang merupakan sumber pengalir keluar sumber cascode dan penguat berlainan dua peringkat. Litar pengesanan yang dicadangkan direka dan disusun menggunakan fabrikasi CMOS Silinder 0.13 μm dengan bekalan 1.2 V. Penggunaan tenaga litar pemangkin sumber yang lebih baik ialah 1.36 μW dan dengan kenaikan 0.998 dB. Penguat berlainan dua peringkat menghasilkan peningkatan voltan 56.02 dB dan nisbah penolakan mod biasa (CMRR) yang tinggi iaitu 90 dB.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CMFET	-	Charge Modulated Field Effect Transistor
ISFET	-	Ion Sensitive Field Effect Transistor
CMOS	-	Complementary Metal-Oxide Semiconductor
dsDNA	-	Double-Stranded Deoxyribonucleic Acid
ssDNA	-	Single-Stranded Deoxyribonucleic Acid
DNA	-	Deoxyribonucleic Acid
EDA	-	Electronic Design Automation
ADC	-	Analog to Digital Converter
MOSFET	-	Metal-Oxide Field Effect Transistor
POC	-	Point-Of-Care
SPICE	-	Simulation Program with Integrated Circuit Emphasis
FYP1	-	Final Year Project 1
FYP2	-	Final Year Project 2
UTM	-	Universiti Teknologi Malaysia

LIST OF SYMBOLS

ω	-	frequency
μ	-	micro
Ø	-	Phase
L	-	Length of Channel
V_{DD}	-	Supply voltage
V_{DS}	-	Drain to source voltage
$V_{DS(SAT)}$	-	Saturation voltage
V_{GS}	-	Gate to source voltage
V_{bias}	-	Bias voltage
A_V	-	Voltage gain
V_{TH}	-	Threshold voltage
W	-	Width of the channel

CHAPTER 1

INTRODUCTION

1.1 Background

As the demand of the small, inexpensive and rapid handheld of the biosensor increasing exponentially every year, the research and development on it also increasing as well. Most of the demand comes from the testing of point-of-care (POC)(Massimo Barbaro et al., 2006b; Maruyama, Terao, & Sawada, 2009). As the technology of Complementary Metal-Oxide Semiconductor (CMOS) introduces, this allows the integrating sensing unit with the transducer in a single chip become possible(B. Kim, Uno, & Nakazato, 2012). The main focus of scientists nowadays is more focusing on biosensor to detect deoxyribonucleic acid (DNA)(Maruyama et al., 2009).

Label-based DNA such as optical DNA microarray is matured method for health care and biological researchers. However, this method comes with bulky equipment and expensive price. This problem can be solved by using the method of label-free electrochemical DNA detection which can provide significant features such as low cost, high sensitivity, faster,

small size and also its compatibility with standard CMOS fabrication for future development and integration(Kaisti, 2017).

The architecture of the sensor as shown in Figure 1.1. The sensor is used to catch the response signal from the chemical, physical or biological property that were used to be tested. The sensor device can be categorized into three types of sensor and transducer namely electrochemical, mechanical and optical(W. Il Lee et al., 2017; Maruyama et al., 2009).

The sensor is used to convert the sample signal from the tested element to the output signal. After that, this output signal from the sensor then is converted into the understandable electric signal by using transducer. The output of the transducer is very small that has to be amplified by using the amplifier circuit and processing unit. The amplified signals from the amplifier circuit then are converted into digital form by using analog to digital converter unit before the output ready to be processed for signal processing unit(Kaisti, 2017).

Figure 1.1 shows the flow of the signal start form the sensory element detached to the sample used to test then go to the transducer circuit to convert to understandable signal then to the electronic system which consists of signal amplification circuit, analog to digital circuit and signal processing unit.

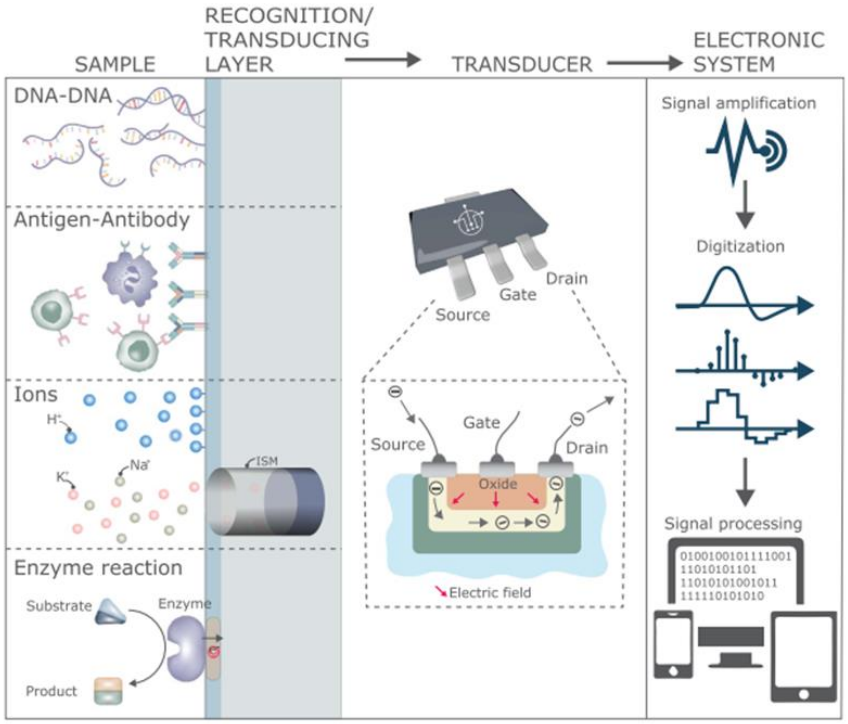

Figure 1.1: Architecture of the typical sensor system(Kaisti, 2017).

1.1.1 Deoxyribonucleic Acid

From generation to generation, Deoxyribonucleic Acid (DNA) is used for transmitting, copying and preserving information. Human's DNA contains genetic information such as height, eyes color and so on. Inside DNA contains a block called Nucleotides. Nucleotide is made up from deoxyribose and

phosphate group as a nitrogen base and sugar(Cai et al., 2016). There are four different nitrogen bases: adenine(A), guanine(G), cytosine(C) and thymine(T).

DNA is made up of two single strands that complementary to each other. The nitrogen base pairs, guanine(G) and cytosine(C) will only bond with each other, while adenine(A) and thymine(T) only will bond with each other(Yang, Chang, Yin, & Kuo, 2008). Figure 1.2 shows the double helix of DNA. As example, in order to form a double helix DNA, two single strands have to complementary to each other like one single strand contain a sequence such as CTAGG and the other strands should have GATCC to form a double helix. The double helix structure can be separated into two single-stranded by increasing temperature (approximate 95°C) or mechanical force(Massimo Barbaro et al., 2006a; Tracy, 2002; Wang et al., 2017).

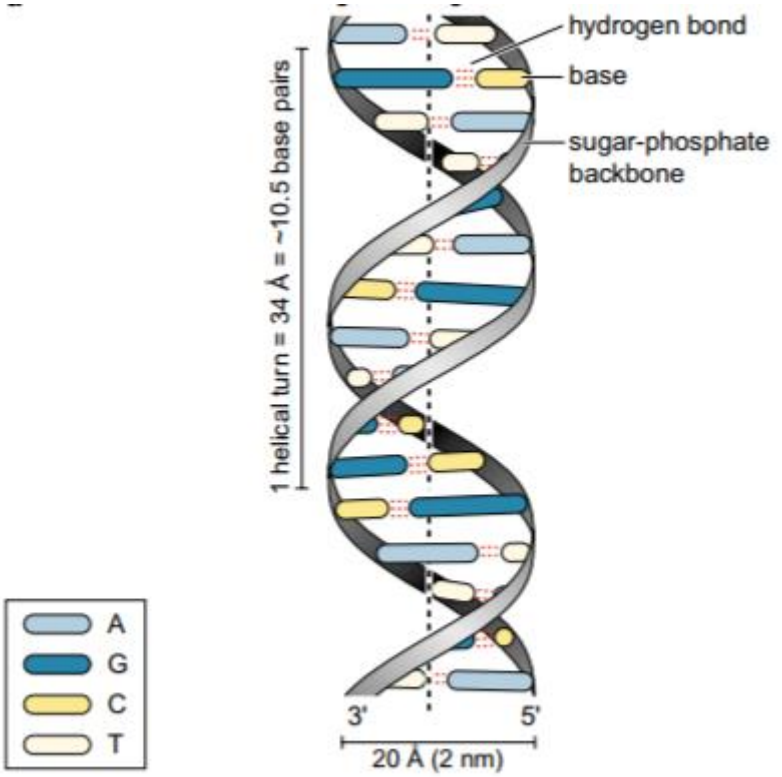

Figure 1.2: Diagram of the DNA double helix(Tracy, 2002)

DNA hybridization process is a binding event between two complementary single-stranded DNA (ssDNA) to form the double stranded DNA (dsDNA)(Tracy, 2002). The commonly used DNA detection method is shown in Figure 1.3. First, ssDNA(probe) will paced on the sensor area by using a chemical approach. Then, ssDNA with unknown sequence (target) will be in injected into the solution and hybridized if its sequence is complementary to the probe. If it is non-complimentary, then the hybridization will not occur(K. H. Lee et al., 2011). For the last step is wash process, the unbind target will be washed away and

only left dsDNA if the result is complementary hybridization(Maruyama et al., 2009)(Thewes et al., 2005).

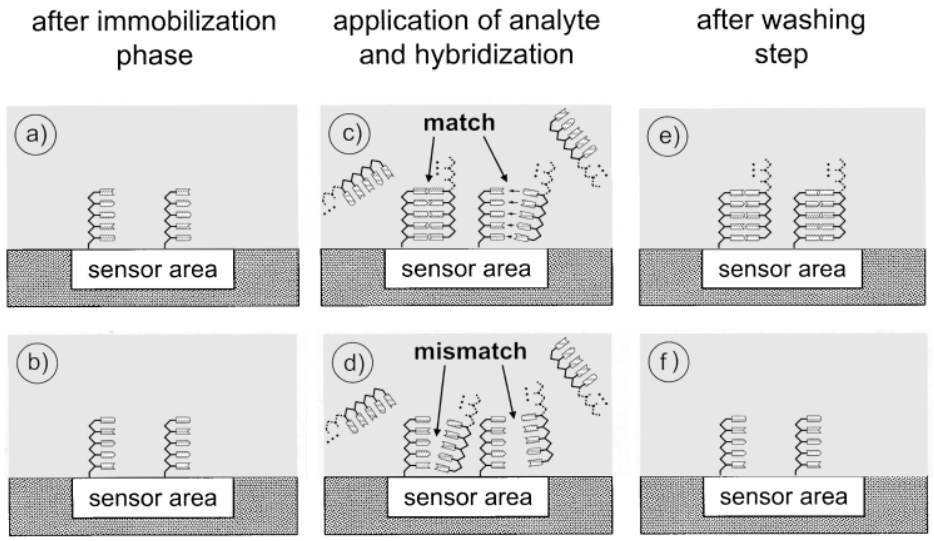

Figure 1.3: Hybridization of DNA. (a) and (b) Immobilization of ssDNA (probe) on the sensor area. (c) Hybridization occurs between complementary ssDNAs. (d) Hybridization will not occur for non-complementary ssDNAs. (e) Sensor area will left with dsDNA (f) Sensor area is left with ssDNAs (non-complementary hybridization) (Thewes et al., 2005)

1.1.2 Application of DNA Testing

As the DNA testing technology that comes from research and development CMOS sensor, this technology has resolved a lot of problems from different kind of aspects. For example,

cancer diagnosis, gene-based disease detection, and also infection or viral bacteria identification. Furthermore, this technology also used by the police department for DNA testing to identify criminals or victims in forensic investigation.

As the development of the microarray circuit for the sensing unit in a single detection circuit, the high volume of outputs will be generated in a single experiment. This will result on low cost for testing the genetic for consumer. Affordable price will encourage more people to take DNA testing to avoid any fatal diseases and also health monitoring.

1.2 Statement of the Problem

As the concern on growing issues such as health care, infectious disease and tailor-made medicine, a portable gene-based point-of-care testing (POC) system is needed. In order to develop a new system which can give the portability device so that it can be operated for anyone and anywhere with immediate results, a new biosensor chip must be developed(Kaisti, 2017). By using electrical detection approach with complementary metal oxide semiconductor (CMOS) integrated circuits, it has the advantages in eliminates the labeling process, real-time detection, high accuracy, compact equipment and low-cost.

1.3 Objectives of the Study

This project is conducted to achieve the following objective:

1. To design a label-free and fully integrated CMOS DNA biosensor based on potentiometric detection circuit.
2. To analyze the gain, power and others performance of the designed detection circuit

1.4 Scope of the Study

The scopes of the study are as below:

i. CMFET device is used as the potentiometric sensor in the detection circuit.
ii. DNA is chosen as the target biomolecules.
iii. Silterra 0.13 µm standard technology with 1.2 V supply is used in the design process.
iv. Mentor Graphic Pyxis is used as the simulation software in the design process.

1.5 Significant of the Study

The development of biosensor gives a lot of benefits towards mankind. The most common problems happen today is the portability of the device. The device for DNA detection is so bulky and complex. Therefore, the DNA testing only can be done in the laboratory. With the CMOS technology biosensor, all the readout and the electronic system integrated into a single circuit. Furthermore, as the consumption of the voltage supply of CMOS technology become smaller, the possibility for the biosensor circuit to be mobile and battery-operated become possible. In addition, the cost for a single test is very high. As the CMOS technology is used in the design of biosensor, it causing DNA test to become affordable since it can reduce in term of cost. This actually can help the middle group income to have the DNA test for early stage detection of the viral diseases.

1.6 Highlight on Research Methodology

In order to get the great output, the plan must be great. Therefore, it is important to plan the research methodology to ensure that all the work progressing well in order to achieve the goal. The research methodology that used in this project is as shown in Figure 1.2 below. First, the literature review on the available potentiometric sensor and array circuit is done in the beginning of the research.

Then, the next process is designing the schematics of the detection circuit. This circuit must be work together with the chosen potentiometric sensor. The technology used in the circuit is 0.13 µm standard CMOS. The expected 0.13 µm technology should be done in this project is in final year project 2. For final year project 1, this circuit been designed by using technology 0.18 µm CMOS technology.

The schematics design for final year project 1 is by using LTSPICE simulator. The expected simulator software used in the final year project 2 is Mentor Graphic Pyxis. If the circuit performance meet the requirements, then this circuit can move to the next process which is analyze performance target, then this project will considered finished.

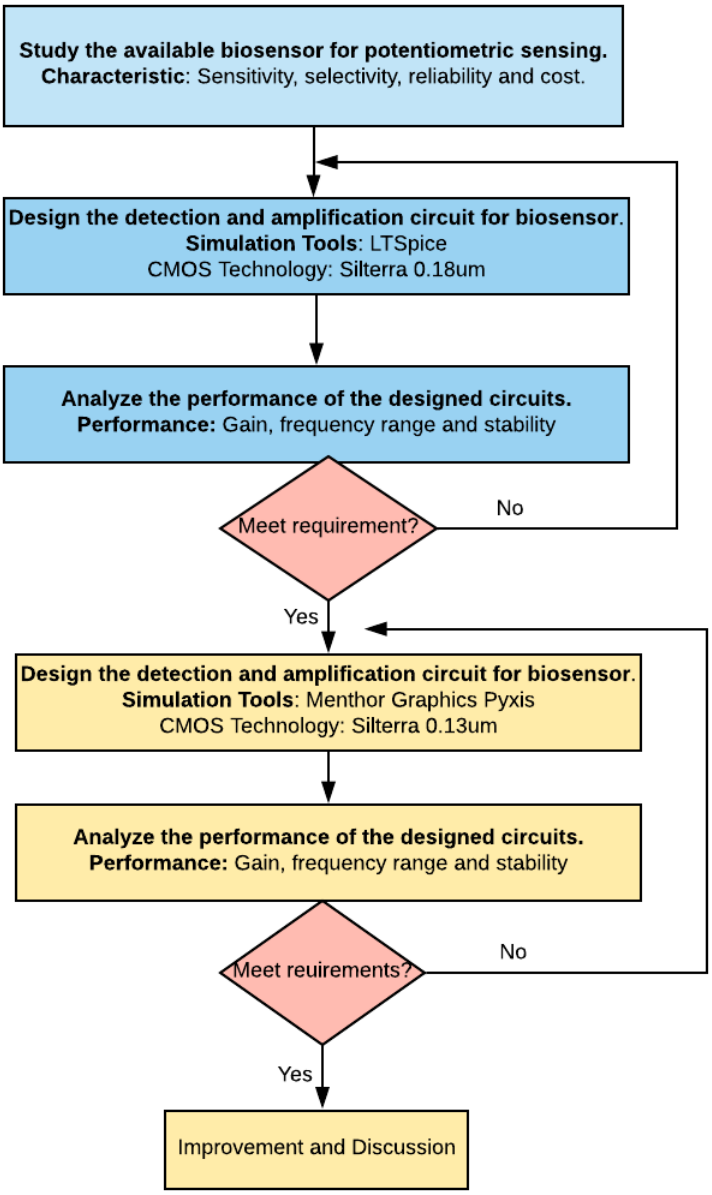

Figure 1.4 Research methodology used in this research

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