INTEGRATED OPTICAL MACH-ZEHNDER INTERFEROMETER FOR BIOSENSOR APPLICATION

by

KHOR KANG NAN

(1130110614)

A thesis submitted in fulfillment of the requirements for the degree of
Master of Science (Microelectronic Engineering)

School of Microelectronic Engineering
UNIVERSITI MALAYSIA PERLIS

2015

DECLARATION OF THESIS

Authors' full name : KHOR KANG NAN
Date of Birth : 6 JUNE 1988
Title : INTEGRATED OPTICAL MACH-ZEHNDER INTERFEROMETER FOR BIOSENSOR APPLICATION
Academic Session : 2011 – 2014

I hereby declare that the thesis becomes the property of Universiti Malaysia Perlis (UniMAP) and to be placed at the library of UniMAP. This thesis is classified as:

☐ **CONFIDENTIAL**	(Contains confidential information under the Official Secret Act 1972)*
☐ **RESTRICTED**	(Contains restricted information as specified by the organization where research was done)*
☐ **OPEN ACCESS**	I agree that my thesis is to be made immediately available as hard copy or on-line open access (full text)

I, the author, give permission to the UniMAP to reproduce the thesis in whole or in part for the purpose of research or academic exchange only (except during a period of ___ years, if so requested above).

Certified by:

____________________	____________________
SIGNATURE	**SIGNATURE OF SUPERVISOR**
KHOR KANG NAN	**DR. MUKHZEER MOHAMMAD SHAHIMIN**
IC NO: 880602-35-5377	
Date:	**Date:**

GRADUATE SCHOOL

UNIVERSITI MALAYSIA PERLIS

PERMISSION TO USE

In presenting this thesis in fulfillment of a post graduate degree from Universiti Malaysia Perlis, I agree that permission for copying of this thesis in any manner, in whole or in part, for scholarly purposes may be granted by my supervisor or, in their absence, by Dean of the Graduate School. It is understood that any copying or publication or use of this thesis or parts thereof for financial gain shall not be allowed without my supervisor's written permission. It is also understood that due recognition shall be given to me and to Universiti Malaysia Perlis for any scholarly use which may be made of any material from my thesis.

Requests for permission to copy or make other use of material in whole or in part of this thesis are to be addressed to:

Dean of Centre for Graduate Studies

Universiti Malaysia Perlis

No. 112 & 114, Tingkat 1,Blok A, Taman Pertiwi Indah

Jalan Kangar-Alor Setar, Seriab

01000 Kangar

Perlis Indera Kayangan

Malaysia

ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to my supervisor, Dr Mukhzeer Mohamad Shahimin for his assistance, patience and continued support throughout my project. His guidance his been essential to the progress of this project.

I would like to thank the staff of University of Malaysia Perlis, School of Microelectronic Engineering, Institute Nanoelectronic Engineering (INEE), School of Material Engineering for thier endless help in my project.

I also extend my special thanks to my family; my parents; Khor Hee Chuan and Heng Lang Hwang who have been tireless in giving me moral support and whom always pray for my success. I would like to thank my friend who have accompanied and supported me which had made my life bearable. Special thank to my girlfriend, Chong Pei Tee who has been supportive and patience throughout my project.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION

CHAPTER 2: LABEL-FREE OPTICAL BIOSENSOR FOR IDEAL SURVEILLANCE RDT

CHAPTER 3: METHODOLOGY

CHAPTER 4: RESULT AND DISCUSSION

CHAPTER 5: CONCLUSION AND FUTURE WORKS

LIST OF TABLES

LIST OF FIGURES

LIST OF NOMENCLATURE

μTAS	Miniaturized total analysis system
3D	Three dimensions
AC	Alternating current
AFM	Atomic force microscopy
AFRIM	Armed Forces Research Institue of Medical
Ar	Argon
ASSURED	Affordable; Sensitive; Specific; User-friendly; Rapid; Equipment free; Delivered to those who need it
BAW	Bulk acoustic wave
BPM	Beam propagation method
CDC	Center for disease control
CF	Complement fixation test
CF_4	Tetrafluoromethane
CFR	Case fatality rate
CMOS	Complementary metal-oxide silicon transistor
CMOS	Complementary metal-oxide-semiconductor
dB	Decibels
DC	Direct current
DENV	Dengue virus
DF	Dengue fever
DHF	Dengue hemorrhagic fever
DI	Deionized water
DL	Detection limit
DSS	Dengue shock syndrome
ELISA	Enzyme linked immunosorbent assay

F-20	Filmetric 20
FCCS	Fluorescence cross-correlation spectroscopy
FD-BPM	Finite difference beam propagation method
FET	Field effect transistor
FFT	Fast fourier transform
FWHM	Full width at half maximum
GIS	Geographical information system
GOF	Goodness of fit
HI	Hemaggluitnation inhibition assay
HPM	High power microscope
HRP	Horse-raidsh peroxidase
ICP	Inductive coupled power
ICT	Immunochromatography
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IO	Integrated optic
IO-MZI	Integrated optical Mach-Zehnder Interferometer
IUPAC	International Union of Pure and Applied Chemistry
JEV	Japanese encephalitis virus
LED	Light emitting diode
LPCVD	Low pressure chemical vapor deposition
LSPR	Long range SPR
MZI_250	MZI with waveguide thickness of 250nm
MZI_75	MZI with waveguide thickness of 75nm
NAAT	Nucleic acid amplification test

NEP	Noise equivalent power
NS1	Non-structural protein 1
OFIS	Optical fiber immunosesnor
PCR	Polymerase chain reaction
PMT	Photomultiplier tube
POC	Point of care
POI	Power overlap integral
PRNT	Plaque reduction neutralization technique
PVDI	Pediatric Dengue Vaccine Initiative
QCM	Quartz crystal microbalance
RDT	Rapid diagnostic test
RF	Radio frequency
RIU	Refractive index unit
RPD	Relative power versus distance
S/N	Signal to noise ratio
SAW	Surface acoustic wave
SDS	Sodium dodecyl sulfate
SF_6	Sulfur hexafluoride
Si_3N_4	Silicon nitride
SiON	Silicon oxynitride
SMF	Single-mode fibre
SOI	Silicon-on-insulator
SPR	Surface Plasmon resonance
TBEV	Thick-borne encephalitis virus
TE	Transverse electric
TIR	Total internal reflection
TM	Transverse magnetic

UV	Ultraviolet
VCSEL	Vertical-cavity-surface-emitting laser
WG_250	Rib waveguide with thickness of 250nm, depth of 1nm and width of 4µm
WG_75	Rib waveguide with thickness of 75nm, depth of 1nm and width of 3µm
WHO	World Health Organization
WNV	West Nile virus
XRD	X-ray diffraction
YFV	Yellow Fever virus
Sensitivity	Sensitivity of IO-MZI sensor which is defined as rate of change of phase of guided mode as cover refractive index varies. $\partial\varphi/\partial n_c$
Bulk Sensitivity	Sensitivity of evanescent field on cover layer which is defined as rate of change of effective index of guided mode as cover refractive index varies, $\partial N_{eff}/\partial N_c$
Surface Sensitivity	Sensitivity of evanescent field on adlayer layer which is defined as rate of change of effective index of guided mode as thickness of adlayer varies, $\partial N_{eff}/\partial d_f$

LIST OF SYMBOLS

$\partial N_{eff}/\partial\ d_f$	Surface sensitivity
$\partial N_{eff}/\partial\ N_c$	Bulk sensitivity
Δd_f	Change in adlayer thickness
Δn_c	Change in bulk index
ΔN_{eff}	Change in effective index
$\Delta \varphi_{min}$	Minimum phase change detectable
A and B	Process coefficient of oxidation process
A *and* B	Process coefficient of oxidation process
d	Rib depth
d_c	Penetration depth of mode into cladding layer
d_{eff}	Effective thickness
d_s	Penetration depth of mode into substrate layer
E_o	Electric field strength (V/m)
E_m	Electric field intensity
H	Rib height or thickness
h	Height of slab region of rib waveguide
h	Strain of polysilicon
H_x	Lateral width of Gaussian beam
H_c	Cladding thickness
H_m	Magnetic Field
H_o	Thickness of waveguide for single mode behavior
H_{opt}	Optimized thickness
H_s	Substrate thickness

H_y	Vertical width of Gaussian beam
k	wavevector of optical ray
k_x	transverse wavevector
L	Wafer length of simulation window
L_{in}	Input waveguide length
L_y	Y-branch bending length
L_{int}	Interaction length of sensing window
m	Mode index
N_{ad}	Refractive index of antibody
N_c	Refractive index of cladding layer
N_{eff}	Effective index
N_{effm}	Discrete effective index
N_g	Refractive index of guide layer
N_s	Refractive index of substrate layer
N_{si}	Refractive index of silicon wafer
$P(z)$	Power as function of propagation distance
$P_{2\pi}$	Maximum power detectable by photodetector
P_{in}	Power of laser source
P_{min}	Minimum power change detectable
Pol	Polarization
P_{out}	Output power of IO-MZI
P_x	Lateral position of Gaussian beam
P_y	Vertical position of Gaussian beam
S	Sensitivity of IO-MZI
S_{ad}	Surface sensitivity

S_c	Bulk sensitivity of waveguide
S_{sur}	Surface sensitivity
t	Oxidation time
t_{ox}	Oxide thickness
V	Visibility factor of power transfer function
W	Rib width
WTl	Lower wafer thickness of simulation window
WTu	Upper wafer thickness of simulation window
WW	Wafer width of simulation window
α / α_{total}	Total insertion loss
α_{in}	Input insertion loss
α_y	Excess loss of Y-branch splitter
α_p	Propagation loss of rib waveguide
β	Longitudinal wavevector or propagation constant
β_m	Discrete propagation constants
Δx	Lateral mesh for simulation
Δy	Vertical mesh for simulation
Δz	Propagation constant
$\theta_{c,c}$	Critical angle at cladding interface
$\theta_{c,s}$	Critical angle at substrate interface
θ_{im}	Incidence angle of each mode (mth)
λ	Wavelength of laser source
P	Power
ρ	Index for polarization

Interferometer Mach-Zehnder Bersepadu Optik untuk Aplikasi Penderia Biologi

ABSTRAK

Denggi merupakan masalah kesihatan yang semakin ketara dan melibatkan lebih daripada separuh populasi dunia. Disebabkan oleh kepesatan pertumbuhan penduduk dan perubahan iklim dunia, lebih 2.5-3 bilion orang, merangkumi lebih daripada 40% daripada penduduk dunia kini berisiko tinggi untuk menghidapi deman denggi. Malaysia, yang terletak berhampiran dengan garisan khatulistiwa, merupakan salah satu negara yang paling terjejas oleh denggi di rantau Pasifik Barat. Kes-kes deman denggi di Malaysia telah melebihi sasaran negara, iaitu 50 kadar insiden deman denggi bagi setiap 100,000 penduduk sejak 2005 sehingga kini. Kit ujian denggi amat diperlukan kerana ia boleh mempercepatkan process pengesanan awal denggi di mana-mana dengan masa yang singkat. Namun begitu, penggunaan kit ujian ini bagi pengawasan denggi amat terhad kerana disebabkan kos ujian yang tinggi dan kelemahan ketepatan ujian. Oleh sebab itu, kajian ini bertujuan untuk membangunkan penderia biologi yang menenuhi keperluan kit ujian bagi pengawasan denggi terutamanya di negara-negara membanggun, di mana sumber adalah terhad. Kajian ini menggunakan teknologi penderia biologi optik tanpa tanda dalam mereka-bentuk penderia biologi ini. Reka-bentuk Interferometer Mach-Zehnder bersepadu optik telah dijalankan berdasarkan kaedah simulasi yang menggunakan perbezaan terhingga tiga dimensi secara perambatan alur. Perisian OptiBPM dipilih kerana ia adalah mesra-pengguna dan ia membolehkan simulasi tiga dimensi yang diperlukan dalam kajian ini dilaksanakan. Konsep utama kajian ini adalah untuk mengoptimumkan prestasi Interferometer Mach-Zehnder bersepadu optik melalui pengoptimuman setiap komponen, iaitu pandu gelombang optik rabung, pemecah-Y dan penukar mod-saiz. Prestasi optima telah mencapai had pengesanan 5.448×10^{-7} unit indeks biasan, yang merupakan dapatan yang baru bagi penyelidikan seumpamanya, dengan menggunakan pandu gelombang rabung dengan lebar 3.5µm, kedalaman 1nm dan ketebalan 75nm. Tambahan pula, kepekaan penderia ini telah meningkat ke 5011* 2π rad disebabkan oleh panjang interaksi yang optima, iaitu 16mm.

Integrated Optical Mach-Zehnder Interferometer for Biosensor Application

ABSTRACT

Dengue is an emerging global health problem affecting over half the world's population. With the rapid pace of population growth and climate change, the population at risk of dengue has reached the figure of 2.5-3.0 billions, approximately 40% of the world's population. Malaysia, a dengue hyperendemic country located near the equator, is one of the most affected countries by dengue in Western-Pacific region. The national target for the incidence rate of DF/DHF cases, 50 cases per 100,000 populations, has long been exceeded since 2005 until now. Rapid diagnostic test is in great demand ever since, however the current RDT is not sufficient as an effective passive surveillance system due to the high cost and lack of accuracy. Hence, this study aimed to develop a dengue RDT that is not only have the characteristics of point-of-care (POC) diagnostic but also suits the criteria needed to achieve a large scale disease surveillance in most developing countries where resources are limited. Label-free optical biosensor had been proposed to realized an ideal surveillance RDT. The design of integrated optic Mach-Zehnder Interferometer (IO-MZI) biosensor had been carried out based on the simulation and fabrication method. Simulation of IO-MZI was carried out by using three-dimensional finite difference beam propagation method with the aim of sensitivity and detection limit optimization. OptiBPM software is selected because it is user-friendly and it allows three-dimensional simulation which is needed in this research. The main concept of this research is to optimize performance of IO-MZI through the optimization of each individual component which are rib waveguide, Y-branch splitter and mode-size converter. The optimized IO-MZI achieved detection limit of 5.448×10^{-7} RIU, which is the novelty of this research, with the use of rib waveguide with width of 3.5µm, depth of 1nm and thickness of 75nm. Besides, the sensitivity, S of the IO-MZI biosensor has been improved to 5011*2π rad because of the optimized interaction length of 16mm.

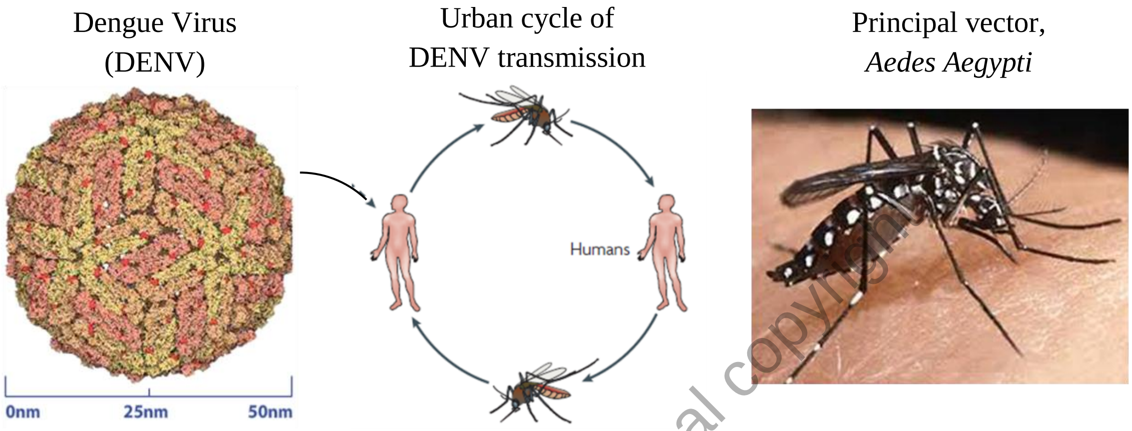
CHAPTER 1

INTRODUCTION

1.1 Background

Dengue is an emerging global health problem affecting over half the world's population (Duane J. Gubler & Clark, 1995; Guzman et al., 2010; Monath, 1994; E.-E. Ooi & Gubler, 2008). Due to the current induced disease burden in developing countries, dengue is considered as neglected tropical disease by World Health Organization (WHO). It is also the most important and widespread arthropod-borne viral infection in tropical and subtropical countries, mostly between latitudes 35^{o}N and 35^{o}S where dengue viruses (DENVs) were easily transmitted by the principal vector, *Aedes aegypti*.

Aedes aegypti, the primary vector of dengue original from Africa had evolved as a peridomestic mosquito species that is highly associated with human habitation (Monath, 1994). Dengue viruses is a flavivirus within the *Flaviviradae* family and there are four distinct serotypes of DENV namely DENV-1, DENV-2, DENV-3 and DENV-4 (WHO, 2009). Each of them can infect human and cause similar spectrum of illness. *Flaviviradae* family contains more than 70 viruses with some of them poses a threat to public health as Yellow Fever virus (YFV), West Nile virus (WNV), Japanese encephalitis virus (JEV) and thick-borne encephalitis virus (TBEV) (Rigau-Perez et al., 1998; Whitehead, Blaney, Durbin, & Murphy, 2007). Non-human primates are the original host of DENVs where the virus evolved slowly and entered urban cycle independently an estimated 500-1,000 years ago (Whitehead et al., 2007). Virus transmission cycle between human and vector mosquito is shown in Figure 1.1. The cycle is started with the non-infective mosquito vector taking a blood meal from a viraemic person and become infective after an incubation period of 8-10 days (Monath, 1994). The infective mosquito can then easily transmit the DENVs by simply probing the skin or taking a blood meal of humans.



(a) (b) (c)

Figure 1.1: Urban cycle (b) of dengue virus (DENV) (a) transmission between *Aedes aegyti* (c) and humans (Whitehead et al., 2007).

After an incubation period of 3-8 days, infection of DENV in human body produce a broad spectrum of clinical presentation ranging from asymptomatic, undifferentiated febrile illness, dengue fever (DF) and more severe dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) (Ministry of Health, 2010; WHO, 2009). The non-complicated dengue fever had been recognized for >200 years. The systemic DF is not life threatening but it can be fatal in its severe form; DHF and DSS. These severe dengue had only been recognized recently and the first report of DHF is being made in 1950s. (Whitehead et al., 2007) The case fatality rate (CFR) of DSS is 12-44% and it is this DSS that claims most life of dengue patients (Rigau-Perez et al., 1998).

With the rapid pace of population growth and climate change, the population at risk of dengue has reached the figure of 2.5-3.0 billion, approximately 40% of the world’s population (Guzman et al., 2010; PDVI, 2009). According to the report of