UNIVERSITI TEKNIKAL MALAYSIA MELAKA

Faculty of Electronic and Computer Engineering

DEVELOPMENT AND ANALYSIS OF NEAR-INFRARED SPECTROSCOPY TECHNIQUE FOR NON-INVASIVE BLOOD GLUCOSE MONITORING SYSTEM

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A thesis submitted
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DECLARATION

I declare that this thesis entitled "Development and Analysis of Near-Infrared Spectroscopy Technique for Non-invasive Blood Glucose Monitoring System" is the result of my own research except as cited in the references. The thesis has not been accepted for any degree and is not concurrently submitted in the candidature of any other degree.

Signature :……………………………………..........……………......….

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Date :……………………………………..........……………….….

APPROVAL

I hereby declare that I have read this thesis and in my opinion this thesis is sufficient in terms of scope and quality for the award of Master of Science in Electronic Engineering.

Signature :……………………………………..........…………….....….

Supervisor Name :…DR. WIRA HIDAYAT BIN MOHD SAAD…

Date :…………………………………................................…....

DEDICATION

For the sake of Allah, my Creator and my Master,

My great messenger, Muhammad S.A.W who taught us the purposes of life,

my beloved mother and father

ABSTRACT

Blood glucose monitoring is necessary for diabetes management therapy, where the common method used is an invasive glucose meter that involves finger prick for blood sample which can cause discomfort and skin injury. Painless monitoring of blood glucose would improve patient's quality of life, therefore the development and analysis of near-infrared (NIR) spectroscopy technique for non-invasive blood glucose monitoring system was proposed in this research. An appropriate conditional circuit for photodiode was constructed and 3D sensor casing was designed for output signal stability and noise elimination. The NIR light-emitting diode (LED) with wavelengths of 1050 nm, 1200 nm, 1300 nm, 1450 nm, and 1550 nm and Indium Gallium Arsenide (InGaAs) photodiode were employed in the in-vitro analysis and the Dextrose solution with different concentrations was used as samples. Based on the analysis on the result of the in-vitro experiment, the NIR LED with the wavelength of 1450 nm had the best coefficient of correlation (R^2) and it is used in the development of non-invasive blood monitoring device system. The in-vivo experiment utilises humans as subjects. The different area of the human body has a different absorption capability based on tissue composition and thickness. By considering that, three sensing areas, which are the finger, the area between the thumb and index finger, and earlobe, were selected for measurement. By referring to the measurement of the conventional invasive glucose meter, the earlobe area showed the best consistency of voltage output compared to other areas and this area was used to place the sensor prop for blood glucose measurement. A prototype of non-invasive blood glucose with the algorithm to convert voltage reading to glucose reading was developed based on the acquisition of the experiments that have been carried out. This prototype device has an LED indicator to alert the user about the condition of glucose level and Android application to monitor the blood glucose reading. In addition, this system of non-invasive blood glucose had also been developed with the temperature and motion parameters control for stability during the measurement. The Clarkson Error Grid (CEG) analysis was used to determine the accuracy of the measurement and the highest value of R^2 indicates a good correlation between the measurement of the proposed device system and conventional invasive glucose meter. Based on the tests performed, the algorithms constructed based on a single subject demonstrate a high reading accuracy The developed device system presented here has been proven to show a good correlation between NIR transmittance and blood glucose reading. However, as such an experimental device is not Food and Drug Administration (FDA) approved, it should only be used for academic or informative purposes, and should not be used for any medical decision-making process.

ABSTRAK

Pemantauan glukosa darah adalah satu keperluan kepada terapi pengurusan diabetes, dimana kaedah lazim yang digunakan adalah meter glukosa invasif yang melibatkan tusukan jarum pada jari untuk mendapatkan sampel darah yang boleh menyebabkan ketidakselesaan dan. kecederaan pada kulit. Pemantauan glukosa darah yang tidak menyakitkan akan meningkatkan kualiti hidup pesakit kencing manis dan oleh sebab itu, pembangunan dan analisis terhadap teknik spektroskopi inframerah dekat (NIR) untuk sistem pemantauan glukosa darah yang tidak invasif dicadangkan dalam kajian ini. Sebuah litar bersyarat yang sesuai untuk fotodiod dibina dan selongsong pengesan 3D direkabentuk untuk kestabilan isyarat keluaran dan penyingkiran bunyi hingar.. Diod pemancar cahaya (LED) NIR dengan jarak gelombang 1050 nm 1200 nm, 1300 nm, 1450 nm, dan 1550 nm dan fotodiod Indium Galium Arsenide (InGaAs) digunakan dalam analisis in-vitro dan larutan Dextrose dengan kepekatan yang berbeza digunakan sebagai sampel. Berdasarkan analisis keputusan eksperimen, NIR LED dengan panjang gelombang 1450 nm mempunyai pekali korelasi (R^2) terbaik dan ianya digunakan dalam pembangunan sistem peranti pengawasan darah yang tidak invasif. Subjek manusia digunakan dalam eksperimen in vivo sebagai sampel. Kawasan yang berbeza pada tubuh badan manusia mempunyai keupayaan penyerapan berbeza berdasarkan komposisi tisu dan ketebalan tisu. Setelah mengambil kira semua itu, tiga kawasan penderiaan, iaitu jari, kawasan antara jari ibu dan jari telunjuk, dan cuping telinga telah dipilih bagi pengukuran. Dengan merujuk kepada ukuran invasif meter glukosa konvensional, kawasan cuping telinga menunjukkan konsistensi terbaik voltan keluaran dan kawasan ini digunakan untuk meletakkan peralatan pengesan untuk pengukuran glukosa darah. Sebuah prototaip glukosa darah tidak invasif dengan algoritma untuk menukar bacaan voltan kepada bacaan glukosa dibangunkan berdasarkan hasil eksperimen yang telah dijalankan. Peranti prototaip ini mempunyai penunjuk LED untuk memberi amaran kepada pengguna mengenai keadaan aras glukosa dan aplikasi Android untuk memantau bacaan glukosa darah. Sebagai tambahan, sistem ini juga telah dibangunkan dengan kawalan suhu dan pergerakan parameter untuk kestabilan semasa ukuran. Analisis Grid Ralat Clarkson (CEG) digunakan untuk menentukan ketepatan pengukuran dan nilai R^2 yang tertinggi menunjukkan korelasi yang baik antara pengukuran sistem peranti yang dicadangkan dan meter glukosa invasif konvensional. Berdasarkan kepada ujian yang telah dijalankan, algoritma yang dibina berdasarkan subjek tunggal menunjukkan ketepatan bacaan yang tinggi. Sistem peranti yang dibangunkan telah terbukti menunjukkan korelasi yang baik antara kehantaran NIR dan glukosa darah. Walau bagaimanapun, kerana peranti percubaan itu tidak diluluskan oleh Pentadbiran Makanan dan Ubat-Ubatan (FDA), ia hanya boleh digunakan untuk tujuan akademik atau dapatan data, dan tidak boleh digunakan untuk proses membuat keputusan dalam perubatan.

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LIST OF ABBREVIATIONS

CGMS	-	Continuous Glucose Monitoring System
NIR	-	Near-infrared
UI	-	User Interface
BLE	-	Bluetooth Low Energy
3D	-	Three-Dimensional
LED	-	Light-Emitting Diode
InGaAs	-	Indium Gallium Arsenide
WHO	-	World Health Organization
ISF	-	Interstitial Fluid
FDA	-	US Food and Drug Administration
CE Mark	-	European Commission
CO2	-	Carbon Dioxide
MIR	-	Mid-infrared
IR	-	Infrared
OCT	-	Optical Coherence Tomography
ConA	-	Concanavalin A
MHC	-	Metabolic Heat Conformation
Hb	-	Haemoglobin
SNR	-	Signal-to-Noise Ratio

Ge	-	Germanium
Si	-	Silicon
PbS	-	Lead Sulfide
Insb	-	Indium Antionide
PbSe	-	Lead Selenide
FGT	-	Fasting Glucose Test
OGTT	-	Oral Glucose Tolerance Test
RMSEP	-	Root-Mean Square Error of Prediction
R2	-	Prediction Correlation Coefficient
Ge	-	Germanium
Si	-	Silicon
PbS	-	Lead Sulfide
SEP	-	Standard Error of Predictions
EGA	-	Error Grid Analysis
PCB	-	Printed Circuit Board
PLA	-	Polylactide
DC	-	Direct Current
PTC	-	Positive Temperature Coefficient
NTC	-	Negative Temperature Coefficient
UV	-	Ultraviolet
IDE	-	Integrated Development Environment
SMBG	-	Self-Monitoring Blood Glucose
ADC	-	Analogue to Digital Converter
IC	-	Integrated Circuit

LIST OF PUBLICATIONS

The research papers produced and published during the course of this research are as follows:

1. Salam, N.A.B.A., bin Mohd Saad, W.H., and Salehuddin, F., Manap, Z.B., Karim, S.A. and Radzi, S.A., 2017. Comparative Study of Different Near-Infrared (NIR) Wavelengths on Glucose Concentration Detection. Journal of Telecommunication, Electronic and Computer Engineering (JTEC) 10(1), pp.2-6.
2. Saad, W.M., Salam, N.A., Salehuddin, F., Ali, M.A. and Karim, S.A., 2017. Study on Different Range of NIR Sensor Measurement for Different Concentration of Glucose Solution. International Journal of Human and Technology Interaction (IJHaTI), 1(1), pp.13-18.
3. Salam, N.A.B.A., bin Mohd Saad, W.H., Manap, Z.B. and Salehuddin, F., 2016. The Evolution of Non-invasive Blood Glucose Monitoring System for Personal Application. Journal of Telecommunication, Electronic and Computer Engineering (JTEC), 8(1), pp.59-65.

Attended conference:

1. International Conference on Telecommunication, Electronic and Computer Engineering (ICTEC) 2017
2. International Conference on Telecommunication, Electronic and Computer Engineering (ICTEC) 2015

CHAPTER 1

INTRODUCTION

1.1 Project background

Diabetes is described as a syndrome of metabolism diseases due to abnormal blood glucose levels in the body. Among Malaysians nowadays, diabetes has become one of the most common diseases (World Health Organization (WHO), 2016). Diabetes is a lifelong illness as the patient is fully dependent on medicines that should be taken on the advice of the doctor to help supply or improve insulin function in the body itself. It can also cause many other diseases that can lead to several complications to the patients. Diabetes is a condition where there is an abnormal level of glucose in the human blood. In the human organism, glucose is the main carrier of the energy and the recommended glucose level varies from 4.9 mmol/L to 5.9 mmol/L within two to three hours after a meal for a healthy individual (Frederick Chee and Tyrone Fernando, 2007). Normally, blood glucose level increases slightly after the meal is taken and the abnormal increases of glucose level in the blood may be caused by the body that loses the ability to produce sufficient insulin or the failure of the body to respond properly to the insulin that has been produced by the pancreas.

In the long term, diabetes can affect other health complications to the patients. Diabetes-related complications include damage to large and small blood vessels, which can lead to heart attack and stroke, and problems with the kidneys, eyes, feet, nerves, and skin as illustrated in Figure 1.1. The risk of most diabetes-related complications can be reduced