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A Multiplexed Impedance Analyser for Biosensing Applications

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Report submitted in partial fulfilment of the requirements of the module Project (E) 448 for the degree Baccalaureus in Engineering in the Department of Electrical and Electronic Engineering at Stellenbosch University.

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Abstract

English

The English abstract.

Afrikaans

Die Afrikaanse uittreksel.

Contents

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Nomenclature

Variables and functions

$p(x)$	Probability density function with respect to variable x.
$P(A)$	Probability of event A occurring.
ε	The Bayes error.
ε_u	The Bhattacharyya bound.
B	The Bhattacharyya distance.
s	An HMM state. A subscript is used to refer to a particular state, e.g. s_i refers to the i^{th} state of an HMM.
$\mathbf{S}$	A set of HMM states.
$\mathbf{F}$	A set of frames.
$\mathbf{o}_f$	Observation (feature) vector associated with frame f.
$\gamma_s(\mathbf{o}_f)$	A posteriori probability of the observation vector $\mathbf{o}_f$ being generated by HMM state s.
μ	Statistical mean vector.
Σ	Statistical covariance matrix.
$L(\mathbf{S})$	Log likelihood of the set of HMM states $\mathbf{S}$ generating the training set observation vectors assigned to the states in that set.
$\mathcal{N}(\mathbf{x}\|\mu, \Sigma)$	Multivariate Gaussian PDF with mean μ and covariance matrix Σ.
a_{ij}	The probability of a transition from HMM state s_i to state s_j.
N	Total number of frames or number of tokens, depending on the context.
D	Number of deletion errors.
I	Number of insertion errors.
S	Number of substitution errors.

Acronyms and abbreviations

AE	Afrikaans English
AID	accent identification
ASR	automatic speech recognition
AST	African Speech Technology
CE	Cape Flats English
DCD	dialect-context-dependent
DNN	deep neural network
G2P	grapheme-to-phoneme
GMM	Gaussian mixture model
HMM	hidden Markov model
HTK	Hidden Markov Model Toolkit
IE	Indian South African English
IPA	International Phonetic Alphabet
LM	language model
LMS	language model scaling factor
MFCC	Mel-frequency cepstral coefficient
MLLR	maximum likelihood linear regression
OOV	out-of-vocabulary
PD	pronunciation dictionary
PDF	probability density function
SAE	South African English
SAMPA	Speech Assessment Methods Phonetic Alphabet

Chapter 1

Introduction

1.1. Background

Biosensors are defined as devices that measures biological and chemical reactions through the use of a physical transducer mechanism which in turn generates signals porportional to the concentration of an analyte in a sample. [1] This allows for the detection of various biological elements such as biomarkers which can be used to monitor health conditions or diagnose diseases.

Designing a low-cost easy to use device to take readings from biosensors, would thus provide a valuable tool for the early detection of diseases such as cancer. This would decrease the need for expensive labratory testing and allow for lower cost and more regular testing of patients using a point-of-care device. Having a multiplexed device, able to take readings from multiple biosensors, would allow a single blood sample to be taken and multiple tests to be run on it with minimum involvement from a healthcare professional.

1.2. Project Objectives

This is a multifaceted project that aims to develop a low-cost, easy-to-use device for reading biosensors. The system design objectives for the device include:

- Developing a circuit that allows a microcontroller to read a biosensor through the use of Electrochemical Impedance Spectroscopy (EIS). This entails conditioning the sinusoidal signal generated by a DAC and measuring the current response from the biosensor through an ADC.
- This measurement circuitry needs to be multiplexed to allow for multiple biosensors to be read in turn without the need for human intervention.
- The microcontroller should be able to filter and process the biosensor data to determine the concentration of the analyte in the sample.
- The device needs to be able to communicate these results in a clear and user-friendly manner. This will be done through the use of a LCD screen on the device as well as a web interface that can be accessed through a smartphone or computer.

- The device should be battery powered, low-cost and easy to use, thus allowing for widespread adoption and use in various environments.

1.3. Project Scope

NOT THE DESIGN OF Biosensors NOT TESTING WITH REAL BLOOD (We arent qualified for that)

1.4. Chapter Overview

Chapter 1: Introduction

Provides an overview of the motivation, background, objectives, scope, and structure of the report.

Chapter 2: Literature Review

Reviews relevant research and technologies in speech recognition and neural networks.

Chapter 3: Methodology

Describes the methods and approaches used in the project, including data collection and model development.

Chapter 4: Experiments and Results

Presents experimental setup, results, and analysis.

Chapter 5: Discussion

Discusses findings, limitations, and implications of the results.

Chapter 6: Conclusion and Future Work

Summarizes the work and suggests directions for future research.

Chapter 2

Literature Review

2.1. Biosensors

Biosensors are employed in applications such as disease monitoring, drug discovery, and detection of pollutants, disease-causing micro-organisms and markers that are indicators of a disease in bodily fluids (blood, urine, saliva, sweat). [1]

2.1.1. Background on Biomarkers

A biomarker is an objective measure that that gives an indication of the biological processes happening inside the body at a given moment. [2] They are physical substances found in the body that can be measured. The concentration of biomarkers differs between healthy individuals and individuals with diseases, thereby aiding in diagnosis and monitoring of diseases. [3] Some biomarkers are easy to measure (such as blood pressure, body weight, etc.) while others require tests of blood, urine or tissue samples. [2]

This project will focus on the detection of biomarkers found in blood samples such as the CA-19 biomarker used for pancreatic cancer detection. Note: Verduidelik bietjie oor CA-19. The concentration of these biomarkers in blood can give an indication of the presence and progression of a variety of diseases, including many types of cancer. [4]

2.1.2. Types of Biosensors

A biosensor consists of an analyte, a bioreceptor and a transducer mechanism combined with the electronics needed to process the signal. [1] The analyte is the substance of interest (such as biomarkers) that needs detection. Bioreceptors are molecules such as enzymes, cells, DNA or antibodies that specifically recognise the analyte. These bioreceptors produce a signal (in the form of light, heat, pH, charge or mass change, etc.) when they interact with the analyte. [1] Antibody based biosensors are the type of biosensor that will be used to detect biomarkers in this project.

Antibodies are produced by vertebrates as part of their immune response to foreign organisms or substances (called antigens). They are the most common biorecognition element used in biosensors. [5] Antibodies are Y-shaped cells that can be divided into two

distinct regions. The top of the Y is variable and binds to a specific antigen depending on the amino acids present in this region. The amino acids present in the constant region (the bottom of the Y) is similar between different classes of antibodies (within the same species of animal). [5] This constant region binds to the substrate of the biosensor during immobilization, leaving the variable region free to bind with antigens. [6]

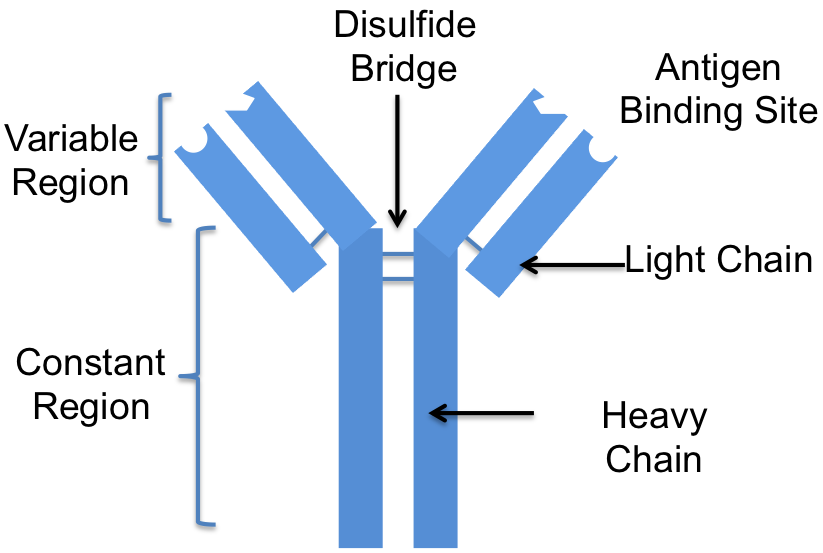

Figure 2.1: Example figure inserted using a LaTeX Workshop snippet.

2.1.3. Transducer Mechanisms

The number of biological binding events indicates the concentration of the analyte in the sample. These binding events change the electrical properties of the biosensor, specifically the complex impedance. Thus, in order to convert the bio-recognition event into a measurable signal, a transducer mechanism is needed [1]. There are various types of transducer mechanisms that can be used in biosensors, including optical, piezoelectric and electrochemical transducers. EIS Noem fardaic vs Capacitive sensors. Ons is capacitive.

2.2. Signal Processing

2.2.1. Analogue Electronics

2.2.2. Digital Processing

2.2.3. Calculating Impedance

2.2.4. Extrapolating from Impedance to Concentration

2.3. Interface

2.3.1. ESP32

2.4. Related Works

Chapter 3

Design

3.1. Functional Design Overview

Discuss wat ons wil bereik en hoe ons dit gan opbreek. Beskryf hoe die circuit die beginsels van biosensors en EIS in ag moet neem, basies wat dit moet doen, hoekom multiplexing en ja dan hoe daai overall doel in gedeeltes opgebreek word.

3.1.1. DUT

3.1.2. Multiplexer

3.1.3. Excitation

3.1.4. Voltage Measurement

3.1.5. Current Measurement

3.1.6. DSP (STM)

3.1.7. User Interface (ESP etc)

3.2. Detailed Design

Gaan meer in diepte oor circuitry maar steeds met generic/ideal coponents. Cover circuitry van elke section, design requirements etc soos 10mV excitation bv. Wat wil ons bereik en dan hoe daai translate na technical requirements en dan die circuitry. Wys LT Spice circuits en sims van elke seksie en combined. Cost is n spec (¡R4500).

3.2.1. DUT

Data van Dr Ebrahim, en dan kry circuit model van daai af.

3.2.2. Voltage Reference

Verduidelik dat ons bipolar signaling kort sonder DC offset, en ipv +- 1.65V doen ons 1.65V virtual ground.

3.2.3. Excitation Stage

Verduidelik hoekom ons 3.3V output signal van DAC gebruik (maximise range theory). Verduidelik hoekom ons 10mV soek gebasseer op DUT circuit model. Gee brief overview van beginsels van opamp em somme. Verduidelik dan hoekom LPF Anti Aliasing nodig is gebasseer op Frequency domain theory en al daai. Calcs rondom hoe naby aan signal freq cutoff moet wees, dus variable LPF. Te expenny om self te bou dus eerder IC. Was voor en na Filter van DAC sims.

3.2.4. Voltage Measurement

Why is voltage measurement needed when we already know our output voltage. Discuss what to consider when amplifying signal. Discuss LPF en hoekom n volle variable een nie needed is nie (dit is meestal vir noise nie vir anti aliasing van sampling nie, want DAC AA behoort dit te keer).

3.2.5. Current Measurement

Beskryf hoekom current measurement so belangrik is. Wat ons range van currents is. Beskryf beginsels van TIA including somme en circuit analysis. Dan hoekom TIA nie al die amplifications doen nie en why PGA needed is. Raak dan briefly ook op die LPF beginsel selfde as voltage.

3.2.6. Multiplexing

Discuss why multiplexing needed (both why multiple sensors are useful and why not just dedicated circuitry for each sensor, including why thats not needed). Discuss options that I considered and why we settled on signal relays. Briefly discuss tree design and why that saves on relays (Double pole double throw vs net manually connect disconnect each relay to central line).

3.2.7. DSP

Discuss why DSP needed, why microcontroller and not other DSP. Beskryf basies hoe ons filtering gaan doen etc. Die formules en konsepte van freq domain en hoe ons capacitance calc en dan na concentration gaan. Los die details van code en libraries en issues vir Firmware Design section.

3.2.8. User Interface

Baie briefly discuss wat ons vereis van

3.3. Component Selection

Watse komponente ons kies, why en watse aspekte ons consider het en hoekom daai specs belangrik is. How een komponent die ander beinvloed. Wys sims met spesifieke komponent seleksies. Wys calcs vir passive compoinent selections.

3.4. PCB Design

Beskryf filosofie en idees wat mee ingegaa het. Briefly discuss general PCB design principles wat design geguide het (Analogue ground plane etc). Beskryf beperkings van PCB manufactures wat inag geneem moes word (PCB size, layers, trace width via diamtre etc.). Noem briefly hoekom PCB in China eerder as Uni laat maak. Gaan deur design logic en discuss probleem met TIA. Include maybe final PCB diagram en langs dit foto van manufactured PCB.

3.5. Firmware Design

Inculde flow diagram.

3.5.1. ESP

Vertel van wat ons wil bereik en hoekom. Discuss libraries used. Discuss maybe issues rondom C6 en hoe dit gesolve is en hoekom die C6 steeds die rgete keuse was.

3.5.2. STM

Probleme met arm library te groot. Discuss met flow chart hoe DMA en als met DAC en ADC interact en dan UART en badies program flow. Delve into limits van STM en maybe briefly setup van DAC en ADC.

Chapter 4

Testing & Validation

4.1. PCB Testing

4.1.1. Voltage Reference Load Testing

4.1.2. Excitation Stage Testing

4.1.3. Voltage Measurement Testing

4.1.4. Current Measurement Testing

4.1.5. Multiplexing Testing

4.1.6. Complete System Test Without & With MCU

4.2. Validation

4.2.1. Test on Calibration Cell

4.2.2. Test on Saline Solution

4.2.3. Discussion of Results

Chapter 5

Summary and Conclusion

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Appendix A

Project Planning Schedule

This is an appendix.

Appendix B

Outcomes Compliance

This is another appendix.