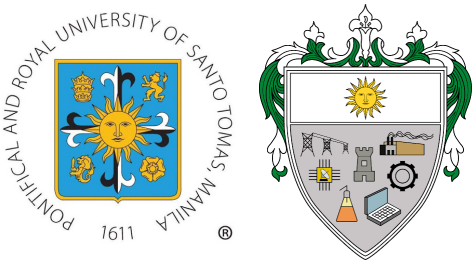

Write the title of your thesis here

A thesis submitted in partial fulfilment
of the requirements for the degree of
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Abstract

This is just a sample abstract for demonstration purposes only. Understanding the brain functions requires the exploration of the activity dynamics and interactions of large neuronal circuits. Two-photon calcium imaging, coupled with the use of genetically encoded calcium indicators (GECIs), is widely used in monitoring large targeted neuronal populations because of its capability to provide single-cell spatial resolution recording in deep brain structures. However, although revolutionary GECIs have sufficient signal-to-noise ratio to resolve single action potentials, there are still several issues that need to be addressed to accurately infer neural activity from raw calcium imaging data. Issues such as neuropil contamination and movement artefacts during imaging of animal models pose problems for the automatic detection and segmentation of neuronal signal sources in two-photon calcium imaging data. In this study, the author presents a standardised computational pipeline that is capable of accurately extracting activity information from automatically segmented cells when performing a comprehensive analysis and exploration of imaging data of any cell model. The whole framework was tested on *in vivo* two-photon calcium imaging data obtained from the mouse hippocampus. Furthermore, the proposed hybrid cell detection and segmentation method was tested on a manually labelled dataset and compared its performance with other existing approaches. It has been shown that *NeuroSEE* has clearly outperformed the other methods in detecting and segmenting cells resulting to a success rate of 75.4%, as compared to the highest success rate of 67.5% of other methods. Hence, the proposed pipeline has shown promising results and has demonstrated that efficient artefact correction and the integration of morphology- and activity-based approaches lead to a more accurate extraction of neural information.

Acknowledgements

[NOTE]: This is just a sample acknowledgement statement. Kindly modify this accordingly.

This work could not have been successfully accomplished without the help of many people.

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Chapter 1

Introduction and Literature Review

[NOTE]: This is just a sample text for the purpose of demonstration only. Please ignore the succeeding texts and edit the contents below accordingly. Elucidating how the brain works remains an immense challenge within science. There is still a huge gap between microscopic brain structures and their associated functions. Bridging this gap demands the exploration of the activity dynamics and interactions of large neuronal populations.

Disruption of complex neuronal circuits can often result to brain disorders, where the destabilisation of neuronal network activity could contribute to cognitive impairments. [1] One of the most common types of brain disorders is dementia – a neurodegenerative disease that is associated mainly with loss of memory. According to the World Health Organization (WHO), approximately 50 million people in the world are suffering from this neurodegenerative disease, but as many as 78% of which do not have proper diagnosis. If trends continue and no action is taken, these numbers are expected to increase to 82 million in 2030 and to an alarming number of 152 million in 2050. More particularly, about 60-70% of these patients are suffering from AD, which is characterised by the death of nerve cells and loss of connections between them.

In order to understand the biology of different brain disorders and to make substantial advances in the treatment of neurodegenerative diseases, it is necessary to improve our understanding of how neural circuits process information. Although much is known about the neural circuits and molecular pathways required for normal hippocampal functions, the processes by which AD disables the brain region remain to be defined. Furthermore, despite much research, there is still no acceptable cure for any neurodegenerative disease. While there are a number of disease models and even several promising treatment approaches, there have been difficulties in transferring apparent success in animal models into successful human trials. One potential reason is that the effect of neurodegenerative disease on memory circuit dynamics is not well understood, nor is the effect of therapeutic strategies on information flow in hippocampal-cortical circuits.

Several methods have been proposed to facilitate the exploration of the activity dynamics and interactions of large neuronal populations in the hippocampus – the part of the brain responsible during learning and behaviour. In recent years, two-photon calcium imaging – a state-of-the-art imaging and optogenetics technique – has become a popular choice in studying the dynamics of large neuronal circuits. It has the capability of providing single-cell spatial resolution recording and monitoring of large targeted neuronal populations in deep brain structures over a relatively long

period of time.

Additionally, various image analysis tools have been proposed to aid the analysis of two-photon calcium imaging data. However, these existing tools usually vary from lab to lab and may differ based on the cell models they used. The aim of this project, therefore, is to develop a standardised computational pipeline that is capable of accurately extracting activity information from automatically segmented cells when performing a comprehensive analysis and exploration of two-photon calcium imaging data of any cell model. The proposed framework was made compatible with other analysis tools in order to promote interoperability and reuse of data. This will set the foundation for the characterisation of the spatiotemporal dynamics of neural cortical circuits involved in memory encoding and recall during the progression of Alzheimer's disease.

1.1 Two-Photon Imaging

One of the most widely used imaging techniques in neuroscience today is two-photon imaging - a technique proposed by Denk et al. in 1990 [2]. It is a three-dimensional imaging technology based on the nonlinear excitation of fluorophores. It has gained much interest among experimental neuroscientists due to its capability of providing long-term single-cell spatial resolution recording and monitoring of large targeted neuronal populations, while providing high sensitivity, lower phototoxicity and greater penetration depths in deep brain structures.

Chapter 2

Problem Statement and Research Objectives

2.1 Problem Statement

One of the most widely used imaging techniques in neuroscience today is two-photon imaging - a technique proposed by Denk et al. in 1990 [2]. It is a three-dimensional imaging technology based on the nonlinear excitation of fluorophores. It has gained much interest among experimental neuroscientists due to its capability of providing long-term single-cell spatial resolution recording and monitoring of large targeted neuronal populations, while providing high sensitivity, lower phototoxicity and greater penetration depths in deep brain structures.

2.2 Research Objectives

2.2.1 Main Objective

2.2.2 Specific Objectives

Chapter 3

Methods and Research Design

3.1 Automated Analysis Pipeline

The proposed *NeuroSEE* pipeline consists of two parallel stages that separately process two-photon movies and behavioural magnetic tracking data. This framework is made compatible with other analysis tools through the integration of the *NWB* format. It is also made compatible with either single-channel or two-channel two-photon calcium imaging data that consists of green (GCaMP6) and red (mRuby) channels.

Appendix A

Other Supplementary Figures

Appendix B

Source Codes

Bibliography

[1] S. A. Romano, V. Pérez-Schuster, A. Jouary, J. Boulanger-Weill, A. Candeo, T. Pietri, and G. Sumbre, "An integrated calcium imaging processing toolbox for the analysis of neuronal population dynamics," *PLoS computational biology*, vol. 13, no. 6, p. e1005526, 2017.

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