DETERMINING THE MULTI-CURRENT SOURCES OF MAGNETOENCEPHALOGRAPHY BY USING FUZZY TOPOGRAPHIC TOPOLOGICAL MAPPING

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ABSTRACT

The human brain is an extremely complex system performing demanding information processing tasks rapidly. It consists of billions of neurons, each connected to others through thousands of synapses or interconnections. This huge network has many electric and chemical processes that can be measured in various ways. Magnetoencephalography (MEG) is a technique of measuring and recording the minute and very weak magnetic fields generated by the currents in the neurons. There are two types of problems in MEG, the forward problem and the backward or the inverse problem. The forward problem deals with finding the magnetic fields when the current source distribution is given or known. On the other hand, the inverse problem is to find the neural current source distribution given a series of magnetic fields measurements. This study has proposed the model FTTM2 (Fuzzy Topographic Topological Mapping Version 2) which is an extension to the novel mathematical modeling FTTM1 (Fuzzy Topographic Topological Mapping Version 1). The model FTTM2 comprises four components namely the Image Contour Plane (IC), Base Image Plane (BI), Fuzzy Image Field (FI) and Topographic Image Field (TI). In the process of applying FTTM2, emphasis is made on its first component, the IC where two different algorithms are being applied to the data. The first is the fuzzy *c*-means (FCM) algorithm which is used to determine the region where the current sources lie and also to approximate the number of current sources. The second is the seed-based region growing (SBRG) algorithm which is used to confirm the number of current sources available in the system by automation. Two theorems and three corollaries are derived and proven as theoretical basis of the proposed system. Finally, FTTM2 is tested on the generated and experimental data and subsequently verified using forward and backward calculations.

ABSTRAK

Otak manusia adalah suatu struktur yang kompleks yang melaksanakan pemprosesan maklumat dengan tangkas. Otak terdiri daripada ribuan juta neuron yang berkait antara satu sama lain melalui ribuan jaringan. Jaringan ini pula mengandungi banyak proses elektrik dan kimia yang boleh diukur dengan pelbagai cara. Magnetoencephalography (MEG) adalah suatu teknik mengukur dan merekod medan magnet yang amat kecil dan lemah yang dihasilkan oleh arus yang mana arus itu pula terhasil oleh tindakan neuron. Terdapat dua permasaalahan di dalam MEG iaitu masalah ke hadapan dan masalah ke belakang. Masalah ke hadapan melibatkan pengiraan medan magnet apabila kedudukan arus diketahui. Sebaliknya, pengiraan ke belakang melibatkan pengiraan kedudukan arus apabila hanya nilai-nilai medan magnet diketahui. Penyelidikan ini telah mengesyorkan model FTTM2 ("Fuzzy Topographic Topological Mapping Version 2") yang mana ia adalah model yang telah diunjurkan dari FTTM1 ("Fuzzy Topographic Topological Mapping Version 1"). Model FTTM2 ini terdiri dari empat komponen iaitu Image Contour Plane (IC), Base Image Plane (BI), Fuzzy Image Field (FI) dan Topographic Image Field (TI). Dalam proses mengaplikasikan FTTM2, tumpuan diberikan pada komponen pertama (IC) yang mana dua algoritma berbeza digunakan. Algoritma pertama ialah penggunaan fuzzy c-means (FCM) yang dapat menentukan lokasi bagi kedudukan arus dan dapat menganggarkan bilangan arus. Algoritma yang kedua melibatkan penggunaan seed-based region growing (SBRG) yang berupaya menentupastikan bilangan arus secara automasi. Untuk menguji kebolehgunaan kedua-dua algoritma ini, dua teorem beserta tiga korolari diterbitkan dan dibuktikan. Akhir sekali, FTTM2 diujikan ke atas data yang diperolehi dari simulasi dan juga dari ujikaji dan seterusnya dibuktikan dengan pengiraan ke depan dan ke belakang.

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LIST OF SYMBOLS AND ABBREVIATIONS

General symbols

A, B, C,	-	Arbitrary set (crisp or fuzzy)
A = B	-	Set equality
$A \neq B$	-	Set inequality
$A \subset B$	-	Proper set inclusion
$A \subseteq B$	-	Set inclusion
$A \cap B$	-	Set intersection
$A \cup B$	-	Set union
$A \setminus B$	-	Set difference
[a, b]	-	Closed interval of real numbers between a and b
(a, b]	-	Interval of real numbers open in a and closed in b
[a,b)	-	Interval of real numbers closed in a and open in b
(a, b)	-	Open interval of real numbers between a and b
G_{min}	-	The smallest possible gray level value
G_{max}	-	The largest possible gray level value
$\{x_1, x_{2}, x_3,\}$	-	Set of elements x_1, x_2, x_3, \dots
$\{x: p(x)\}$	-	Set determined by property p
$(x_1, x_{2_1}, x_3,)$	-	<i>n</i> -tuple
i, j, k,	-	Arbitrary identifiers (indices)
$N_4(p)$	-	The 4-neighbours of <i>p</i>
$\left[x_{ij}\right]$	-	Matrix
E	-	Element of
¢	-	Not an element of
Э	-	There exist (at least one)

-	For all
-	Set of real numbers
-	Set of n-tuple of real numbers
-	Universal set
-	Empty set
-	Membership grade of <i>x</i> in fuzzy set A
-	Euclidean norm
-	Definition
-	Intersection of two fuzzy sets
-	Union of two fuzzy sets
-	Minimum of $x_1, x_2, x_3,, x_n$
-	Maximum of $x_1, x_2, x_3, \dots, x_n$
-	The weighting exponent
-	Fuzzy partition matrix
-	Set of cluster centres

Magnetism

B _z	- The magnetic fields data measured on the top of the head (at $z = 0$)
$\boldsymbol{B}_{y(\text{left})}$	- The magnetic fields data measured on the left side of the head (at $y = 0$)
$\boldsymbol{B}_{y(right)}$	- The magnetic fields data measured on the right side of the head (at $y = 0.15$)
μ_0	- The permeability in free space
μ	- Material permeability
Ι	- The magnitude of current flow in a conductor
θ_1	- The angle between a line parallel to the segment in the direction of the current flow and the line joining the starting point of the segment A to the measurement point
θ_2	- The angle between a line parallel to the segment in the direction of the current flow and the line joining the end point of the current segment to the measurement point

r	-	The perpendicular distance between the current source and the measurement point on a plane
ŕ		The unit perpendicular distance
BZ	-	The absolute value of B_z
max(BZ)	-	The maximum value of <i>BZ</i>
min(BZ)	-	The maximum value of <i>BZ</i>
max(max(BZ))	-	The maximum among all the maximum values of BZ
max(max(BZ))	-	The minimum among all the minimum values of BZ
I_z	-	The image data in the range of [0, 255]
$\max(I_z)$	-	The maximum value of the fuzzified data
$min(I_z)$	-	The minimum value of the fuzzified data
μ_{I_z}	-	The fuzzified image data in the range [0, 1]
μ_{B_z}	-	The fuzzified magnetic fields values in the range [0, 1]
<i>x</i> , <i>y</i> , <i>z</i>	-	Cartesian coordinates
B_{x}	-	The <i>x</i> -component of the magnetic fields
B_{y}	-	The <i>y</i> -component of the magnetic fields
B_0	-	The magnetic fields data when current is not flowing
B_c	-	The magnetic fields data when current is flowing
B_n	-	The net magnetic fields data obtained from the difference between B_c and B_0
h	-	The distance between the current source and the measurement plane
d	-	The distance between the two extrema of the magnetic field contours
Ζ	-	The defuzzified values

В	- Magnetic fields vector
Н	- Magnetic field intensity
$\hat{\mathbf{a}}_{\phi}$	- The unit vector along the concentric circular path of the magnetic field lines
â _r	- The unit vector along the perpendicular line from the line current to the field point
$\hat{\mathbf{a}}_{\mathbf{I}}$	- The unit vector along the line current

Abbreviations

MEG	-	Magnetoencephalography
SQUID	-	Superconducting Quantum Interference Device
FTTM1	-	Fuzzy Topographic Topological Mapping Version 1
FTTM2	-	Fuzzy Topographic Topological Mapping Version 2
FCM	-	Fuzzy c-Means
SBRG	-	Seed-Based Region Growing
MC	-	Magnetic contour plane
BM	-	Base magnetic plane
FM	-	Fuzzy magnetic field
TM	-	Topographic magnetic field
IC	-	Image contour plane
BI	-	Base image plane
FI	-	Fuzzy image field
TI	-	Topographic image field
ROI	-	Region of interest
S 1	-	Current segment 1
S2	-	Current segment 2
MUSIC	-	Multiple signal classification
FEM	-	Finite element method
BEM	-	Boundary element method
ICA	-	Independent component analysis

- ECD Equivalent current dipole
- SEFs Somatically evoked magnetic fields
- VEFs Visually evoked magnetic fields
- PC Partition coefficient
- PE Partition entropy
- Prop_E Proportion exponent
- CSV Compactness and separation validity
- PSPs Postsynaptic potentials
- MNE Minimum norm estimates
- LHe Liquid helium
- RHR Right-Hand Rule
- MLE Maximum likelihood estimation

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CHAPTER 1

INTRODUCTION

1.1 Introduction

The human brain is the most important organ in our body. It is also the most sophisticated creation known to exist. Therefore, understanding how the brain works is one of the greatest challenges ever faced by mankind. The brain fulfills several important functions such as processing of sensory information, the programming of motor and emotional responses, the storage of information and learning. These complex tasks are carried out by the interconnected sets of neurons. There are at least 10^{10} neurons in the outermost layer of the brain, the cerebral cortex (Penfield and Rasmussen, 1950). This is the part which differs most from the brain of other animals (Devinsky, 2001). This cerebral cortex is a greatly convoluted sheet of cells, about 3 mm thick, consisting of small grooves (sulci), large grooves (fissures) and bulges between them (gyri). The neurons are the active cells units in a vast signal handling network, which include 10^{14} interconnections or synapses. When information is being processed, small currents flow in the neural system and produced a weak magnetic field, which can be measured noninvasively by a device known as Superconducting Quantum Interference Device (SQUID) magnetometer, placed outside the skull, provided that thousands of nearby neurons act synchronously (Hamalainen et al., 1993).

The brain consists of two hemispheres, separated by the longitudinal fissure. The left and right halves, in turn are divided into lobes by two deep grooves. The Rolandic fissure runs down the side of both hemispheres, while the Sylvian fissure is almost horizontal (see Figure 1.1). There are four lobes in both halves of the cortex: frontal, parietal, temporal and occipital. Each lobe contains many different areas that have different functions. Most regions of the cortex have been mapped functionally (Hamalainen *et al.*, 1993). Figure 1.1 below shows some of the important structural landmarks and special areas of the cerebral cortex.



Figure 1.1 The important parts of the human brain (left side)

The primary somatosensory cortex, which receives tactile stimuli from the skin, is located posterior to the Rolandic fissure. The area in the frontal lobe just anterior to the Rolandic fissure contains neurons concerned with the integration of muscular activity: each site of the primary motor cortex is involved in the movement of a specific part of the body (Hamalainen *et al.*, 1993).

The nervous system is the most complex and delicate of all the body systems. At the center of the nervous system is the brain. The brain sends and receives messages through a network of nerves. These nerve cells or the neurons are the basic functional unit of the nervous system. Figure 1.2 is an illustration of the structure of the neuron.



Figure 1.2 (a) Schematic illustration of a pyramidal neuron and three magnified synapses, (b) pyramidal neuron (Hamalainen *et al.*, 1993).

The neuron is a nerve cell specialized for the reception, interpretation and the transmission of electrical messages. They function like computer chips, analyzing and processing information and then sending signals through the nerve fibers. Basically, a neuron consists of a cell body that receives electrical messages from other neurons through contacts called synapses located on the dendrites or on the cell body. The dendrites are the parts of the neuron specialized for receiving information from stimuli or from other cells. If the stimulus is strong enough, the neurons transmit an electrical signal outward along a fiber called an axon. The axon or nerve

fibre, which may be as long as 1 meter carries the electrical signal to the muscles, glands or other neurons.

The two principal groups of cortical neurons are the pyramidal and the stellate cells. The former are relatively large; their apical dendrites from above reach out parallel to each other, so that they tend to be perpendicular to the cortical surface. Since neurons guide the current flow, the resultant direction of the electric current flowing in the dendrites is also perpendicular to the cortical sheet of gray matter.

In the human brain, there are more than several hundred millions of neurons connecting with each other and working for auditory and visual information processing. In these neurons, ion currents flow while these neurons are involved in the information processing. The ion current goes out of the neurons and flows in the conductive brain. It is these ion currents that produce the magnetic fields which flows according to the Right-Hand Rule (RHR) (Sadiku, 1995). Amazingly, this magnetic field can emerge out of the head through the brain, the skull, the cerebrospinal fluid and the scalp without receiving any distortion. This outstanding characteristic of magnetic fields becomes important in the studies of Magnetoencephalography (MEG).

MEG is a revolutionary medical imaging technology that provides unprecedented insight into the workings of the human brain through the measurement of electromagnetic activity. It is a technique of recording and measuring the minute and very weak magnetic fields produced by electrical activites in the brain (Hamalainen *et al.*, 1993). By measuring the magnetic fields created by the electric current flowing within the neurons, MEG identifies brain activities associated with various functions in real time with millimeter spatial accuracy. MEG is also completely non-hazardous since the human subject is not exposed to x-rays, radioactive tracers or to time-varying and strong static magnetic fields. Furthermore, MEG is noninvasive since it permits studies of the brain without opening the skull.

Different parts of the brain produce different patterns of magnetic waves (signals). Diseased brains can produce abnormal magnetic signals. The special feature of MEG is that it can be used to determine which brain regions are malfunctioning. It can also identify specific foundation regions of the brain such as auditory and visual cortex. Stimuli such as sounds or pictures will activate specific portions of the brain in characteristic sequences. MEG examines neuromagnetic (a near synonym of MEG, meaning the study of neuronal activity by means of magnetic fields) activity changes during this stimulation and pinpoints the location of functional regions. This helps determine if the sequence of activation has been perturbed by disease. MEG can be used to accurately localize sources within the brain. This information is useful in the field of medicine especially for pre-surgical functional mapping assessment of pathological functional deficits, neuropharmocological investigations, trauma assessment and a growing list of research investigations in neuroscience and psychiatry. Furthermore, by using MEG, one can measure the activity of the brain in real time. This means that the brain can be observed "in action" rather than just viewing a still image.

In MEG studies, the weak magnetic fields are measured with the sensitive device known as SQUID magnetometer. This device only works at a temperature of -270 degrees Celcius, which requires that it be kept in a large container of liquid helium. Figure 1.3 illustrates the arrangement of the magnetometer that is placed above a patient's head while the patient is in a lying position.



Figure 1.3 Detection of cerebral magnetic fields using a SQUID magnetometer (Hamalainen *et al.*, 1993)

MEG measurements are normally carried out inside a special magnetically shielded metal room. This is due to the fact that the magnetic signals from the brain are extremely weak as compared to the ambient magnetic field variations. Thus, the rejection of the outside disturbances is of utmost importance. Significant magnetic noise is caused for example, by fluctuations in the earth's geomagnetic field, moving vehicles and elevators, radio, television and microwave transmitters and the omnipresent power-line fields.

1.2 Background of the Research

The neurons in the brain normally generate electrochemical impulses that act on other neurons, glands, and muscles to produce human thoughts, feelings and actions. When there is any disruption of the electrical processes, the neurons may function abnormally. Epilepsy or seizure disorder is a condition in which clusters of nerve cells, or neurons in the brain sometimes signal abnormally. In epilepsy, the normal pattern of neuronal activity becomes disturbed (Penfield and Jasper, 1954), causing strange sensations, emotions and behaviors, or sometimes convulsions, muscle spasms and loss of consciousness. During an epileptic seizure, neurons may fire as many as 500 times a second, much faster than the normal rate of about 80 times a second. These seizures can last anywhere from a few seconds to a few minutes, and are usually spontaneous and uncontrolled. According to Hari (1996), the first clinical application of MEG is in the determination of epileptic foci. Physiologically, the epileptic foci refer to the location of the current sources, which generate the corresponding magnetic fields.

In spite of advances in antiepileptic medication, seizures in some patients cannot be controlled adequately. About 10 % - 20 % of all epileptic patients ultimately suffer from medically intractable epileptic seizures (Yung and Hsiang, 2002). Neurologists often suggest surgery to resect the problematic cells. However, the surgery can never be successful unless treated at the exact location of those problematic cells. Hence, it is crucial to determine the epileptogenic focus precisely before choosing the surgical procedure, that is, a presurgical localization plays an essential role in neurosurgical planning. This is to avoid injury to the primary sensory-motor cortices during the procedures (Lueders et al., 1983; Gallen et al., 1995), thus reducing the risk of the patient being left with a permanent functional deficit such as paralysis or loss of speech and sensation. As MEG is an established technique that can measure and record the very weak magnetic fields, it can therefore be adopted to determine or locate the epileptogenic focus in epileptic patients. The weak magnetic fields produced by the cerebral electrical activities in the brain that occurs during epileptic seizure measured by the MEG can serve as a presurgical measure. The main purpose of measuring these magnetic fields is to locate the electrical activity and to determine its distribution in the brain (Risto et al., 1994).

In MEG, there exist two types of problems involving the forward and the backward (inverse) problems. The forward problem involves calculating the observable variables (magnetic fields) caused by the current sources. On the other hand, the inverse problem involves estimating the location, orientation and the magnitude of the current sources from the results of the magnetic fields measurements. These two problems can be presented using the corresponding models: the forward model and the backward model. Figure 1.4 below illustrates the forward model.



Figure 1.4 The forward neuromagnetic modeling

The backward model is illustrated in Figure 1.5 below;



Figure 1.5 The inverse neuromagnetic modeling

Until now, all methods used to solve the inverse problems depended on prior data. Clarke (1989), Hamalainen *et al.* (1993), Baillet and Garnero (1997), Philips *et al.* (1997) and Hasson and Swithenby (1999) applied the Bayesian approach, which allows the introduction of *a priori* information. Ricardo *et al.* (2000) applied the independent component approach (ICA) to the analysis of MEG recordings. Boris *et al.* (2004) and De Munck *et al.* (2004) used the maximum likelihood estimation (MLE) approach. These approaches are based on statistical methods that involve

loads of data. These kinds of models are also said to be the data-based models. Unfortunately, these models are limited by the computational burden where the computing time is unnecessarily long and hence makes the process of solving the problem tedious.

As opposed to the above model, Tahir *et al.* (2000) proposed a novel structured-based model known as Fuzzy Topographic Topological Mapping Version 1 (FTTM1). The FTTM1 model requires only instantaneous data. As a consequence of this, the computing time is consequently reduced, unlike the statistical-based models. Figure 1.6 illustrates the FTTM1 model, which is based on the backward model as illustrated in Figure 1.5.



Figure 1.6 Inverse neuromagnetic modeling: FTTM1

Basically, this newly developed model is a topological mapping which contains some fuzzy structures and it comprises four components linked by three different algorithms. The four components are magnetic contour plane (MC), base magnetic plane (BM), fuzzy magnetic field (FM) and topographic magnetic field (TM). Figure 1.7 illustrates the FTTM1 model;



Figure 1.7 Fuzzy Topographic Topological Mapping Version 1 (FTTM1)

Traditionally, the MEG data used for analyses are obtained using the SQUID measurements made above the head. However, to test the applicability of the newly developed model FTTM1, simulated data were used (Fauziah *et al.*, 2000). As the model is structured-based, it does not need *a priori* data and hence, it is anticipated that the computing time can be reduced. Initially, this model was applied to simulated data of single and unbounded current sources and has provided fairly good results (Fauziah, 2002).

In this research, an extended version of FTTM1 which will be known as FTTM2 is proposed. Unlike FTTM1, this new model uses image data, which are transformed from the magnetic fields data. The use of the image data is to incorporate the image processing techniques that will provide better visualization of the image. The model will then be used to solve the inverse problem of single bounded and multiple bounded current sources.

1.3 Objective and Scope of Study

The main objective of this study is to solve the backward (inverse) problem of MEG. This involves finding the location of the current sources from the measured magnetic fields. Physiologically, this implies finding the epileptic foci in epilepsy disorder patients. Before the backward problem can be solved, the forward problem must first be taken care of. The forward problem deals with writing an algorithm to generate the magnetic fields data for multiple bounded current sources. This includes the generation of data measured at three different planes where this kind of measurement is especially useful for overlapping current sources. The magnetic fields data generated can then be used to find the parameters for multi-current sources. This includes the number of current sources present, the location of the current sources, its orientation and also its magnitude.

The newly proposed inverse model, FTTM2 is incorporated with a fuzzy clustering technique known as fuzzy *c*-means (FCM) and an image processing technique known as the seed-based region growing (SBRG). Because of the topological structure of FTTM2, it has the biggest advantage in that it can be applied anywhere on a patient's head (top or the sides). In other words, it is invariant with regards to the measured space in a given time. Consequently, new algorithms in solving the inverse problem of MEG are introduced. Since this study deals with testing the applicability of the newly developed inverse model, the scope of this study is limited to the use of simulated magnetic fields data obtained from single bounded and multiple bounded current sources. Experimental works are also undertaken to test the applicability as well as the performance of the developed model.

1.4 The Significance of this Research

This research adopts the techniques of image processing in solving the inverse problem of MEG. In doing so, a new model is formulated which can consequently be used to further enhance the applications of MEG. The new model, FTTM2, is a structured-based model. This implies that the model is constructed by studying the characteristics of the current sources and its corresponding magnetic fields. This model also uses instantaneous data which implies that the model does not require much time in providing the results.

Since the model is able to pinpoint the location of current sources, it will be useful in the presurgical localization of the current focus where only the problematic cells will be resected. Hence, this will give minimum or no side effects to the patients when undergoing surgery. This discovery serves as a significant contribution in the neurosurgical field specifically for epileptic disorder or any other problem areas analogous to it.

1.5 Research Framework

This research comprises two main phases namely solving the forward problem and the backward problem. Solving the forward problem deals with generating the magnetic fields data. This will be accomplished by using MATLAB simulations and experimental work in the laboratory. The backward problem deals with using these data and applying the proposed model to determine the number of current sources, its location and also its magnitude. Figure 1.8 illustrates the general procedures. Data gathered by simulations and experiments in phase 1 are used in the second phase where FTTM2, incorporated with fuzzy *c*-means (FCM) and seed-based region growing (SBRG), is adopted to produce an output. This process produces the number of current sources, its location as well as its magnitude.



Figure 1.8 Research framework

1.6 Outline of Presentation

This chapter gives an overview of the research undertaken. Chapter 2 begins with a review of previous studies on Magnetoencephalography, its measurement and the methods used to solve the forward and the inverse problems.

Chapter 3 explains the essential mathematical background that are used in this research. This includes substantial topics on magnetism, crisp set, fuzzy set, image processing, seed-based region growing and clustering.

The main contributions of this study are presented in the next four chapters. Chapter 4 describes the procedure to calculate the magnetic fields from known location of current sources. The detailed algorithms are given. In order to facilitate their uses, the algorithms are coded in MATLAB. The outputs of the algorithms are presented in the form of magnetic fields data and its corresponding contour plots. This is to examine the patterns generated with the associated known current location and orientation of the current sources. This information will be useful in solving the inverse problem later. In addition to this, the characteristics of the magnetic fields data are also examined by means of equations and geometries.

Chapter 5 describes the inverse model of FTTM2 in detail. This involves the use of a clustering algorithm known as fuzzy *c*-means (FCM) that is used to cluster the data into foreground and background regions. Another algorithm is the seed-based region growing (SBRG) which can be used to determine the number of current sources present in the system by automation. Once these two algorithms are applied, the data will be processed further by going through the other processes in FTTM2.

In Chapter 6, we propose the theoretical bases supporting Chapters 5 and 7 by proving two theorems and three corollaries. These theorems and corollaries showed that the partitioning applied to the first component is preserved during the transformation from the first component to the fourth component. Since this involves some concepts of topology, some preliminaries on topology are also included. To verify these theorems and corollaries, they are implemented on the data as described in the next chapter.

The detailed implementation of the FTTM2 is illustrated in Chapter 7 where the topological structure of FTTM2 plays another main role in localizing the current sources. The implementation starts with the acquisition of magnetic fields data via two different methods. In the first method, the data is acquired through MATLAB simulations while in the second method, the data is acquired through laboratory experiments. These data acquisition is also called the forward calculations, which provides data to be used in solving the backward problem. In the backward problem, the data is then processed by applying FCM clustering algorithm and the SBRG algorithm and the developed FTTM2 algorithm. The results are also shown in this chapter.

Finally, Chapter 8 concludes the thesis with a summary of the study and recommendations for further research into this area of study. The thesis outline is summarized in Figure 1.9.



Figure 1.9 Thesis outline

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