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PARALLEL ALGORITHM OF NAVIER-STOKES MODEL FOR MAGNETIC NANOPARTICLES DRUG DELIVERY SYSTEM ON DISTRIBUTED PARALLEL COMPUTING SYSTEM

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UNIVERSITI TEKNOLOGI MALAYSIA

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SAKINAH ABDUL HANAN

A thesis submitted in fulfillment of the
requirements for the award of the degree of
Master of Philosophy

Faculty of Science
Universiti Teknologi Malaysia

JUNE 2017

To

my beloved husband,

mother, father,

and brothers

who have always given me love,

care and cheer

and whose prayers have always been a source of great inspiration

for me.

May Allah bless you all...

ACKNOWLEDGEMENT

All praises and thanks are due to Allah for making the completion of this thesis possible. Peace and blessing of Allah be upon Prophet Muhammad (peace be upon him).

First of all, I would like to express my deepest gratitude and thanks to my supervisor, PM Dr Norma Alias for their generous contribution in term of knowledge, expertise and advice that help bring this work to completion. I am especially indebted to PM Dr Norma Alias, for providing me with many years of continuous coaching, guidance, motivation and support. Without her understanding, time and patience, I may not have made it this far. Not to forget she the one who building up my interest and inspired me to develop confidence in this research.

Next, I am grateful to the individuals who have kindly offered their assistance in my time of needs. My special thanks go to Nadia Nofri Yeni, Hazidatul Akma, Siti Hafilah, Masyitah, Maizatul Nadhirah, Nur Hafizah, Akhtar and Imran for their wonderful deeds in sharing with me their knowledge and skills that are relevant to the development of this research. I am also thankful for the valuable friendship that I have obtained from my friends and colleagues who have given me constant advice, help, and encouragement throughout the years of my studies.

I acknowledge the Senate and the Management of Universiti Teknologi Malaysia for giving me the opportunity to pursue my Master studies. I am also pleased to acknowledge the University for sponsoring my studies and provide necessary facilities for the preparation of this thesis. I acknowledge the Ibnu Sina Institute for Fundamental Science Studies, UTM, for giving me the permission to use their facilities.

My special and sincere thanks are for my beloved family. I thanks my parents, Prof Dr Abdul Hanan Abdullah and Puan Rohana Yusof, and my brothers for their help, understanding, prayers, and support for always giving me hope and confidence. Last but not least, I am especially grateful to my supportive and loving husband, Muhammad Fiqry Aiman Md.Zubadi who has always believed in me and inspired me to keep on striving despite the challenges along the way. I truly appreciate all of them sacrifices, patience, and understanding. Without the support and motivation from all of them, I would not have done this project successfully.

ABSTRACT

Integrated mathematical Navier-Stokes model for transportation of drug across the blood flow medium by partial differential equations (PDE) with one dimensional (1D) and two dimensional (2D) parabolic type in cylindrical coordinates system are considered. The process of magnetic nanoparticle drug delivery system is made measurable by identifying some parameter such as magnetic nanoparticle targeted delivery, blood flow, momentum transport, density and viscosity on drug release through blood medium, the intensity of magnetic fields, the radius of the capillary and controllability expression to control the concentration of blood. Finite difference method (FDM) with centre difference formula was used to discretization the mathematical model. This research focuses on two types of discretization controlled by weighted parameter $\theta = 1$ and $\theta = \frac{1}{2}$ which are implicit (IMP) and Crank Nicolson (CN) schemes respectively. The implementation of several numerical iterative methods such as Alternating Group Explicit (AGE), Red Black Gauss Seidel (RBGS) and Jacobi (JB) method are used to solve the linear system equation (LSE) and is one of the contributions of this research. The sequential algorithm was developed by using C Microsoft Visual Studio 2010 Software. The numerical result was analysed based on execution time, number of iteration, maximum error, root mean square error, and computational complexity. The grid generation process involved fine grained of large sparse matrix by minimizing the size of interval, increasing the dimension of model and level of time steps. Parallel algorithm was proposed for increasing the speedup of computations and reducing computational complexity problem. The parallel algorithms for solution of large sparse systems were design and implemented supported by the distributed parallel computing system (DPCS) containing 8 processors Intel CORE i3 CPUs employing the Parallel Virtual Machine (PVM) software. The parallel performance evaluation (PPE) in term of execution time, speedup, efficiency, effectiveness, temporal performance, granularity, computational complexity and communication cost were analysed for the performance of parallel algorithm. As a conclusion, the thesis proved that the 1D and 2D Navier-Stokes model is able to be parallelized and parallel AGE method is the alternative solution for the large sparse simulation. Based on numerical result and PPE, the parallel algorithm is able to reduce the execution time and computational complexity compared to the sequential algorithm.

ABSTRAK

Navier-Stokes pemodelan matematik bersepadu bagi pengangkutan ubat melalui aliran darah dengan menggunakan persamaan pembezaan separa (PDE) dengan satu dimensi (1D) dan dua dimensi (2D), berjenis parabola dalam sistem koordinat silinder dipertimbangkan. Proses nanopartikel magnet melalui sistem peredaran ubat dalam aliran darah diukur dengan mengenal pasti beberapa parameter seperti penghantaran nanopartikel magnet sasaran, aliran darah, pengangkutan momentum, ketumpatan dan kelikatan bagi perlepasan ubat melalui pengantaraan darah, keamatan medan magnet, jejari kapilari dan juga ungkapan pengawalan yang mengawal kelikatan darah. Kaedah beza terhingga (FDM) dengan formula pembezaan tengah telah digunakan untuk mendiskretasikan model matematik tersebut. Kajian ini tertumpu kepada dua jenis pendiskretan yang dikawal oleh parameter pemberat $\theta = 1$ dan $\theta = \frac{1}{2}$ yang melibatkan skim tersirat (IMP) dan skim Crank Nicolson (CN) secara khususnya. Perlaksanaan beberapa kaedah berangka seperti Kelas Tak Tersirat Kumpulan Berarah Berselang-seli (AGE), Gauss Seidel Merah Hitam (RBGS) dan Kaedah Jacobi (JB) digunakan untuk menyelesaikan persamaan sistem linear (LSE) dan merupakan salah satu sumbangan dalam kajian ini. Algoritma berjujukan dibangunkan menggunakan perisisan C Microsoft Visual Studio 2010. Keputusan berangka dianalisis berdasarkan masa perlaksanaan, bilangan lelaran, ralat maksima, ralat punca min kuasa dua, dan kekompleksan pengiraan. Proses penjanaan grid yang dihaluskan lagi bagi matrik berskala besar dengan meminimumkan saiz selang ruang, meningkatkan dimensi model dan peringkat paras masa. Algoritma selari dicadangkan untuk meningkatkan kecepatan pengiraan dan mengurangkan masalah kekompleksan pengiraan. Algoritma selari bagi menyelesaikan masalah sistem yang berskala besar dirangkakan dan dilaksanakan serta disokong oleh sistem pengkomputeran selari teragih (DPCS) yang mengandungi 8 pemproses Intel CORE i3 CPUs menggunakan perisian Parallel Virtual Machine (PVM). Penilaian prestasi selari (PPE) berdasarkan masa pelaksanaan, kecepatan, kecekapan, keberkesanan, prestasi sementara, granulariti, kekompleksan pengiraan dan kos komunikasi dianalisis untuk menilai prestasi algoritma selari. Sebagai kesimpulan, kajian ini membuktikan pemodelan Navier-Stokes bagi 1D dan 2D dapat diselarikan dan kaedah selari AGE merupakan penyelesaian alternatif bagi simulasi berskala besar. Berdasarkan keputusan berangka dan PPE, algoritma selari dapat mengurangkan masa pelaksanaan dan kekompleksan pengiraan apabila dibandingkan dengan algoritma berjujukan.

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LIST OF SYMBOLS

u	-	Velocity of blood (m/s)
v	-	Velocity of magnetic nanoparticles (m/s)
P	-	Pressure (Pa)
μ	-	Viscosity of blood (kg/ms)
R_M	-	Radius of magnetic nanoparticles (m)
υ	-	Kinematic viscosity
R	-	Radius of capillary (m)
H	-	Magnetic intensity
M	-	Magnetization of particles (A/ m^{-1})
B	-	Magnetic induction
χ	-	Magnetic susceptibility of the particle
μ_o	-	Permeability of free space
V_M	-	Volume of MNP (m^3)
m	-	Mass of MNP (kg)
ρ	-	Density of blood (kg/m^3)
ρ_p	-	Density of MNP (kg/m^3)
N	-	Number density of suspended nanoparticles
A	-	Stokes' coefficient
t	-	Time (s)
r	-	Grid in r direction (m)
x	-	Grid in x direction (m)

z	-	Grid in z direction (m)
T_p	-	Execution time
S_p	-	Speedup
E_p	-	Efficiency
F_p	-	Effectiveness
L_p	-	Temporal performance
G	-	Granularity
T_{comp}	-	Computational time
T_{comm}	-	Communication time
T_{idle}	-	Idle time
T_{comm1}	-	Communication cost for minimal data item

LIST OF ABBREVIATIONS

1D	-	One Dimension
2D	-	Two Dimension
AGE	-	Alternating Group Explicit
DPCS	-	Distributed Parallel Computing System
FDM	-	Finite Difference Method
JB	-	Jacobi
LSE	-	Linear System Equation
MDCS	-	MATLAB Distributed Computing Server
MNPs	-	Magnetic Nanoparticles
MPI	-	Message Passing Interface
ODE	-	Ordinary Differential Equation
PAGE	-	Parallel Alternating Group Explicit
PDE	-	Partial Differential Equation
PJB	-	Parallel Jacobi
PRBGS	-	Parallel Red Black Gauss Seidel
PVM	-	Parallel Virtual Machines
RBGS	-	Red Black Gauss Seidel
SAGE	-	Sequential Alternating Group Explicit
SJB	-	Sequential Jacobi
SRBGS	-	Sequential Red Black Gauss Seidel

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CHAPTER 1

INTRODUCTION

1.1 Research Background

Nanotechnology is a general purpose technology because of its important effects that are related to most of the industries and people. Nanotechnology can be applied to many areas of research and development such as medicine, manufacturing, computing, textiles and cosmetics (Dutta, 2015). Nanotechnology is defined as 'engineering at a very small scale' which is shown through a nanoparticle range from 1 to 100 nanometers (nm) (Gupta, 2014). In others description, Figure 1.1 shows structure of nanoparticles with a range of structure size starting from 1 to 100 nm (Taylor *et al*, 2013).

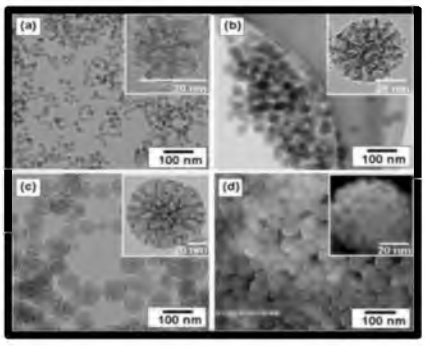

Figure 1.1 Structure of Nanoparticle

In nanoparticle manufacturing, a variety of compositions can be achieved as it may have many practical applications in a variety of areas such as engineering and medicine. The nanoparticles of drug delivery and related to pharmaceutical

development in the context of nanomedicine should be viewed as science and technology of nanometer scale complex systems. The nanoparticles that are created for drug delivery purposes are defined as small particles (< 100nm). This definition includes nanospheres which the drug is absorbed, dissolved or dispersed throughout the matrix; and nanocapsules in which the drugs are limited to an oily core that surrounded by the shell-like wall (Kreuter, 2004).

The nanoscale devices allow the chemotherapeutic drug to be discharged into the blood vessels, spreading out through the tissue and gaining access to the tumour cells location. Nowadays, drug delivery system is notable for its capabilities when compared to traditional delivery via bolus injection (Allen and Cullis, 2004). The structure of nanoparticle platforms for drug delivery is shown in Figure 1.2 (Schoonen and van Hest, 2014).

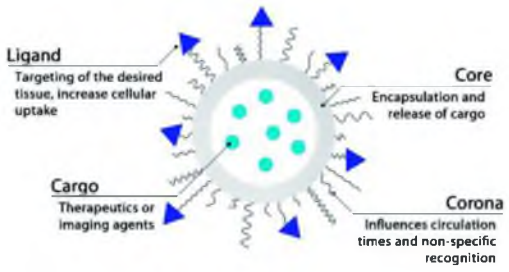

Figure 1.2 Structure of nanoparticle platforms for drug delivery

The potential of nanoparticles delivery systems provides chances to diversify the drug delivery approaches or therapeutic options in cancer disease treatment (Gabathuler, 2010). However, Timchack (2008) said that the drug delivery system is being designed to ensure an efficient therapy which meant that no harmful side effects for the body cells and therefore improving the patient life quality. In other words, there should be minimal damage inflicted to the healthy cells within the body while ensuring a good recovery progress.

Lifelong diseases such as cancers or tumour growths are common among people nowadays. Hence, more studies and researches are needed to be carried out so that the crucial effects of nanoparticles drug delivery systems can be understood more thoroughly. Drug delivery systems are recommended particularly as the alternatives

in the form of nanoparticles in order to maintain the effectiveness of the new drugs that been developed which are more potent and more complex ever before. Magnetic nanoparticles platform has the ability to let the physicians detect and treat diseases such as cancer and cardiovascular disease more effectively than before (Baptista *et al*, 2013).

The unique advantages of an external magnetic field control have achieved the purpose of targeted delivery because they can be remotely navigated to the intended site via application of an external magnetic field gradient. Magnetic therapy is widely used to assist in curing various diseases. The drug that possessed magnetic nanoparticles properties will be easier to be controlled by external magnetic field and it has potential therapeutic usage in the cancer cells as well as helps in controlling the blood pressure in the blood medium (Kumar and Mohammad, 2011). At stationary position, the transverse magnetic field is applied externally to a moving electrically conducting fluid where electrical currents are induced in the fluid. The interaction between these induced currents and the applied magnetic field produces body forces with a tendency to move slowly along with the movement of blood and bring the drug to the targeted cells (Sun et al, 2008).

Mathematical models have been developed in order to understand the process of magnetic nanoparticle drug delivery system. The development of mathematical model is to predict, design and control the movement of drug delivery through blood medium controlling by external magnetic fields. Parameters during the process can be range from very simple to complex in order to upgrade the quality of the system. Some authors in the area of blood flow feel that blood can be assumed as Newtonion in nature especially in large blood vessels. In Wang *et al.* (2014), the flow treatment of blood has been assumed to be Newtonian fluid and flow as laminar, incompressible, unsteady and the flow field is simulated by solving the Navier-Stokes equation.

Numerical methods are capable to solve a complex system of partial differential equation (PDE) which is almost impossible to be solved analytically. The Finite Element Method (FEM), Finite Volume Method (FVM) and Finite Difference Methods (FDM) are some alternative methods to solve the PDE (Peiro and Sherwin, 2005). For other application of drug delivery system, the FDM and FEM have been

widely used to solve the models (Siepmann, 2008; Palazzo *et al*, 2005; Dev *et al*, 2003). However, the FDM scheme is chosen because this method is simple to formulate a set of discretized equations from the transport differential equations in a differential manner (Mitchell and Griffiths, 1980). Besides, this method is straightforward in determining the unknown values. Only a few researchers in magnetic nanoparticles drug delivery system solved the model using numerical methods. Thus, due to this reason, the mathematical Navier-Stokes model magnetic nanoparticles drug delivery system in this research is solved using FDM. Further details of FDM will be discussed in Chapter 2.

A large scale of system linear of equations is discretized from the FDM for simulation and visualization. However, one central processing unit (CPU) is not enough to compute the large computation. Therefore, the parallelization in solving the large scale of system linear of equations is great importance. The objective is to speed up the computation and increase the efficiency by using massively parallel computers. The domain problem is partitioned into subdomain or equal sized tasks. Then, the tasks are connected to each other local and global communication. Static mapping strategy is implemented because this research focuses on the distributed parallel computing architecture. Further detail to describe the parallel algorithm design methodology is discussed in Chapter 2.

The magnetic nanoparticle drug delivery system to treat the cancer cell problem is very interesting. Mishra *et al* (2008) has conducted the application of magnetic nanoparticle drug delivery system. However, from the existing work by Mishra *et al* (2008), this research implement the parallel algorithm of Navier-Stokes model in magnetic nanoparticle drug delivery system for 1D and 2D model. Thus, this research which involved a large scale matrix of the discretization model, a large sparse computational complexity, intensive large-scale parallel computing system and a huge memory space to support the simulation with a high-speed solution. All the numerical methods and parallel programming that are used in visualizing and observing the changing parameters of phase change simulation models run on Linux operating system by using distributed parallel computing system (DPCS). The parallel algorithms are programmed in C language while the communication software tool involves the use of Parallel Virtual Machines (PVM). The parallel performances are

analysed in reference to the numerical result and parallel performances evaluation (PPE).

1.2 Problem Statement

Magnetic nanoparticle drug delivery system is closely related with biomechanical researchers due to its relationship with cancerous cell or tumour. Some problem statements will be explored and discussed through this research. Firstly, on how to model the mathematical modelling and illustrating the visualization of magnetic nanoparticles drug within its delivery to the specific targeted cell. The integrated mathematical modelling that uses Navier-Stokes model with continuity and momentum equations that are related to parameter changes is developed. Thereafter, the 1D and 2D model with parabolic type equations are solved by the weighted parameter central FDM in order to obtain the results. The discretized computational is conducted for $\theta = 1$ and $\theta = \frac{1}{2}$, which represent Implicit (IMP) and Crank Nicolson (CN) schemes respectively. Dealing with nanoscale phenomena system with large sparse matrices. By applying some iterative numerical methods, the impact of domain decomposition techniques, message passing model and grid generation technique can be stimulated. Furthermore, the implementation of sequential and parallel algorithms on the PDE is generated by some numerical iterative methods such as Alternating Group Explicit (AGE), Red Black Gauss Seidel (RBGS) and Jacobi (JB). PPE will be conducted to measure the superiority of generate FDM schemes in solving the PDEs.

1.3 Objectives

The objectives of the study are:

1. To formulate and visualize the mathematical Navier-Stokes model for magnetic nanoparticles on the delivery of the drug through blood flow for cancer cell treatment.

2. To discretize the mathematical models using weighted parameter central FDM involving a number of parameter changes for the large sparse data set.

3. To develop the sequential and parallel algorithms for the Navier-Stokes model based on three different numerical iterative methods; AGE, RBGS and JB.

4. To analyze the results of 1D and 2D based on the numerical results and PPE in solving the Navier-Stokes model.

1.4 Scope of Study

In real phenomenon, mathematics provides a broad foundation in each of these overlapping areas: pure mathematics, applied mathematics, and statistics. This research will focus on the mathematical modelling for drug delivery via magnetic nanoparticle system through the blood flow within the cancer cell treatment application by using PDE. The non Newtonian fluid in blood medium is derived from the theory that is based on Navier-Stokes model, which emphasizes on the continuity and momentum equation. The flow scope of the research in Figure 1.3 shows that this study is focused on the applied mathematics that deals with mathematical modelling PDE with parabolic type in order to predict the magnetic nanoparticles drug delivery system. The mathematical modelling involved the continuity and momentum equation with the initial and boundary conditions are made to be known. Controllability expression to control the concentration blood is also considered. The 1D and 2D problems are discretized by using the weighted parameter method. The numerical iterative methods that are being considered to be used in the comparison are AGE, RBGS and JB method. The mathematical modelling of the sequential and parallel algorithms are implemented to solve the problem of drug delivery for the purpose of dealing with the cancer cell. The approximate solution that uses COMSOL is utilized for 3D visualization, Matlab for the 1D and 2D visualization and the DPCS with the communication platform PVM and C programming is applied. The superior iterative

method of FDM is being observed and utilized in the solution process of the Navier-Stokes model.

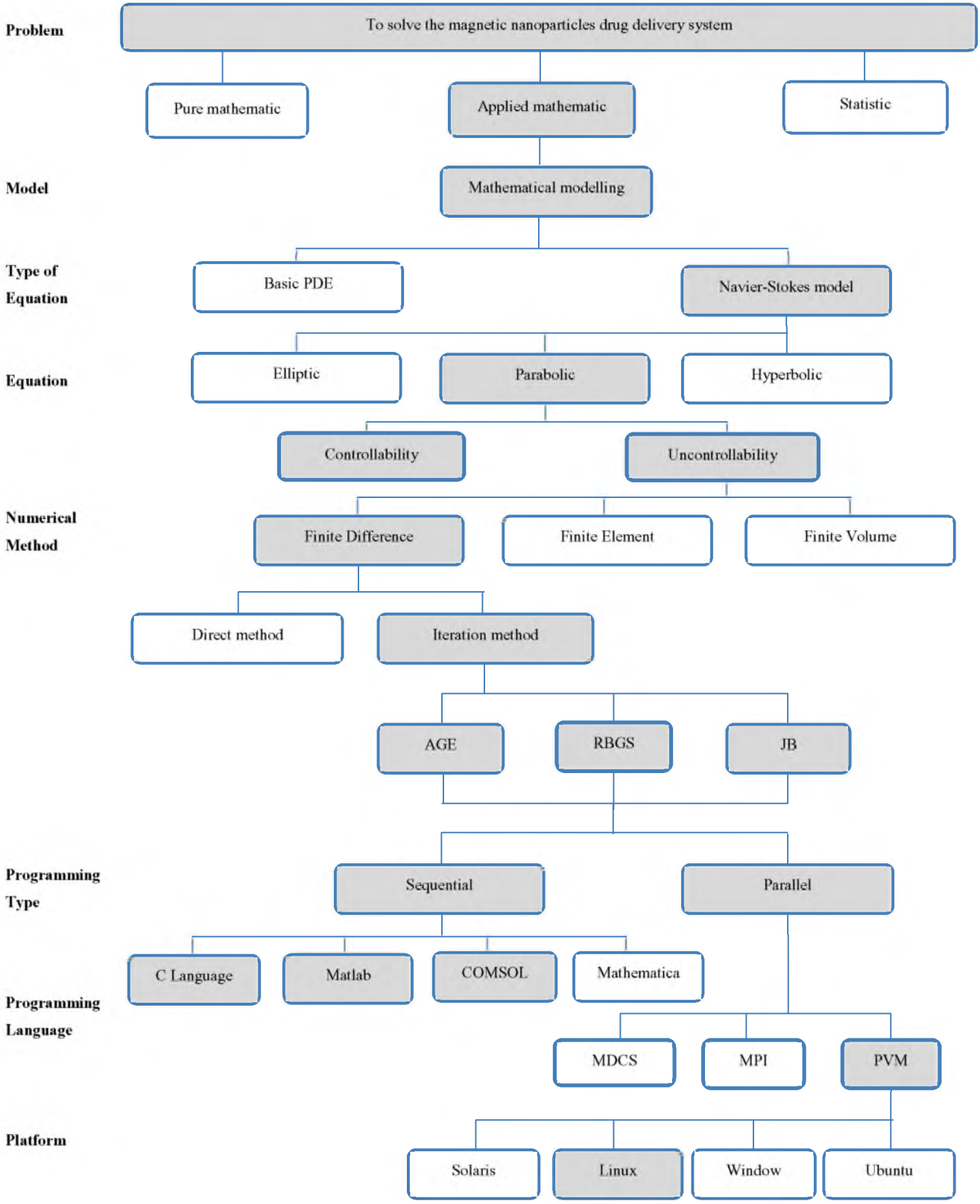

Figure 1.3 The scope of research.

1.5 Significance of Study

The magnetic nanoparticles for the drug delivery model are significant in the process of developing the alternative numerical simulation for the treatment of the cancer cell growth. The application of nanoparticles is assumed to be the solution for early detection of tumour cell growth. The importance of the Navier-Stokes model in predicting and visualizing the parameters involved to deliver the magnetic nanoparticles towards the targeted cells. The implementation of the numerical iterative methods such as AGE, RBGS and JB methods are suitable to solve the 1D and 2D model. Besides, the simulation of large sparse matrix for the multidimensional models on DPCS will help reduce the execution time and increases the performance of speedup. In addition, the approximation result uses parallel computing which is a fast prediction of the movement of the magnetic nanoparticles through the blood medium. This medical practice is related to the evolution of biological systems in cancer cells treatment. Furthermore, this research is beneficial to the cancer patients and doctors who are working on the cancer diagnostics and cancer treatments through efficient stimulation and coordination.

1.6 Thesis Outline

The contents of this research can be divided into seven chapters which includes an introduction, literature review, mathematical modelling, implementation of the sequential algorithm, implementation of the parallel algorithm, result, discussion, and conclusion. Chapter 1 starts with a brief discussion on the introduction, problem formulating, research objectives, the scope of research, significance of study and the thesis outlines.

Chapter 2 focused on the review regarding the problem, solution of problem, methodology, computing platform and analysis. The discussion regarding the problems includes the cancer related issues, the growth of tumours and magnetic nanoparticles. The mathematical Navier-Stokes model on the magnetic nanoparticle

drug delivery is portrayed as the solution to the problem. The mathematical modelling is used to deal with PDE with parabolic type. Some common methods that are used to solve this mathematical modelling are the formulation of FDM and weighted average parameter. The classical and advanced iterative methods are also being highlighted. Besides, the computational solution of the sequential and parallel algorithm with the use of common mathematical software and DPCS are also being studied. This chapter also includes the importance and purpose of mathematical modelling in predicting the magnetic nanoparticle drug delivery within the cancer cell treatment. Some important terms that are related to numerical analysis and PPE such as convergence, consistency, stability, speedup, efficiency, effectiveness, temporal performance and granularity are also discussed in the chapter.

The scope in Chapter 3 is focused on the integrated mathematical modelling that is based on the theory of Navier-Stokes model in the fluid dynamic for blood flow which are the mass (continuity) and momentum conservation equation for 1D and 2D model. The flow is expected to take place under the influence of externally applied magnetic field in the axial direction. The equation of continuity is integrated into each other together with the equation of momentum equation. The governing equations for 1D and 2D are written in the cylindrical coordinate system (r, z, θ). Discretization by weighted parameter with the usage of the central FDM as well as LSE is also being discussed in this chapter. Finally, the presence of controllability expression is injected to 1D Navier-Stokes model due to control of the concentration of blood in capillary that influenced the magnetic nanoparticle drug delivery system will be developed.

The contribution of Chapter 4 is the development of sequential algorithms of the magnetic nanoparticle drug delivery model for 1D and 2D. The continuity and momentum equation will be solved using some numerical iterative methods. The numerical iterative methods mentioned are AGE (1D SAGE and 2D SAGE), RBGS (1D SRBGS and 2D SRBGS) and JB (1D SJB and 2D SJB) method. These numerical method are compared according to the execution times, number of iterations, maximum errors and root mean square errors (RMSE).

Chapter 5 convert the iterative methods are being presented in Chapter 4 into the parallel algorithms which aims to improve the time execution when dealing with

large sparse matrix and nanoscale problem. The parallelization of the multidimensional equation will use the same numerical methods discussed in Chapter 4. The parallel algorithm is implemented on PVM with distributed memory within the message passing environment. The numerical methods are parallelized into 1D PAGE, 2D PAGE, 1D PRBGS, 2D PRBGS, 1D PJB and 2D PJB. The performances are measured based on speedup, efficiency, effectiveness, temporal performance and granularity.

The numerical results and the PPE obtained from Chapter 4 and Chapter 5 are then discussed in Chapter 6. The visualization of the mathematical model is simulated by using Comsol Multiphysic in 3D simulation and Matlab R2013a stimulation for 1D and 2D mathematical model. To validate the results obtained, a comparison of the velocity of the blood and velocity of drug magnetic nanoparticle is made with Mishra *et al.* (2008) as a limiting case where it involved 1D model. Simulation of controllability expression in 1D mathematical modelling is simulated by using Matlab R2013a. The mathematical modelling which are related to Navier-Stokes magnetic nanoparticle drug delivery model of 1D and 2D model are analysed based on the numerical analysis and PPE by comparing between two type of schemes and three types of numerical iterative method.

Lastly, Chapter 7 draws on the conclusion of the thesis. Contributions are highlighted and further studies are suggested. An overview of the thesis research is described in Figure 1.4.

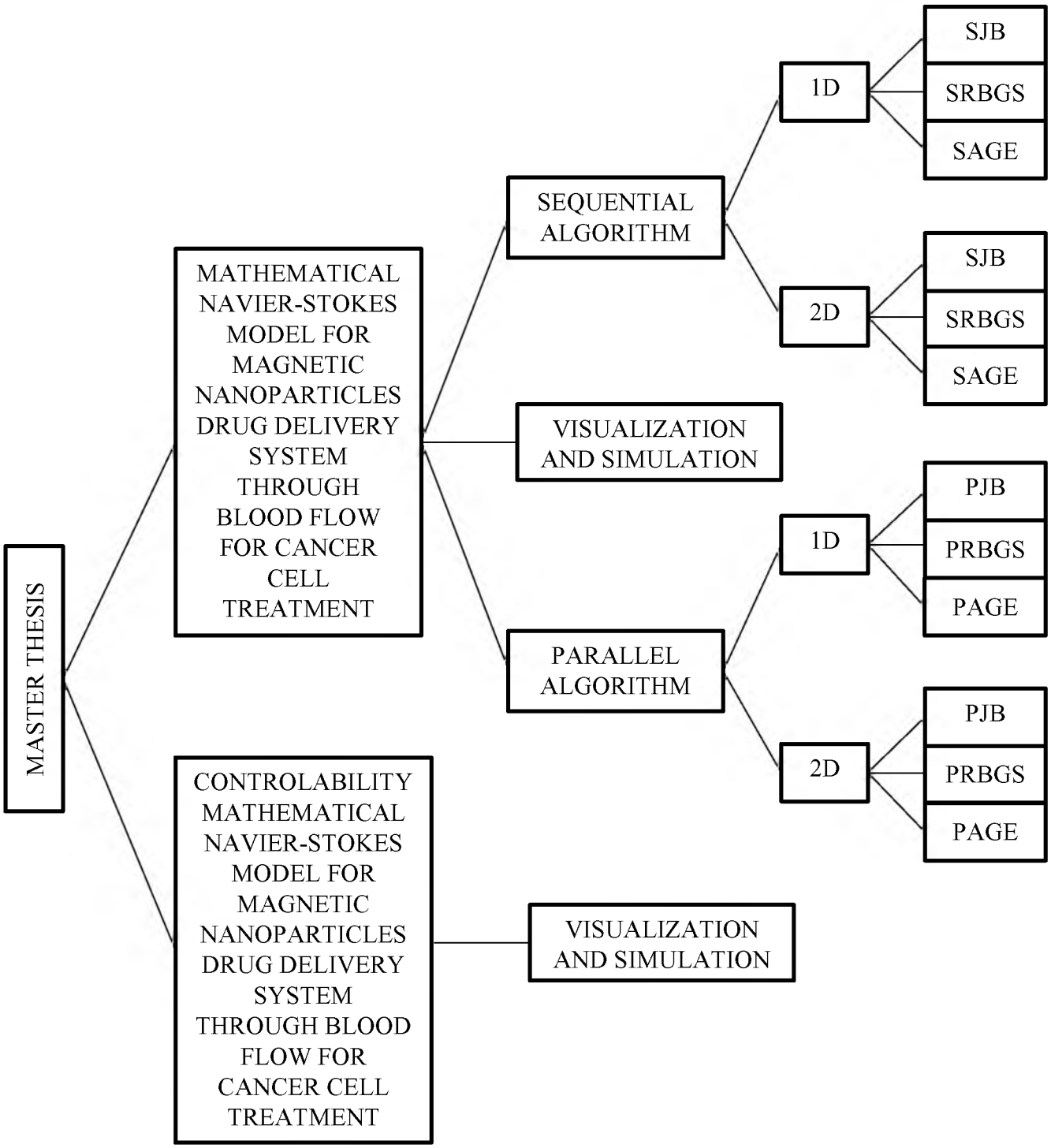

Figure 1.4 An overview of the thesis research

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