

**HIGH PERFORMANCE SIMULATION OF DRUG RELEASE
MODEL AND MASS TRANSPORT MODEL
BY USING HYBRID PLATFORM**

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To my parents and family for their continuous moral support during whole of my
academic career

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ABSTRACT

The controlled drug delivery in drug eluting stents exerts an important influence in decreasing restenosis in intravascular stenting. These stents are coated with drug to avoid the re-narrowing of the arterial wall. The drug is directly associated with the original bare metal stents. Drug eluting stents have plus point of a flexible time delivery of a curative drug to the neighboring arterial tissue. It treats the required injuries efficiently having negligible systemic drug interaction. This thesis aims to develop a mathematical model for describing the procedure of drug distribution from stent coating and from arterial wall. For this purpose, a mathematical model of two phase is presented to simulate the transportation of drug between coating and arterial tissue. This two-phase model explores the impact of non-dimensional parameters such as solid liquid mass transfer rate γ_1 , ratio of accessible void volume to solid volume e_1 and Peclet number P_e on drug release and mass concentrations from coating and tissue layers. For better understanding a 2D mathematical model of biodurable stent coating is developed, where the intravascular distribution of drug from an implanted drug eluting stent in arterial wall is simulated. The model integrates reversible drug binding and diffusion of drug in the stent coating. The arterial wall and coating drug diffusivities are examined for the impact of arterial drug uptake and drug release in the coating. The diffusion coefficient of drug D_c , the diffusion coefficients of wall D_w , D_{wx} , D_{wy} and strut embedment play an important role to regulate the drug release. Moreover, a 3D model of mass concentrations and drug release from the cross section of artery is investigated. The impact of advective and diffusive velocities is explored and these forces can be used to control the mass concentrations of drug. FEM and FDM is used for spatial and temporal discretization of model equations. The sequential and parallel algorithms are developed for numerical simulations. Furthermore, the motivation for using GPU accelerators with CUDA is explained to handle computational complexities. A hybrid CPU/GPU algorithm for the proposed models is designed and satisfactory results for parallel performance indicators such as; speedups S_p , temporal performance T_p , efficiency E_p and effectiveness F_p are obtained. The CN method gives better sequential results because it has less RMSE than GD and BD methods. However, the BD method gives good results for parallel indicators because it involves less computation than GD and CN methods. The sequential and parallel performance of BM method is better as compared to NM and PM methods. The BM method has least RMSE for both sequential and parallel algorithms. The parallel performance indicators S_p , T_p , E_p and F_p for BM method gives better performance than the other methods. Therefore, it is a superior method than the NM and PM methods. Hybrid algorithms are more efficient in large-scale problem simulations as shown in parallel performance results. The governing models in this research provide the basis of a design tool for studying and calculating drug distribution in coating and arterial wall in the application of stent-based drug delivery. The models propose in this research are used for monitoring purpose and to determine drug release, mass transport, visualization and observation. The simulations support to offer a good perception into the potential effects of different parameters such as γ_1 , e_1 , P_e , D_c , D_w , D_{wx} , D_{wy} and strut embedment can affect the efficiency of drug release.

ABSTRAK

Kawalan penghantaran ubat dalam sten elusi ubat menghasilkan pengaruh yang penting dalam mengurangkan stenosis semula dalam sten intravaskular. Sten ini disaluti dengan ubat untuk mengelakkan penyempitan semula dinding arteri. Ubat ini berkait rapat dengan sten logam terdedah asli. Sten elusi ubat mempunyai kelebihan dari segi masa penghantaran ubat penyembuhan yang fleksibel kepada tisu arterial bersebelahan. Ia merawat kecederaan secara efisien dengan interaksi ubat bersistem yang sedikit. Tesis ini bertujuan untuk membangunkan model matematik untuk menerangkan prosedur pengagihan ubat dari salutan sten dan dinding arteri. Bagi tujuan ini, model matematik dua fasa dikemukakan untuk simulasi pengangkutan ubat dari salutan ke tisu arteri. Model matematik dua fasa ini meneroka impak parameter tanpa matra seperti kadar pemindahan jisim antara pepejal dan cecair γ_1 , nisbah isipadu kosong yang boleh diakses dengan isipadu pepejal, e_1 dan nombor Peclet, P_e terhadap pelepasan ubat dan kepekatan jisim daripada salutan dan lapisan tisu. Untuk pemahaman yang lebih baik, satu model matematik 2D bagi sten bersalut biotahan lama telah dibangunkan, di mana pengagihan ubat secara intravaskular daripada sten elusi ubat yang diimplan dalam dinding arteri telah disimulasikan. Model ini mengintegrasikan ikatan ubat boleh balik dan penyerapan ubat dalam salutan sten. Penyerapan ubat di dinding arteri dan penyerapan ubat salutan diperiksa untuk impak penyerapan ubat arteri dan pelepasan ubat dari salutannya. Pekali penyerapan ubat D_c , pekali penyerapan dinding D_w , D_{wx} , D_{wy} dan penyemakan topang memainkan peranan penting untuk mengawal pelepasan ubat. Tambahan pula, suatu model 3D untuk pengaruh kepekatan jisim dan pelepasan ubat daripada keratan rentas arteri dikaji. Impak hadlaju advectif dan penyerapan diterokai dan daya ini boleh digunakan untuk mengawal kepekatan jisim ubat. FEM dan FDM digunakan untuk pendiskretan persamaan model secara ruangan dan secara temporal. Algoritma berturut dan selari telah dibangunkan bagi simulasi berangka. Selain itu, dorongan untuk menggunakan pemecut GPU dengan CUDA diterangkan bagi mengendalikan kerumitan komputasi. Algoritma hibrid CPU/GPU telah dibentuk bagi model yang dicadangkan dan memperoleh hasil prestasi selari memuaskan seperti kelajuan tambahan S_p , prestasi temporal T_p , kecekapan E_p dan keberkesanan F_p . Kaedah CN memberi hasil berturut yang lebih baik kerana ia mempunyai RMSE yang kurang daripada kaedah GD dan BD. Namun, kaedah BD memberikan hasil selari yang lebih baik kerana kaedah ini melibatkan pengiraan yang kurang berbanding kaedah GD dan CN. Prestasi berturut dan selari bagi kaedah BM adalah lebih baik berbanding kaedah NM dan PM. Kaedah BM mempunyai RMSE yang terkecil bagi algoritma berturut dan selari. Indikator prestasi selari S_p , T_p , E_p dan F_p yang ditunjukkan oleh kaedah BM adalah lebih baik berbanding kaedah lain. Oleh itu, ia adalah kaedah yang lebih unggul berbanding kaedah NM dan PM. Algoritma hibrid adalah lebih cekap dalam simulasi masalah berskala besar seperti yang ditunjukkan dalam hasil prestasi selari. Model tadbir dalam kajian ini menyediakan asas reka bentuk alat bagi mempelajari dan mengira pengagihan ubat dalam salutan dan dinding arteri dalam aplikasi penghantaran ubat berdasarkan sten. Model yang dicadangkan dalam kajian ini digunakan untuk tujuan pemantauan dan untuk menentukan pelepasan ubat, pengangkutan jisim, visualisasi dan pemerhatian. Simulasi dapat menyokong persepsi yang baik mengenai kesan potensi parameter berbeza seperti γ_1 , e_1 , P_e , D_c , D_w , D_{wx} , D_{wy} dan pembenaman topang yang boleh mempengaruhi kecekapan pelepasan ubat.

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LIST OF ABBREVIATIONS

1D	-	One Dimensional
2D	-	Two Dimensional
3D	-	Three Dimensional
BM	-	Backward Method
BM	-	Broyden's Method
BMS	-	Bare Metal Stents
CBSG	-	Characteristic Based Split Galerkin
CFX	-	Central Florida Expressway Authority
CN	-	Crank Niclson Method
CPU	-	Central Processing Unit
CSR	-	Compressed Row Storage
CUDA	-	Compute Unified Device Architecture
DES	-	Drug Eluting Stents
fd	-	Degrees of Freedom
FDM	-	Finite Difference Method
FEM	-	Finite Element Method
GM	-	Galerkin Method
GPU	-	Graphic Processing Unit
MEX	-	Matlab Executable
NM	-	Newton Raphson Method
PDEs	-	Partial Differential Equations
PLGA	-	Poly lactic-co-glycolic acid
PM	-	Picard's Method
PPI	-	Parallel Performance Indicators
RAM	-	Random Access Memory
SIMD	-	Single Instruction Multiple Data

- SLE - System of Linear Equations
- SM - Shared Memory
- SNLE - System of Nonlinear Equations
- WHO - World Health Organization

LIST OF SYMBOLS

Pe	- Peclet number
C_0	- Initial Drug Concentration in Coating
D_1	- Diffusion Coefficient in Coating
D_2	- Effective Diffusivity of Free Drug
D_c	- Diffusivity of Drug Coating
D_w	- Isotropic Vascular Drug Diffusivity
D_{wx}	- Transmural Vascular Drug Diffusivity
D_{wy}	- Circumferential Vascular Drug Diffusivity
K_2	- Equilibrium Dissociation Constant
L_1	- Thicknesses of Coating
L_1	- Thicknesses of Coating
L_2	- Thicknesses of Tissue
L_p	- Stent Strut Embedment
L_x	- Thickness of Artery Wall
L_y	- Inter-Strut Distance
R_{wp}	- Resistance at Perivascular Boundary
S_0	- Initial Binding Site Concentration
e_1	- Ratio of Accessible Void Volume to Solid Volume in Coating Layer
e_2	- Ratio of Accessible Voide Volume to Solid Volume in Tissue Layer
k_1	- Partition Coefficient in Coating
k_2	- Partition Coefficient in Tissue
k_a	- Binding Rate Constant
k_{cw}	- Partition Coefficient at the Coating Arterial Wall Interface

k_d	- Unbinding Rate Constant
k_{wp}	- Partition Coefficient at the Perivascular Boundary
r_h	- Hydraulic Radius
β_2	- Binding Rate Constants
δ_2	- Unbinding Rate Constants
ϵ_1	- Porosity Coefficient in Coating
ϵ_2	- Porosity Coefficient in Tissue
P	- Permeability of Topcoat
u	- Transmural Velocity
a	- Dimension of Strut
e	- Fraction of Accessible Void Volume to the Solid Volume
$k\varepsilon$	- Available Void Volume
u	- Transmural Velocity
δ	- Coating Thickness of Strut
ε	- Porosity

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CHAPTER 1

INTRODUCTION

1.1 Introduction

Endovascular drug eluting stents are being increasingly applicable for the prevention and cure of restenosis. Stents are devices inserted into arteries to widen their lumen, prevent occlusion and restore blood flow perfusion to the tissues downstream. Drug Eluting Stents (DES) are coated with drugs for decreasing in-stent restenosis after implantation. The drug molecules diffuse from the coating into the blood stream and into the artery wall, when a DES is inserted in the artery wall as shown in Figure 1.1.

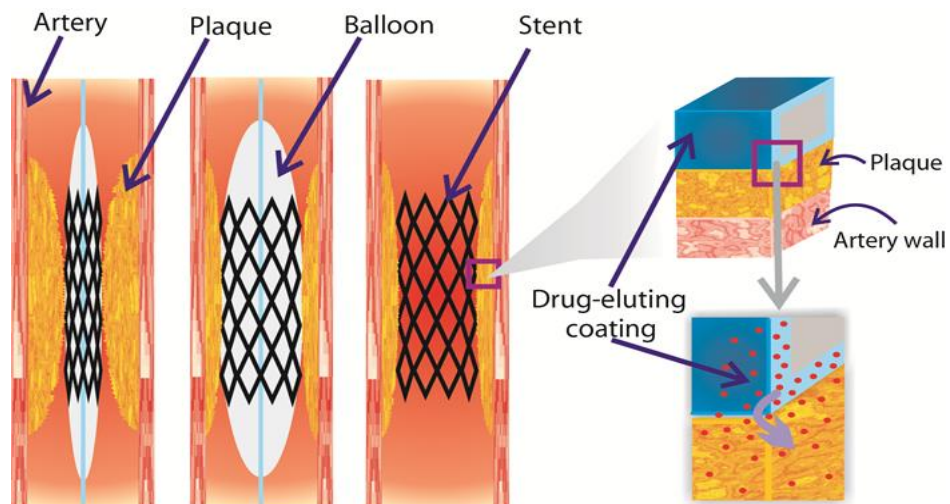


Figure 1.1 A drug eluting stent coated with a drug-loaded polymer and its implantation into a stenotic artery. The drug releases from the stent coating into artery wall to prevent re-blocking due to restenosis (Vo *et al.*, 2016).

Hence, the delivery of drug depends on various aspects, for example physicochemical properties and coating geometry, drug properties such as solubility and diffusivity. In order to achieve optimum results, the therapeutic agent is loaded with biocompatible polymeric layers that are coated on the struts of the stent. These stents work under complex conditions that vary according to time and it is not easy to accurately predict their efficiency and performance over extended periods of time.

The following data show the percentage of coronary artery disease in population. This percentage is huge in some countries. According to the latest WHO data published in May 2016, the death rate due to coronary heart diseases in Malaysia has reached 29363 or 23.10% in the world. On average it becomes 150.11 cases per 100,000 of population. In Pakistan death rate has reached up to 9.87% of total deaths. 110.65 fatal cases per 100,000 of population are occurred according to data. Death rate in the United States due to heart attacks is, approximately 600,000. It is 25% of the total deaths. Among 715,000 Americans who suffered from the heart attacks, only 15% of the people die from the stroke. This stroke affects mostly the Afro- Americans and the wilds. It may cause 24.3% and 24.1% of deaths, respectively.

Mathematical modeling paves the way of deep perception of the drug transport mechanisms in the arterial wall and coating, especially in the drug eluting stents case. In this way it has turn into an effective means to catalyze drug release processes. In spite of the fact that cardiovascular drug transportation shows a very complicated physiological and biochemical phenomenon, yet an improved release model may give comprehension of the release mechanism of the drug from arterial wall tissue to drug coating. The focus of this research is to aquire the behavior of mass transport and drug release from the arteries using mathematical modelling and simulation. This chapter highlights the background of the problem, significance and scope of the research. Several previous researches will provide an interpretation of the background of biodegradable polymer coated drug eluting stents (DES).

1.2 Background of Problem

The background of the problem is divided into two main parts. The first part introduces the background of biodegradable polymer coated DES. The second part signifies the mass transport from DES.

1.2.1 Biodegradable Coated Drug Eluting Stents

This research aims to acquire the behavior of mass transport and drug release from the arteries using mathematical modelling and simulation. DES decrease the intensity of restenosis as compared to the uncovered metal stents. Nowadays, it becomes a widespread method for curing the coronary arteries.

DES have a metallic wire covered by thin polymer layers. These polymer layers enclose a curative drug for the serving hyperplasia of smooth muscle cells. The DES performance improved by optimizing the stent geometry and coating design. The proceeding of non-proliferative remedial drug from DES is directly related to the rate of the discharge of drug (Tzafiriri *et al.*, 2012). Manufacturing and design of DES are facing challenges in terms of biological effects and toxicity of the local area. The optimum drug concentration and absolute dose of tissue are still not enlightened (Venkatraman and Boey, 2007).

The interaction of the mechanical action of the stent on the wall as well as the interface of the blood flow with the drug releasing process from DES are still new in the medical literature. These processes had also been analyzed separately in study of (Migliavacca *et al.*, 2002; Prosi *et al.*, 2005). The role of drug in healing the artery after the insertion and function of the stent is significant (Migliavacca *et al.*, 2007). The flow of blood has a slight effect on the penetration of the drug into the wall. The lumen of artery works to reduce the concentration of the drug. Balakrishnan *et al.* (2005) suggest the justification of these assumptions is not really valued as the drug dissolve into the stream of blood. It affects the deposition of the drug in the part of the artery walls near the surrounding of the stent.

Many issues are directly associated to the slow process of drug release into the bio-durable coatings. The bio-durable or non-erodible polymers are the most frequent kinds of stent coatings to carry the mixtures of active drug (Lüscher *et al.*, 2007; Venkatraman and Boey, 2007). This model is being made for the improvement of functioning and design of DES. Various researchers have proposed the usage of bio-degradable polymer coatings in place of bio-durable coatings (Acharya and Park, 2006). Biocompatible PLGA (poly lactic-co-glycolic acid), has achieved much interest in DES research. PLGA optimize the rates of drug release, based on the weights of polymer molecule (Wang *et al.*, 2006).

Modeling and simulation are used to investigate the distribution of arterial drug around the stent strut. The mathematical models reduce the stent coating difficulties into a source term and provide improved understanding of drug concentration. Such models are used in diffusive and convective transport of drug in the arterial wall (Hwang *et al.*, 2001), stent expansion mechanics, drug distribution (Zunino *et al.*, 2009) and effect of blood flow in the arterial wall (Balakrishnan *et al.*, 2005; Kolachalama *et al.*, 2009).

The distribution of arterial drug has been searched by diffusion of the drug in the coating and in the arterial wall. Some researchers discussed the features related to drug release such as changeable drug bindings, the strut implantation, compression, the viscosity of the coating and structure of the arterial wall of different layers (Balakrishnan *et al.*, 2007; Mongrain *et al.*, 2007; Zhu *et al.*, 2014). A degradable stent coating is formulated artificially by supposing the value of drug diffusion in the coating store. Drug delivery systems have been discussed in numerous models by polymer degradation in PLGA (Borghi *et al.*, 2008; Prabhu and Hossainy, 2007; Versypt *et al.*, 2013). Currently, there is plenty of models that propose the bio-durable coating to understand the discharge of drug from the outer layer and later the diffusion of drug into the arterial wall. In these model's bio-durable coating is clearly formulated with constant release and diffusion of drug (Hossainy and Prabhu, 2008; Rossi *et al.*, 2012; Zhu and Braatz, 2014a). Such models have not been employed to format the intravascular drug delivery from a biodurable stent coating. A systematic model for drug release in the PLGA coating is discussed in this work. It connects the

drug diffusion to the PLGA degradation and erosion in the arterial wall (Zhu and Braatz, 2014b). The movement of drug is formulated as a reversible or two sided binding process by Zhu *et al.* (2014). This study made some improvement in this model by considering convection and diffusion in the modeling of the equation for free and bound drug. Furthermore, an investigation based on parameters such as drug diffusivities, arterial wall diffusivities and strut embedment of stent strut has considered. The effect of strut embedment on arterial wall is investigated for three cases, no embedment, half embedment and full embedment.

1.2.2 Mass Transport from Drug Eluting Stents

The means of mass transport in DES is to transfer drug from the regions of high concentration to the low concentration. The presence of gradients of these concentrations induces diffusion between the DES and the arterial wall. Mass transport can be divided into two types in the human vasculature system. The first type is blood side mass transport. Blood side mass transport transfer the drug into the lumen vessels subject to the haemodynamic. The ability of DES to deliver accurate remedial mass of drug to the wall becomes limited inside the lumen due to the nature of blood flow. So, it efficiently takes the drugs away from the affected parts. This happens only in those regions where recirculation of blood is high. The second type is transport of drug into the arterial wall, known as wall side mass transport. Wall side mass transport depends on the structural conditions of the wall and properties of the drugs. These properties will determine how the drug are being transferred into the arterial wall. If intimal layer of artery wall is damaged , the mass transfer from medial layer is accelerated directly (Hwang *et al.*, 2001).

Modelling of mass transport into the arterial walls needs powerful information about structure of arterial walls. The DES are fixed in seriously blocked regions of arteries. Wall side mass transport is directed by two forces, a convective pressure oriented force and the diffusive force. A dimensionless parameter known as the Peclet number (Pe)s in Equation 1.1, shows the relation of these two forces relatively.

$$Pe = \frac{ua}{D} \quad (1.1)$$

Peclet number plays an important role during mass transfer. If Peclet number is less than one, the transport of species is dominated by diffusion. If this number is greater than one, species are dominated by convection (Friedman, 2012). Mathematical studies convey dynamic material related to mass transport and enhancement of the functioning of DES. The delivery of medication between the tissue coatings of the arterial walls is more important. The distribution of the drug in the lumen by blood flow was published in 2007 (Mongrain *et al.*, 2007). The publications appeared in 2009 (Zunino *et al.*, 2009) and 2010 (Vairo *et al.*, 2010) may be categorized as possessing a mutual methodology.

A model is developed to analyze the diffusion controlled drug release by taking spatially independent velocity (Hwang *et al.*, 2001). Pontrelli and De Monte (2009) has developed a model based on purely mass diffusion. The methodology adopted by Pontrelli and de Monte (2007) for the solution of purely mass diffusion problem is similar as to dealing with heat conduction problems. Pontrelli and De Monte (2010) extends the previous work by taking a porous artery medial layer and porous coating of polymer top coat. This model describes the mass transport through multiple layers. A boundary layer model is discussed to deal the drug distribution by means of lumen blood flow by Rugonyi (2008). A few publications highlight the numerical analysis of drug mass transport from DES in porous arteries (Pontrelli and de Monte, 2007; Zunino, 2004). The variation in the construction of the artery wall due to stent compression and its effects on drug mass transport have not been formatted numerically. O'Connell and Walsh (2010) have investigated the effect of compression on the artery wall by considering porous material. Walsh, specifies the artery wall compression and suggests its existence in all DES computational models. A 3D purely diffusive mass transport model is presented by taking compressed porous media into account and including the compression on artery wall (Denny *et al.*, 2013).

It is interesting and encouraging to explore the effects of the drug distribution and mass transport from DES with the aid of mathematical models. In this study three integrated mathematical models for drug release and mass distribution are considered. The governing equations and the boundary conditions in non-dimensional form have been modified to find the broad range of key parameters. In this thesis numerical approach is used to solve the governing equations. For this purpose, FEM is applied to solve the model problems because FEM is better than the other numerical methods such as FDM and FVM. It has capacity to discretized complex geometries in an efficient way. This study involves the geometries of stent and arteries therefore it is necessary to use FEM. Furthermore, Matlab 2017a, Visual Studio 2010 and CUDA Toolkit 5 are used to develop hybrid platform (CPU-GPU) to tackle large sparse system of equations.

1.3 Statement of the Problem

This study aims to investigate the drug release and mass transfer from a DES. The drug mass transfer and drug release both into the wall regions and coating, are explored through the aid of some computational tool. Since, the perturbation or asymptotic methods are not able to solve the complex fluid flow model. Numerical method seems to be more significant. Therefore, these aims are achieved by modeling the governing equations to illustrate the behavior of drug release and mass transport from DES. A two phase drug release model and mass transport from DES is under exploration. The movement of drug from biodegradable coated DES investigated for better understanding by simulation of 2D model. The governing equations explain the drug release from biodegradable coated DES. This model tends to explain the concentration of free and bound drug into the arterial wall and coating. A 3D mathematical model is considered to investigate the mass transport when blood stream passing into the lumen. The governing equations are numerically solved by applying finite element method. A hybrid platform is developed for large sparse system of discretized equations to reduce the computational cost. Further a sincere attempt is made to investigate the necessary modifications to make the integrated model able to represent dynamics of drug eluting stents.

1.4 Objectives of the Study

The key objectives of this research are to investigate theoretically the characteristics and dynamics of drug release and mass transport from DES. This study includes the construction of suitable mathematical models by appropriate governing equations. These governing equations are solved by applying FEM. The objectives are:

- i. To enhance a two phase mathematical model for the exploration of the effects of key parameters on free and bound drug release in drug eluting stents.
- ii. To integrate a coupled mathematical model for the exploration of drug release from biodegradable coating and arterial wall.
- iii. To develop a mathematical model in order to analyze the mass transport from arterial wall region and lumen.
- iv. To develop sequential and parallel algorithms for discretized equations using numerical methods.

1.5 Significant of the Study

The exact mechanism to understand drug transport and mass distribution in arteries is complicated and incomplete. The previous researches show only a part of this puzzling mystery. It is important to comprehend the development of the DES. A new method can be developed to overcome DES issues. Modelling and simulation techniques encourage the understanding of the functions of DES and improve the efficacy of device. Biodegradable poly coated DES are the best choice to enhance the drug transport. DES decrease the combative consequences in stented arteries in patients. A full understanding about the formation of stents is essential for the prevention of coronary heart diseases. The DES have become the most common treatment for the prevention of these diseases. It is significant to increase the

successfulness of this treatment. The study of the dynamic outcome of the DES on the targeted site is essential to reduce the percentage of the treatment failure.

1.6 Scope of the Study

The Figure 1.2 highlights the scope of the study in detail.

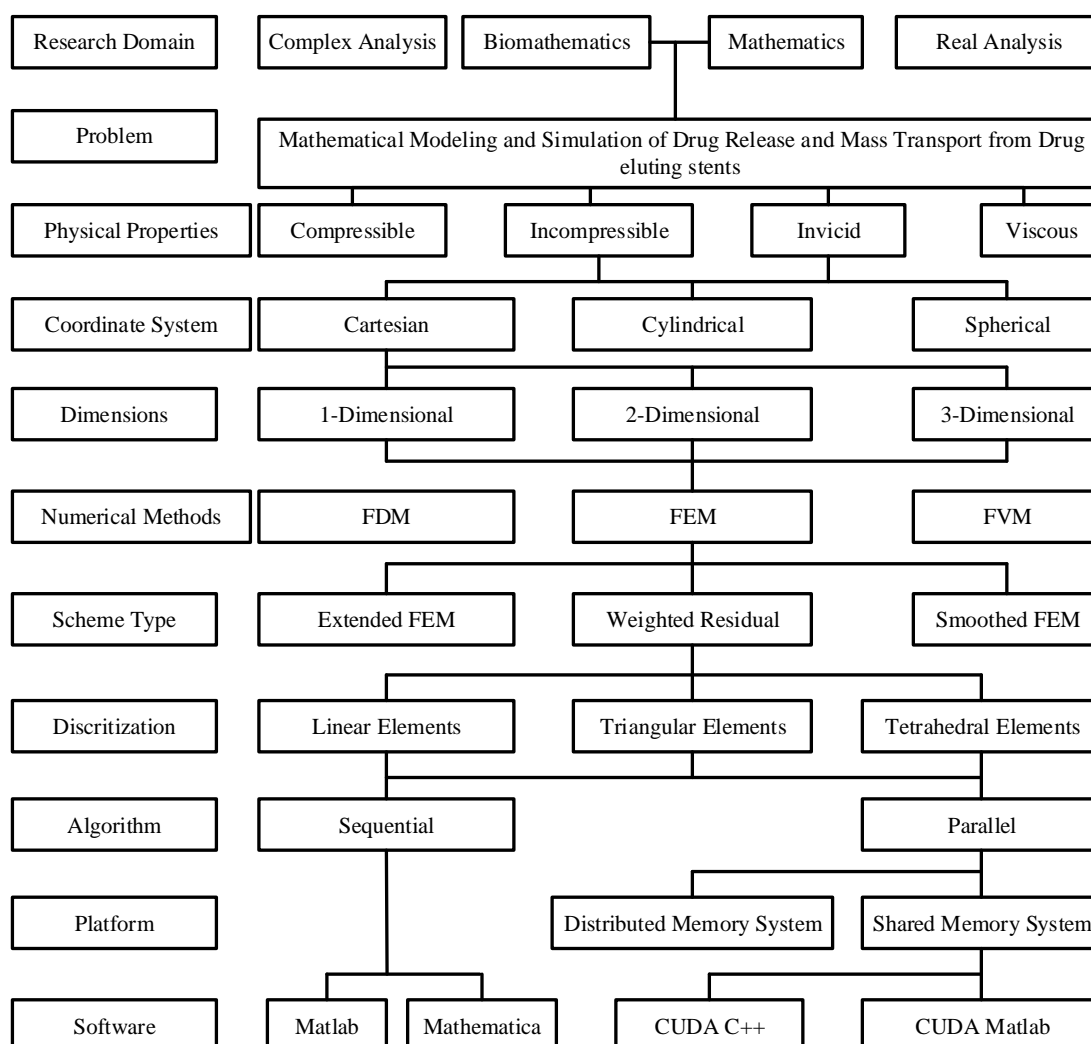


Figure 1.2 Scope of research

The present study focuses on modelling and simulation to encourage the understanding of functions of DES. This in turn could potentially facilitates the enhancement of device efficacy and ultimately contribute to reduction of the number

of heart attacks. The investigation of key parameters may help to optimize the mass concentration and drug release from coated drug eluting stents.

The fluid in the arteries is considered as an incompressible Newtonian fluid as shown in Figure 1.2. The mass distribution both into the artery walls and lumen is considered minutely in this attempt. Three mathematical models with 1D, 2D and 3D are considered in Cartesian coordinate systems to simulate the drug release and mass transport from DES. The governing equations are numerically solved by using the FEM. Linear elements, triangular elements and tetrahedron elements are used to discretize 1D, 2D and 3D models respectively. Sequential and parallel algorithms are developed for discretized equations.

The Matlab 2017b software is used for the computation of sequential and parallel numerical results. There are several parallel architectures, the most widespread many-core architecture are the GPUs (graphics processing units). On the other hand, the most common multi-core architecture are the CPUs (central processing units). The code executed using hybrid algorithm is compared with its respective serial code executed in one CPU core. The advantage of the hybrid algorithm implementation is also observed graphically.

1.7 Organization of Thesis

This thesis contains seven chapters. These are organized as follows:

Chapter 1 highlights the introduction, summary of the background, objectives and scope of the study, significance of DES, and at the end structural organization of thesis.

Chapter 2 provides an overview of the DES for the treatment of arterial problems. Several existing DES; background of this technology; safety and uses, future of DES, role of mathematics and review of FEM and time stepping methods are briefly discussed in this chapter. The introduction of hybrid platform and its

implementation using CUDA are discussed in detail. The parallel performance indicators based on speedup, temporal performance, effectiveness and efficiency are also presented in this chapter.

Chapter 3 details the research methodology of the work. The numerical background, governing equations, dependence of different parameters of the equation and elaborated solution technique have been discussed. The implementation of FEM and time stepping methods have also been discussed in this chapter. The contribution in this chapter is the modification of 1D, 2D and 3D mathematical models.

Chapter 4 gives the idea of two phase mathematical model of drug release and mass transport from DES. This model has a system of partial differential equations (PDEs). The governing equations are spatially discretized by FEM. The temporal discretization is made by three different time marching numerical methods. These numerical methods are compared on the basis of execution time, number of iteration, maximum error and root mean square error. The FEM is parallelized using the hybrid platform to improve the performance of the sequential algorithm. The parallel performance of numerical methods is compared on base of parallel performance indicators such as speedup, efficiency, temporal performance and effectiveness. The main contribution in this chapter is comparison of numerical results and parallel performance results to investigate the role of key parameters. These parameters play an important part in the concentrations of drug and mass transport from DES.

Chapter 5 presents a two dimensional (2D) mathematical model to analyze the drug release from biodurable coating and artery wall. The impact of the stent strut embedment, varied coating diffusivities and vascular drug diffusivities in the arterial wall are focused in this chapter to determine the device efficiency. Numerical solutions are obtained using FEM for governing equations. The governing equations are spatially discretized using FEM and the time derivative are treated by FDM method. The nonlinear system of algebraic equations is solved by three iterative methods known as Picard's method, Newton's Method and Broyden's Method. The sequential results of iterative methods are compared on the base of execution time,

number of iteration, maximum error and root mean square error. The hybrid platform is used to overcome computational costs by converting sequential algorithm to parallel algorithm. The parallel performance of iterative methods is compared on base of parallel performance indicators such as speedup, efficiency, temporal performance and effectiveness.

The contribution of Chapter 6 focuses on the numerical results and parallel performance of the sequential and parallel algorithms for three-dimensional model (3D). This model is also discretized numerically using FEM. The nonlinear system of algebraic equations is solved by three iterative methods as discussed in Chapter 5. The sequential and parallel performance results are measured on the base of parallel performance indicators.

Chapter 7 states the conclusion drawn from the current work and suggests possible directions for the future work.

1.8 Summary

This chapter presents the introduction and background of the study to observe the drug release and mass transport from DES. Problem statement identifying research gaps and future calls of previous studies is discussed. The objectives of research based on problem statement are identified to fill theoretical gaps. Significance, scope of the study and organization of thesis are also enclosed in this chapter.

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