ROLE OF BIDOMAIN MODEL OF CARDIAC TISSUE IN THE DYNAMICS OF PHASE SINGULARITIES

Jianfeng Lv

Submitted to the faculty of the University Graduate School
in partial fulfillment of the requirement
for the degree
Doctor of Philosophy
in the Department of Physics,
Indiana University

February 2012
Accepted by the Graduate Faculty, Indiana University, in partial fulfillment of the requirement for the degree of Doctor of Philosophy.

Sima Setayeshgar, Ph.D.

Shouhong Wang, Ph.D.

Doctoral Committee

Shyh-Yuan Lee, Ph.D.

January 11, 2012

Susan Klein, Ph.D.
ROLE OF BIDOMAIN MODEL OF CARDIAC TISSUE IN THE DYNAMICS OF PHASE SINGULARITIES

Jianfeng Lv

Submitted to the faculty of the University Graduate School
in partial fulfillment of the requirement
for the degree
Doctor of Philosophy
in the Department of Physics,
Indiana University

February 2012
To my parents and my wife Lei.
Acknowledgments

I owe my gratitude to all people who have made this dissertation possible and because of whom my graduate experience has been one that I will cherish forever.

I would like to express my deep and sincere gratitude to my advisor, Dr. Sima Setayeshgar, for her guidance during my research and study at Indiana University, Bloomington. Her perpetual energy and enthusiasm in research had motivated all her advisees, including me. Her understanding, encouraging and personal guidance have provided a good basis for the present thesis. Sima’s patience and support helped me overcome many crisis situations and finish this dissertation.

I would also want to express my thanks and appreciation to my thesis committee members Dr. Shouhong Wang, Dr. Shyh-Yuan Lee and Dr. Susan Klein. I owe my gratitude to them for being in the committee at such a short notice and all their patient and understanding for my dissertation.

I gratefully acknowledge members of my research group: Xianfeng Song, Lin Wang and Yang Yang with whom I worked closely and puzzled many of the same problems.

Finally, none of this would have been possible without the inseparable support of my family. My parents Shaoqiang and Yanxi, and my wife Lei deserve special mention for their love, encouragement and patient.
Jianfeng Lv

Role of Bidomain Model of Cardiac Tissue
in the Dynamics of Phase Singularity

The left ventricle of the heart consists of nested fiber surfaces in which the orientation of fibers in successive layers rotates through the thickness of the ventricle. Previous numerical and analytical works have shown this rotating anisotropy to be important in the generation of scroll wave instabilities in the context of the monodomain description of cardiac tissue. The bidomain model is widely recognized as providing a more accurate description of cardiac tissue than the monodomain model in describing macroscopic electrical wave phenomena in the heart, particularly in studies involving applied current.

In this work, we present a systematic study of the comparison between the bidomain and monodomain descriptions of cardiac tissue in the generation of rotating-anisotropy-induced scroll wave instability. We have implemented a multigrid scheme for simulation of electrical wave propagation in the bidomain model in three dimensions. The effects of tissue thickness and transmural diffusion coefficient were studied systematically. Our simulation results indicate that in both models, rotating-anisotropy induces scroll wave breakup. We have established phase plane diagrams denoting the stable/unstable regions for each model and identified shifts in the boundaries between these regions between the two models. Overall, we find that the bidomain model is inherently more susceptible to rotating-anisotropy induced instability than the monodomain model. These results provide further insight into and complement existing work on the role of the bidomain on the dynamics of phase singularities.
Contents

Acceptance ii

Acknowledgments ii

Abstract iii

Contents iv

List of Figures viii

List of Tables xi

1 Introduction 1

1.1 Organization of this thesis 6

1.2 Glossary of Terms 6

2 Introduction to Cardiac Electrophysiology 11

2.1 Cardiac Physiology 11

2.1.1 Structure of Cardiac Tissue and Action Potential 11

2.1.2 Cardiac Arrhythmia 14

2.2 Mechanisms Underlying Cardiac Arrhythmias 16

2.2.1 Mechanisms of Reentrant Tachycardia 16
## CONTENTS

2.2.2 Mechanism of Ventricular Fibrillation ........................................... 17

2.3 Cardiac Electrophysiology Modeling ................................................. 19
   2.3.1 Monodomain Model ................................................................. 19
   2.3.2 Bidomain Model ................................................................. 21
   2.3.3 Bidomain Reduction ............................................................... 24
   2.3.4 The Membrane Current Models ................................................. 25
      2.3.4.1 FitzHugh-Nagumo Model ................................................. 26
      2.3.4.2 Barkley Model ............................................................... 29

3 Introduction to Numerical Methods .................................................... 35
   3.1 Basics of Finite Difference Methods ............................................ 36
      3.1.1 Finite Difference ................................................................. 36
      3.1.2 Error, Consistency, Stability and Convergence ................................ 39
         3.1.2.1 Error ................................................................. 39
         3.1.2.2 Consistency .............................................................. 40
         3.1.2.3 Stability ................................................................. 41
         3.1.2.4 Convergence .............................................................. 41
   3.2 Numerical Methods for Partial Differential Equation ................................ 42
      3.2.1 Parabolic Equations ............................................................. 42
         3.2.1.1 Explicit (Forward Euler) Scheme ..................................... 43
         3.2.1.2 Implicit Methods ......................................................... 47
         3.2.1.3 The Crank-Nicholson Method ......................................... 50
      3.2.2 Elliptic Equations ................................................................. 52
         3.2.2.1 Direct Matrix Methods .................................................. 53
         3.2.2.2 Iterative Methods ......................................................... 56
         3.2.2.3 Geometric Multigrid Methods ......................................... 62
## 4 Numerical Implementation and Verification

4.1 Model Development ................................................. 75
  4.1.1 Cardiac Tissue Anatomy and Mathematical Model ........ 75
    4.1.1.1 Conductivity tensor and diffusion terms ............ 76
    4.1.1.2 Fiber Rotation ...................................... 78
  4.1.2 Mathematical Model ........................................... 81
4.2 Model Implementation and Verification .......................... 82
  4.2.1 Numerical Simulation ........................................ 82
  4.2.2 Tips and Filament Finding Algorithm ...................... 85
  4.2.3 Convergence Test and Numerical Result Verification ...... 86
    4.2.3.1 Convergence Test .................................... 86
    4.2.3.2 Bidomain Results Verification ....................... 90

## 5 Numerical Results

5.1 Spiral Wave Dynamics in Homogeneous Monodomain 2D Tissue .. 101
5.2 Scroll Wave Dynamics in Homogeneous Monodomain 3D Tissue Slab:
  Does tissue thickness matter? .................................... 104
5.3 Scroll Wave Dynamics in Monodomain 3D Tissue Slab with Rotating
  Anisotropy ....................................................... 107
  5.3.1 The effect of transmural diffusion constant $D_3$ in monodomain
     model with rotating anisotropy ............................. 117
  5.3.2 The role of tissue thickness in monodomain model with rotating
     anisotropy .................................................... 119
  5.3.3 The effects of $D_3$ and $N_z$ in the monodomain model with ro-
     tating anisotropy ............................................. 121
5.4 Scroll Wave Dynamics in Bidomain 3D Tissue Slab with Rotating
  Anisotropy ....................................................... 122
CONTENTS

5.4.1 The effect of transmural diffusion constant $D_3^i$ on bidomain model 124
5.4.2 The role of tissue thickness, $N_z$, in bidomain model . . . . . . 127
5.4.3 The role of $D_3^i$ and $N_z$ in the bidomain model . . . . . . . . . . 129

6 Discussion and Conclusion 132

6.1 Previous Works . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 133

Appendix 138

A.1 Rotating Anisotropy on Fitzhugh-Nagumo-type Dynamics . . . . . . 138

Bibliography 142
# List of Figures

2.1 Schematic description of cardiac muscle cells .................. 12  
2.2 Action potential of cardiac muscle cells ....................... 15  
2.3 The distributed-element model of cardiac fiber ................. 20  
2.4 Bidomain model approximation .................................. 23  
2.5 Phase plane for the generalized FHN model .................... 28  
2.6 Nullcline of piecewise linear model ........................... 30  
2.7 Nullcline of Barkley model .................................... 32  
2.8 Phase diagram for spiral wave states .......................... 34  

3.1 A typical finite-difference grid .................................. 38  
3.2 The computational molecule for Equation 3.16 ................. 44  
3.3 The computational molecule for Equation 3.33 ................. 48  
3.4 Crank-Nicholson finite-difference approximation for Equation 3.42 . 51  
3.5 Matrix structure for discretized Poisson equation ............. 54  
3.6 Mesh point numbering ........................................... 62  
3.7 ADI Scheme calculation procedure ............................. 63  
3.8 A schematic description of V and W cycles ...................... 68  
3.9 Workflows for full multigrid (FMG) method .................... 70  
3.10 The 3D prolongation operator matrix .......................... 73
LIST OF FIGURES

3.11 The 3D restriction operator matrix ........................................ 74
4.1 Typical sequence of photomicrographs from a heart in systole ........ 79
4.2 Schematic view of a slab of cardiac tissue ............................... 80
4.3 Convergence test of multigrid scheme for 3D bidomain model ........ 88
4.4 Alternative convergence test of multigrid scheme ......................... 89
4.5 u vs Time plots for homogeneous monodomain and reduced bidomain
models ................................................................. 91
4.6 Density plots of differences for the differences between models in ho-
mogeneous space ....................................................... 92
4.7 u vs time plots for center points in monodomain and reduced bidomain
model with rotating anisotropy ...................................... 94
4.8 u vs time plots for boundary points in monodomain and reduced bido-
main model with rotating anisotropy ................................ 95
4.9 Density plots of differences between models with rotating anisotropy
at layer 1 ............................................................ 96
4.10 Density plots of differences between models with rotating anisotropy
at layer 4 ............................................................ 97
4.11 Density plots of differences between models with rotating anisotropy
at layer 7 ............................................................ 98
5.1 Monodomain 2D phase diagram with Barkley’s Model ............... 103
5.2 Tip trajectory patterns .................................................. 104
5.3 Monodomain 3D in homogeneous domain ................................ 106
5.4 Monodomain 3D density plot with rotating anisotropy ................ 108
5.5 Monodomain 3D filament dynamics with rotating anisotropy .......... 110
5.6 Monodomain 3D quasi-stable filament dynamic ......................... 112
5.7 Monodomain 3D quasi-stable density layer plot ......................... 113
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.8</td>
<td>Monodomain 3D stable dynamic with rotating anisotropy</td>
<td>114</td>
</tr>
<tr>
<td>5.9</td>
<td>Monodomain 3D phase diagram with rotating anisotropy</td>
<td>116</td>
</tr>
<tr>
<td>5.10</td>
<td>The role of $D_3$ in 3D monodomain model</td>
<td>118</td>
</tr>
<tr>
<td>5.11</td>
<td>The role of tissue thickness $N_z$ in monodomain 3D model</td>
<td>120</td>
</tr>
<tr>
<td>5.12</td>
<td>Phase diagram for the bidomain model along horizontal line in phase plane</td>
<td>123</td>
</tr>
<tr>
<td>5.13</td>
<td>Filament number plots for various $D_3^i$ in the bidomain model, $N_z = 15$</td>
<td>125</td>
</tr>
<tr>
<td>5.14</td>
<td>Filament number plots in bidomain model with various $D_3^i$, $N_z = 7$</td>
<td>127</td>
</tr>
<tr>
<td>5.15</td>
<td>Filament number and length plots in the bidomain model for various slab thicknesses</td>
<td>129</td>
</tr>
<tr>
<td>A1</td>
<td>Three-dimensional wave pattern comparison</td>
<td>140</td>
</tr>
<tr>
<td>A2</td>
<td>Filament number and length plot for Figure A1(b)</td>
<td>141</td>
</tr>
</tbody>
</table>
List of Tables

5.1 Summary of role of $D_3$ and $N_z$ in monodomain 3D model . . . . . . . 121
5.2 Cross effect of $D_3^i$ and $N_z$ in bidomain model for $D_3^e = 0.4$ . . . . . 130
5.3 Cross effect of $D_3^i$ and $N_z$ in bidomain model for $D_3^e = 1.0$ . . . . . 131
A1 Compare with previous study . . . . . . . . . . . . . . . . . . . . . . . . . . . . 139
Chapter 1

Introduction

The mechanical function of pumping blood through the body is controlled by electrical activity propagating in cardiac tissue, which induces rhythmic contractions of the heart chambers. This electrical activity is initiated in a patch of tissue in the right atrium, known as the pacemaker (or sinoatrial node), which is a spontaneously oscillating source of electrical excitation which propagates through the healthy heart’s chambers as a plane wave. This excitation is in the form of an increased transmembrane potential difference, known as an action potential, which in turn triggers flow of various ions (most importantly sodium, potassium, calcium and chloride) across the cardiac cell membrane through membrane ion channels, ultimately triggering coordinated contraction of individual cells and chambers. Modeling transmembrane electric potential propagation, henceforth referred simply as electric potential propagation in cardiac tissue derives from the application of the leaky “cable equation” (proposed by Lord Raleigh for propagation along the trans-Atlantic telegraph cable) to neuronal cables, modified to incorporate details of cardiac electrophysiology [1].

The left ventricle is the chamber primarily responsible for pumping blood to the rest of the body, including the heart itself; as such, abnormalities in its function can
have serious consequences and are the focus of cardiac electrophysiological studies. The term cardiac arrhythmia is used to denote conditions that reflect abnormal electrical activity in one or more of the chambers. Ventricular fibrillation is a common, often fatal form of arrhythmia in which a rapidly developing disturbance in the heart’s rhythm, characterized by disorganized electrical activity, renders it unable to pump blood. In the United States alone, nearly half a million deaths annually are caused by cardiac arrhythmias [2]. Treatment of cardiac arrhythmias can either be pharmacological, e.g., based on the antiarrhythmic drugs, or interventional, e.g., in the form of implantable defibrillators. Despite the success of implantable defibrillators in terminating arrhythmic episodes in patients with diagnosed heart disease, more than half of sudden cardiac deaths arise in individuals with no previous symptoms [2, 3]. The prevention and treatment of cardiac arrhythmias are far from being fully understood and the choice of the appropriate strategy still strongly relies on the personal experience of individual cardiologists.

The heart is a moving, three-dimensional conducting medium with complex muscle fiber architecture. The heart wall is made of directed muscle cells, approximately 100 microns in length and 15 microns wide. Cells are organized in bundles known as fibers, and interconnected via gap junctions, setting up a three-dimensional conducting pathway with uniaxial anisotropy: enhanced conduction along the mean fiber direction. In the direction transverse to the fibers, conduction is significantly reduced given that the lipid cell membrane is normally impermeable to the passage of ions except at ion channels, and the density of gap junctions electrically coupling adjacent cells is much smaller on the periphery of cells than at the ends. A continuous or homogenized model of cardiac tissue is often adopted where the discrete gap junctions are averaged, and the intracellular resistance is accordingly adjusted.

In the thicker-walled ventricles, the muscle fibers are locally parallel and organized in layers, with the fiber orientation smoothly varying by approximate 120 degrees
across the ventricular wall. Hence in three dimensions, the intra- and extracellular spaces are described by anisotropic conductivity tensors. This rotating anisotropy of cardiac tissue as a conducting medium will be central to the analysis in this thesis. In the bidomain description of tissue, the intra- and extracellular spaces are distinguished. As will be shown later in this thesis, in the monodomain reduction, the anisotropy ratio (ratio of conduction velocities, or equivalently diffusion constants, along and perpendicular to the fiber direction) is assumed to be the same for intra- and extracellular spaces, giving rise to a nonlinear, parabolic reaction-diffusion system describing potential propagation. In contrast, the bidomain model gives rise to coupled parabolic and elliptic equations. The bidomain model has been demonstrated to be a more realistic description of cardiac tissue, especially in the presence of external current (for example, during defibrillation shock therapy or pacing) \[4\], \[5\].

The nonlinearity in the equations describing potential propagation in cardiac tissue derives from the resistance of membrane ion channels to the passage of ions across the cell membrane. Unlike Ohmic resistors, the resistance of membrane ion channels is a nonlinear function of the transmembrane potential. The first quantitative modeling of transmembrane ionic currents was carried out in the Nobel prize-winning work of Hodgkin and Huxley \[6\], \[7\], \[8\], \[9\] for the squid giant neuronal axon, later modified to describe ionic currents in heart cells. In the myocardium, the numbers and types of ion channels are larger than in the squid giant axon, and with growing experimental capabilities for measuring different types of ionic contributions to the transmembrane current, the complexity and size of the coupled nonlinear ordinary-differential equation models describing the dynamics of the transmembrane current have grown. At the same time, beginning with the work of Fitzhugh and Nagumo on the Hodgkin-Huxley equations nearly four decades ago, there has remained a trend in developing and using reduced electrophysiological models, which still capture the same qualitative features as higher dimensional, realistic ionic models containing contributions
to the ionic current from many different ion channels. The reduction relies on the difference in time scales describing the dynamics of different channels, often providing ionic models that are analytically and numerically more tractable. Various FitzHugh-Nagumo-type models are commonly utilized in studies of electrical wave propagation in cardiac tissue, and despite their simplicity, they have shed considerable light on the mechanisms underlying instabilities leading to arrhythmias.

As discussed in the next Chapter, transmembrane potential propagation in cardiac tissue is governed by coupled equations describing (i) the conducting properties of tissue, given by the bidomain model or its monodomain reduction, and (ii) the dynamics of membrane ion channels giving rise to the transmembrane current. Normal wave activity under the control of the heart’s pacemaker takes the form of nonlinear plane waves, whose existence and properties follows from singular perturbation analysis of equations governing propagation (see Chapter 2). If a barrier is encountered, such as a region of tissue with reduced conductivity (for example following a heart attack), the wavefront breaks, and under certain conditions, one can show the formation of a pivot point or phase singularity as the front reforms [10] and continues to propagate as a spiral wave. In three dimensions, the loci of pivot points or phase singularities define filamentous organizing centers, referred to as scroll filaments. Unlike target patterns which require a periodic source, spiral waves are self-sustained.

Even slight disturbances of heart tissues electrophysiological and conductive properties can have devastating physiological consequences and can initiate conditions under which the tissue re-excites itself through reentrant spiral/scroll waves [11, 12, 13]. There is growing experimental evidence that cardiac arrhythmias are associated with self-sustained patterns of electrical wave activity [14]. While spiral/scroll waves in the atria or ventricles are not fatal (associated with atrial and ventricular tachychardias), but rather correspond to more rapid and less efficient contraction of the heart chambers, it has been widely conjectured that the instability of a single scroll wave to a
spatiotemporal disordered state, comprised of multiple wavelets, governs the transition from tachycardia to fibrillation [15, 16, 17, 18, 19, 20, 21]. A central question is therefore understanding properties of scroll waves, and the fundamental mechanisms underlying their stability/instability [22]. Several studies [23, 24, 25] have suggested rotating anisotropy of myocardium as a possible mechanism of spiral wave instability.

In this thesis, we will utilize a FitzHugh-Nagumo-like model (Barkley model) [26] for (ii), that has been successfully used and benchmarked in previous studies of spiral wave behavior in excitable media. The focus will be on the understanding the role of the conductive properties of tissue on the generation of electrical wave instabilities; in particular, we carry out a systematic comparison of scroll wave behavior in a tissue slab described by the monodomain and bidomain models with rotating anisotropy. Given tractability of numerical implementation and analytical calculations, most previous studies have either focused only on the monodomain description of tissue [23, 24], or have employed the bidomain model [27, 28, 29] neglecting the anisotropic nature of cardiac tissue, described above. We set out to address whether and to what extent neglecting the realistic bidomain description of cardiac tissue as a conducting medium significantly alters conclusions one may draw from using the monodomain description in determine fundamental mechanisms underlying scroll wave instabilities. To do so, we have developed and implemented a full multigrid method for the bidomain model allowing fast convergence of large scale simulations. We study the effects of tissue thickness and transmural diffusion coefficient on the stability of scrolls in the bidomain and monodomain models. Our results indicate that in both bidomain and monodomain models, rotating anisotropy leads to scroll wave breakup. We have established phase plane diagrams denoting the stable/unstable regions for both models, showing shifts in boundaries between these regions between the two models. Despite the relatively simplified ionic current model employed here and idealized slab geometry, our study provides insight into the role of the bidomain
model on the onset of scroll instabilities: While the behavior of scroll waves is similar for parameter values leading to fully stable and fully unstable states, for marginally stable cases, the monodomain and bidomain results can be significantly different, with scrolls being more unstable in the bidomain model.

1.1 Organization of this thesis

The outline of this dissertation is as follows. In Chapter 2, we present a brief review of cardiac electrophysiology. The mechanisms underlying cardiac arrhythmias are introduced. The two main approaches for modeling cardiac tissue as a conducting medium, leading to monodomain and bidomain models, and their connection are presented here. The relevant membrane current models are discussed at the end of this chapter. In Chapter 3, the numerical methods used in this study are described, which focuses on finite difference methods for solving parabolic and elliptic equations. The full multigrid method used for the bidomain model is also elaborated in this chapter. We describe the construction, implementation and validation of our models in Chapter 4. In Chapter 5, we present our observations of the numerical simulation of both monodomain and bidomain models. The results from bidomain model simulations are compared directly with monodomain model results. Finally in Chapter 6, we summarize our results and possible future research directions.

Before proceeding, we provide below a glossary of key technical terms.

1.2 Glossary of Terms

Heart Physiology:

Atrium Either of the two upper chambers on each side of the heart that receive blood from the veins and in turn force it into the ventricles
**Ventricle** In the heart, ventricle is a chamber receiving blood from atrium and pumps it to the arteries.

**Fiber** The cylindrical cardiac muscle cells are linked to each other at their ends with the longer axis roughly aligned, forming a cable-like structure. We refer this structure in our study as fiber.

**Layer** The cardiac fibers are arranged in surfaces where fibers are approximately parallel in each surface, we refer the surface in our study as layer.

**Anisotropy** Anisotropy is one of the characteristics of cardiac tissue. As a consequence of the fibrous structure of the tissue, the propagation speed of electrical waves is about $2 \sim 3$ times faster along the fiber axis than perpendicular to it. This gives rise to the anisotropy of cardiac tissue.

**Fiber Rotation** The dissection results indicate that cardiac cells are first linked to form fiber structure that is further extended into layers, within which the fibers share approximately the same direction. The layers stack to form heart wall where the mean fiber angle in each layer rotates from the inner to outer wall. We refer this continuously changing fiber direction as fiber rotation.

**Rotating Anisotropy** The cardiac tissue structure has the combined effect of anisotropy and fiber rotation which give rise to rotating anisotropy.

**Modeling:**

**Monodomain Model** A mathematical model used to describe a region with the same characteristics. In our study, monodomain model specifically means a model describes the current flow in the intracellular region of the heart. Monodomain model in 2D or 3D is an extension of the cable equation, which was first introduced in computational neuroscience.
1.2 Glossary of Terms

Bidomain Model In our study, bidomain model means a mathematical model accounts for current flow in intra- and extra-cellular regions.

Ionic Current Models A mathematical model describes electrical characteristics of excitable cells such as neuron and cardiac myocytes.

Dynamics:

Action Potential The change in electrical membrane potential that occurs between the inside and outside of a nerve or cardiac muscle fiber when it is stimulated.

Arrhythmia Any disturbance in the rhythm of the heartbeat.

Tachycardia A state of heart that has abnormally fast heat beat ranging from 120 to 500 beats per minute. Tachycardia is thought to be characterized by scroll waves of electrical wave activity.

Fibrillation It is spatio-temporal incoherent electrical wave activity with heart beat rate greater than 500 beats per minute. It is well established that the fibrillation is a result of the breakup of scroll waves.

Reentry An electrical state of heart that involves action potential recurrently travels in a tight circle within the heart.

Spiral Wave In our study, it is the spatial-temporal state of the action potential in the pattern of spiral. It is usually referred in two-dimensional region.

Scroll Wave Three-dimensional extension of spiral wave.

Phase Plane It is a plot with axes being the values of two state variables, allowing for visualization of the qualitative behavior of the system. The FitzHugh-Nagumo model and Barkley model introduced in our study are two-variable
model. The phase plane of these models are the plotting of nullclines against the two variables. The dynamics can be described using the phase plane.

**Nullcline** The $x$-nullcline is a set of points in the phase plane so that $\frac{dx}{dt} = 0$.

**Phase Singularity** In our study, phase singularity is identified as where the excitation wavefront meets the repolarization waveback. It is a point of which the normal velocity is zero in two dimension. Mathematically it can be calculated as intersection of $V(\vec{r}, t) = V_{iso}$ and $\partial_t V(\vec{r}, t) = 0$, where $V(\vec{r}, t)$ is an arbitrarily chosen isopotential line.

**Spiral Core** For a given $V_{iso}$, the meandering trajectory of the tip is rigid rotating in isotropic medium and elliptical in cardiac tissue. The wavefront and the waveback of a FitzHugh-Nagumo-liked model are thin boundary layers. The trajectories form by various $V_{iso}$ chosen between resting and peak membrane potential are very close to each other. The area covered by these tip trajectories refer as spiral core.

**Spiral Tip** Wavebreak at the core of the spiral, sometimes referred as a point of phase singularity.

**Scroll Filament** Wavebreak at the core of scroll wave, sometime referred as a line of phase singularity. The filament in three dimension is actually cylindrical shape formed by the tip trajectory on each layer instead of a line. Since the core area is small compared to the diameter of the scroll wave in our model, we approximate the scroll core as filament.

**Scroll Twist** The twist in our study is applied by rotating anisotropy on the scroll filament. Twist can be imagined by first drawing a numbers of spirals on planes that are stacked right on top of each other, then rotate the spiral by an angle
relative to the spiral in the plane below. In general, the scroll is not necessary to be straight and the angle needs not be constant.

**Twiston** The disturbances correspond to highly twisted and distorted regions of a filament.
Chapter 2

Introduction to Cardiac Electrophysiology

In this chapter, we will summarize the pertinent concepts of cardiac electrophysiology. In section 2.1 we start with the structure of cardiac muscle, then a brief description of action potential, which is the most significant feature of cardiac muscle tissue for this study. In section 2.2, the mechanisms underlying cardiac arrhythmias are summarized. Two dominant approaches for cardiac tissue modeling: monodomain and bidomain, and their connection are introduced in Section 2.3. A survey of membrane models is also included at the end of Section 2.3.

2.1 Cardiac Physiology

2.1.1 Structure of Cardiac Tissue and Action Potential

The heart pumps blood through blood vessels by rhythmic contractions of cardiac muscles. These contractile cardiac muscles found in myocardium are made up of cardiac muscle cells known as cardiac myocytes, which are relatively small, cable-like,
cylindrical cells averaging $10 \sim 20\,\mu m$ in diameter and $50 \sim 100\,\mu m$ in length [30]. The cardiac myocytes are arranged into fibrous bundles which in turn make contact with adjacent bundles. The brick-like pattern shown in Figure 2.1 gives a schematic description of the arrangement of the cardiac cells.

Figure 2.1: Schematic description of cardiac muscle cells from Ref. [31]. The rectangular box represents a cardiac muscle cell. The cells are interconnected at the ends through gap junctions. The shaded area denotes the extracellular space.

Cardiac myocytes may be linked to each other at their ends. The specialized intercellular connection between the ends of cardiac myocytes is known as gap junction which is approximately $20\,\AA$ in diameter. It is a discrete anatomic entity that directly connects the cytoplasm of two cardiac cells and provides direct ionic pathways from one cell to the next. Gap junctions can also be found along the sides of the cells connecting the cells of adjacent columns into fiber bundles.

Previous study [32] has shown that the myocardial walls are formed by well-ordered, fiber-wound continuum of muscle fibers interconnected through gap junctions. The arrangement of fiber bundles form layered structures each having a common fiber orientation across the chamber walls. This architecture will be discussed in detail in Chapter 4.

One of the most significant features of cardiac muscle tissue is its electrical be-
haviour. The normal electrical conduction in the heart allows the impulse that is generated by the sinoatrial node to be propagated to the myocardium. The myocardium then contracts after the stimulation. It is the ordered stimulation of the myocardium that allows efficient contraction of the heart thereby allowing blood to be pumped throughout the body. This electrical conduction through cardiac tissue occurs by electrodiffusion in the intra-cellular and extra-cellular fluids. Electrical aspects of gap junctions are particularly important for such conduction: the electrical impulse signal is passed efficiently through gap junctions. This enables the heart to be stimulated at only one place, with the electrical impulses passing on to the rest of the heart muscle, causing it to contract. These electrical impulses are called action potential pulses. As the cell membrane is a relatively poor conductor, the action potential propagates more readily in the direction parallel to the longer cell axis as a result of the fibrous arrangement structure of the cells and the gap junctions appeared dominantly at the end of the cells, while the flows in the perpendicular direction is slower.

The cardiac action potential is of great interest to scientists, not only because it elicits the muscle contraction which pumps the bloods, but also because the changes in cardiac action potential may induce cardiac arrhythmias. The cardiac action potential is the transmembrane potential in the heart. It is caused by the changes of membrane permeability of certain ionic species. It involves the movement of various ions into and out of the cells, either actively or passively. The rapid changes of cell electrical potential could in turn excite the neighbouring cells. The properties of the action potential propagation in myocardium is governed by variable permeability of the cell membranes and diffusions. Under normal circumstances, the action potential is a propagating phenomenon either generated by stimulus or by ionic events intrinsic to tissue, and propagates away in all directions until it covers the entire tissue. Each region of the heart has cells with slightly different action potentials. The standard
model used to understand the cardiac action potential is the action potential of the ventricular myocyte, the most common cell of the heart Figure 2.2.

In order to pinpoint the changes of voltage, the cardiac action potential are separated into phases by various parts. At rest, the transmembrane potential is around \(-85 \sim -95\text{mV}\), see Figure 2.2 phase 4. During this period the voltage remains in its lowest level until next excitation. If there is an electric wave propagation approaching, the cell can be excited and then the initial depolarization is generated. It then transits to the next phase—Phase 0. This is the immediate depolarization that sends the voltage to positive millivolt level. The transmembrane potential will increase to approximately of 20mV. The membrane permeability of sodium ions (Na\(^+\)) increases and the permeability of potassium (K\(^+\)) decreases during the rapid change of voltage. Once the high sodium permeability decreases, slight repolarization occurs. The slight drop of voltage constitutes Phase 1. Next in Phase 2 the membrane potential remains steady at around zero. This plateau phase of the cardiac action potential is due to the equality between the inward flow of the calcium ions (Ca\(^{++}\)) and the outward flow of the potassium ions (K\(^+\)). During Phase 3, the calcium permeability declines while the potassium permeability increases. The net outward, positive current causes the cell to repolarize. The membrane potentials continue to restore to about \(-85 \sim -95\text{mV}\) until the next stimulus. The calcium ion (Ca\(^{++}\)) concentration increases \([33]\) when the transmembrane potential is high, which in turn induces the cardiac cells to contract. The cardiac tissue is considered an excitable medium due to its non-linear response.

2.1.2 Cardiac Arrhythmia

Operating under the control of a complex internal electrical system, the heart beats out a continual rhythm. This rhythm is ordinarily even and regular, changing speed
as necessary to adjust to the body’s need for oxygen. But many forms of heart disease can interrupt the normal contract-relax cycle and cause abnormally fast or unusually slow heart rates called cardiac arrhythmias. There are several possible causes of cardiac arrhythmia. The heart’s natural timekeeper - sinus node- can malfunction and develops an abnormal electrical impulse rate. Or any part of the cardiac muscle can interrupt the electrical rhythm or even take over as the heart’s pacemaker, setting off an abnormal heartbeat. Arrhythmias may be classified by rate or by mechanism. Two types of cardiac arrhythmias will be introduced below and discussed in more details in next section: tachycardia and fibrillation.

In the condition of tachycardia, the heart beats independent of the sinus pace-
2.2 Mechanisms Underlying Cardiac Arrhythmias

2.2.1 Mechanisms of Reentrant Tachycardia

One of the basic mechanisms underlying cardiac tachycardia is reentry. Reentry is the arrhythmogenic mechanism by which a wave of excitation fails to die out after normal activation and reenters the tissue it had previously activated. It is responsible for most of the clinically important arrhythmias like atrial/ventricular fibrillation and ventricular tachycardia. Typically, reentrant tachycardia are paroxysmal and may be terminated with a critically timed, paced beat. There are three kinds of reentry: anatomic, functional, and anisotropic. Anatomic reentry can rotate or be terminated. Functional reentry can reproduce itself and result in fibrillation or it can convert into anatomic reentry.

Anatomic reentry, first observed by Mines in 1914 [11], consists of an excitation wave that travels a fixed pathway as if it were a road. Anatomic reentry usually requires electrophysiologic or anatomic obstacle. The propagating wave front splits into two limbs when it passed through the obstacle and the reentry is created around the block. Example of anatomic reentry are supraventricular tachycardia, atrial fibrillation, and ventricular fibrillation (VF) is the main cause of sudden cardiac death in industrialized nations, accounting for more than 200,000 deaths per year in the United States alone, an incidence of $0.08 - 0.16\%$ per year [34, 35, 36]. VF is a fast-developing disturbance to the heart’s rhythm that cause the heart stop pumping. Ventricular tachycardia (VT) which could lead to VF [14], is also life-threatening.
2.2 Mechanisms Underlying Cardiac Arrhythmias

2.2.2 Mechanism of Ventricular Fibrillation

Cardiac arrhythmias are caused by abnormal electric activities of the heart, of which the most dangerous is ventricular fibrillation that can lead to sudden death. It is well established that ventricular fibrillation is a result of turbulent propagation of
the electrical excitation waves. These circulating waves have high frequency and lead to localized contractions. The definite mechanism of its initiation and maintenance is still unclear. Experimental tools for the visualization of the excitation wave as well as advanced three-dimensional computer models have intensified attempts to understand ventricular fibrillation. It is well recognized that during fibrillation at least one or possibly many three-dimensional spiral or scroll waves are present [14, 14, 38, 41, 42, 43, 44, 46, 47, 48]. And these chaotically wandering wavelets cause chaotic uncoordinated contractions of atrial and ventricular fibrillation. One of the hypotheses that has been most actively discussed is the *spiral-breakup* hypothesis. The hypothesis may lead to a breakthrough in our understanding of the factors that cause this deadly arrhythmia.

The spiral-break-up hypothesis emphasizes that the wavelets are generated by the fragmentation of an initial spiral/scroll wave: behavior observed in numerous numerical experiments [16, 17, 19, 22, 48, 49, 50, 51]. The transition from single scroll wave into wavelets qualitatively reproduce the experimentally-observed transition from ventricular tachycardia to ventricular fibrillation. Despite the popularity of the spiral-break-up hypothesis, we are still unclear about the precise mechanism of the breakup. One of the possible causes of the breakup is due to rotating anisotropy [23, 24].

Worth to mention and it’s also closely related to our study that spiral/scroll wave breaks up only when the domain size is sufficiently large through numerical studies [16, 52]. If the domain size doesn’t reach the threshold, the spiral/scroll wave either remains stable or breaks up but shrinks quickly. This observation is consistent with the clinical result that larger hearts are more susceptible to heart attacks [47, 53, 54, 55].
2.3 Cardiac Electrophysiology Modeling

2.3.1 Monodomain Model

In order to understand the patterns of electrical conduction and propagation from the scale of a single tissue to whole heart, some physical models were constructed in which the cell membrane is viewed as an electrical network with the fibers of myocardial cells constituting a cable. In the model, we can then represent the cardiac fiber as a chain of identical modules [56] which represents cylindrical slices of the membrane (see Figure 2.3). Current can flow both through the interior fluid or through the surrounding extracellular fluid. This simplified structure inspires using the cable equation, borrowed from neural science, to describe the electrical wave dynamics. The "cable equation" in two-dimensional form is sometimes called the monodomain equation, since it involves principally the intracellular domain only.

Here we introduce the derivation of cable equation. We first write down the condition of charge conservation for one cylindrical slice. Thus:

$$-\frac{dI_x}{dx}dx = I_x(x) - I_x(x + dx)$$

$$= 2\pi a \left( C_m \frac{du}{dt} + j_{ion}(x) \right) dx,$$

in which $j_{ion}$ is the transmembrane current density, $C_m$ is the membrane capacitance per unit area and $a$ is the radius of the cable.

From Ohm’s law, which holds that the axial current at a point $x$ of our cable equals the potential drop along the short distance divided by the axial resistance $dR_x$, we obtain
2.3 Cardiac Electrophysiology Modeling

Figure 2.3: The distributed-element model of cardiac fiber, from Ref. [56]. The cylinder module is an abstraction of cardiac cell bundles. The surfaces of the cylinders represent the membrane which separate the intra- and extra-cellular spaces. The electrical representation of the cylinder module is denoted inside the dash box.
\[ I_x(x) = -\frac{du}{dR_x} \]  \hspace{1cm} (2.3)

\[ = -\pi a^2 D \frac{du}{dx} \]  \hspace{1cm} (2.4)

since \( dR_x = dx/(\pi a^2 D) \) in which \( D \) is the fiber’s electrical conductivity.

Inserting Equation 2.4 into Equation 2.2, we can easily obtain the one-dimensional cable equation:

\[ D \frac{d^2 u}{dx^2} = \chi \left( C_m \frac{du}{dt} + j_{ion} \right) \]  \hspace{1cm} (2.5)

in which \( \chi = 2/ak \) is the membrane surface-to-volume ratio. In three-dimensional space, the cable equation can be rewritten as

\[ \nabla \cdot (D \nabla u) = \chi \left( C_m \frac{du}{dt} + j_{ion} \right) \]  \hspace{1cm} (2.6)

Monodomain model has its advantages of simplicity but it lacks of capturing the characteristics of extracellular space which is important for the present of injecting current.

### 2.3.2 Bidomain Model

As discussed in the previous section, in the early models, cardiac conductions were considered along a representative one-dimensional fiber that was continuous and cylindrical. When the monodomain model was extended to two and three dimensions, the effects of anisotropy on conduction become important. We can not ignore the extracellular conductivity as we did in the simple one-dimensional fiber model. Before bidomain model, even if both intracellular and extracellular conductivities are included in some modified monodomain models, the two conductivity matrices are
treated proportional to each other which it is essentially monodomain as we will shown in Section 2.3.3. In this case, the cardiac tissue is said to have equal anisotropy ratios under monodomain modeling assumption.

The cable equation introduced in the above section applies either to the intracellular space or the extracellular space. Indeed, inside the myocardial tissue, the signal is the transmembrane potential between these two inter-winded spaces. In order to model the electrical wave propagation inside the heart, one must apply the cable equation in both spaces. Whereas the monodomain model only describes the current flow in the intracellular regions or treat the intracellular and extracellular conductivities proportionally, bidomain model is a representation of cardiac tissue that explicitly accounts for current flow in both regions. Therefore bidomain model is considered a more accurate description of the electric wave activities than monodomain model.

Even in bidomain models we still can not take into account the fine-structure details, the model represents the cardiac tissue at a macroscopic scale in that the microstructure can be treated homogeneously that the intracellular and extracellular spaces are uniformly continuous. Therefore a commonly adapted treatment is to average the fine structure to yield equations that describe the potentials in an average or smoothed sense, which is adequate for most purposes [1]. The transmembrane current is also volume averaged and is defined at each point. In this sense, the cardiac tissue is viewed as a two-phase medium. Every point in space is composed of a certain fraction of intracellular space and a fraction of extracellular space. Accordingly, at each point in space there are two electrical potentials \( u_i \) and \( u_e \), as well as two currents \( i_i \) and \( i_e \), where \( i \) and \( e \) denote the intracellular and extracellular spaces, respectively (See Figure 2.4).

The bidomain model consists of a system of two nonlinear partial differential equations coupled to a system of ordinary differential equations. To deduct the bidomain equation system, we first start with Ohmic relation that is obeyed by any point in
Figure 2.4: The electrical circuit approximation of bidomain model from Ref. [57]. The intracellular and extracellular spaces are both represented by resistor grids. The two spaces are coupled by the cell membrane, represented as a parallel combination of a resistor and a capacitor.

the domain,

\[ \vec{i}_i = -\vec{D}_i \cdot \vec{\nabla}u_i, \quad (2.7) \]
\[ \vec{i}_e = -\vec{D}_e \cdot \vec{\nabla}u_e, \quad (2.8) \]

where \( \vec{D}_i \) and \( \vec{D}_e \) are the conductivities of the intracellular and extracellular spaces respectively. Since the total current

\[ \vec{i}_t = \vec{i}_i + \vec{i}_e \quad (2.9) \]

should be conserved because there are no extraneous current sources inside the cardiac fibers, we have

\[ \vec{\nabla} \cdot (\vec{D}_i \cdot \vec{\nabla}u_i + \vec{D}_e \cdot \vec{\nabla}u_e) = 0 \quad (2.10) \]
2.3 Cardiac Electrophysiology Modeling

From the cable equation, we can also get

\[ \chi \left( C_m \frac{\partial u}{\partial t} + j_{ion} \right) = \nabla \cdot \left( D_i \cdot \nabla u_i \right) = \nabla \cdot \left( D_e \cdot \nabla u_e \right), \]

(2.11)
in which

\[ u = u_i - u_e \]

(2.12)
is the transmembrane potential.

Equation 2.10 together with Equation 2.11 are usually known as the bidomain model, which was first proposed by Tung and Geselowitz [58] in the late 1970s. The transmembrane current \( j_{ion} \) in Equation 2.11 is usually determined by a valid physiological model and the boundaries usually adopt no-flux boundary conditions.

Although the bidomain model is a more accurate model, it is computationally very expensive from numerical point of view. Notice that the newly introduced, coupled elliptic equation is usually challenging to solve numerically. It turns out to be dominant in computational cost in numerical implementation. Also the requirement of the demanding fine grid structure in order to get a realistic simulation imposes more difficulties on the numerical simulation.

2.3.3 Bidomain Reduction

The monodomain model can be derived from the bidomain model by assuming that the monodomain conductivity tensors \( D_i \) and \( D_e \) are proportional to each other. From the equations of total current and transmembrane potential,

\[ \tilde{i}_t = -D_i \cdot \nabla u_i - D_e \cdot \nabla u_e, \]

(2.13)

\[ u_e = u_i - u, \]

(2.14)

we can have
\[ \vec{\nabla} u_i = (D_i + D_e)^{-1}(D_e \cdot \vec{\nabla} u - \vec{i}_t). \]  

(2.15)

Plugging this equation into Equation 2.11, we can get:

\[ \chi(C_m \frac{\partial u}{\partial t} + I_{ion}) = \vec{\nabla}(D_i ((D_i + D_e)^{-1}D_e \cdot \vec{\nabla} V) - \vec{\nabla} \cdot D_i (D_i + D_e)^{-1}i_t. \]  

(2.16)

Since we know \( \vec{\nabla} \cdot i_t = 0 \), considering the case where \( D_i (D_i + D_e)^{-1} \) is equal to a constant matrix, the governing equation can be rewritten as:

\[ \chi(C_m \frac{\partial u}{\partial t} + j_{ion}) = \vec{\nabla} \cdot (D \cdot \vec{\nabla} u), \]  

(2.17)

in which \( D = D_i (D_i + D_e)^{-1}D_e \). \( D \) is the "bulk conductivity tensor" [59, 60]. And the result Equation 2.17 is a so-called monodomain equation. The condition \( D_i = \alpha D_e \) can be interpreted as describing the case where the tissue has the same anisotropy ratios (of transverse to longitudinal conductivities with respect to the fiber orientation) in both the intracellular and extracellular spaces.

Since the monodomain equation is one parabolic type equation, with \( j_{ion} \) described by several ordinary differential equations, depending on the underlying physiological model; there are well-established numerical scheme (Section 3.2.1) that can solve it efficiently. However, the bidomain model constitutes two coupled equations, in particular the integration of elliptic equation is considered challenging [61]. In our study, we have implemented numerical scheme, which allows solving the bidomain equation system efficiently and makes practical study of bidomain model feasible.

### 2.3.4 The Membrane Current Models

Progress in treating heart disease, especially ventricular fibrillation, requires understanding the electrical behavior of cardiac membrane. There are two basic types of
2.3 Cardiac Electrophysiology Modeling

equations for membrane current: Hodgkin Huxley [6, 7, 8, 9] type and FitzHugh-Nagumo type [62, 63]. Early extensions of the Hodgkin-Huxley equations to cardiac cells were introduced for the Purkinje fiber. Beeler and Reuter [64] introduced the first model for the dynamics of a ventricular myocyte (myocardial fiber), also based on the ideas of Hodgkin and Huxley. More complicated models (e.g., Luo and Rudy [65]), based on sophisticated experiments, including single-cell and single-channel measurements, were developed later. The quantitative descriptions of ionic currents in cardiac tissue are continually being revised. There is not yet complete agreement on the best model.

2.3.4.1 FitzHugh-Nagumo Model

FitzHugh reduced the Hodgkin-Huxley model, a system of four coupled ODEs to two-variable action potential system. The FitzHugh-Nagumo (FHN) equations capture the core qualitative features of the original neuronal and cardiac system while have the advantage of simplicity and the ability to connect the effects observed in these models with basic properties of excitable medium. And of course benefits the numerical computations.

We will first list the Hodgkin-Huxley equations here for illustration purpose, for more details about this model, refer to [9].

\[
\frac{dV}{dt} = -\frac{1}{C}[\langle g_{Na} m^3 h (V - E_{Na}) + g_K n^4 (V - E_K) 
+ g_L (V - E_L) + I_{stim}\rangle,
\]

(2.18)

\[
\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m,
\]

(2.19)

\[
\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h,
\]

(2.20)

\[
\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n,
\]

(2.21)
where $L$ denotes leak, $I_{stim}$ is the total stimulus current.

FitzHugh-Nagumo model reduces Hodgkin-Huxley model by combining the variables $V$ and $m$ into a single variable $u$, and variables $n$ and $h$ into $v$ noticing that the gating variables $n$ and $h$ are slow kinetics relative to $m$. In the reduced two-variable model, the fast variable can be viewed as being representative of the transmembrane potential. The slow variable is usually denoted as a gate variable.

The generalized form of FHN model is:

$$
\epsilon \frac{du}{dt} = f(u, v) + I_{\text{external}},
$$

$$
\frac{dv}{dt} = g(u, v),
$$

in which $\epsilon$ is a small constant and $I$ is the current from external sources [1].

The two-variable feature of FHN models facilitates the phase plane analysis and singular perturbation theory. The phase plane in Figure 2.5 illustrates excitability in FHN system. Small perturbation can either quickly return to equilibrium, or depart on a large excursion.

- $u$-nullcline, which is ”cubic” shape obtained from the condition $f(u, v) = 0$.

- $v$-nullcline, which is a straight line obtained through $g(u, v) = 0$

The intersection of the nullclines is an equilibrium point, which may be unstable if it is on the middle branch of the $u$-nullcline.

**Piecewise linear FHN** One common tool for the analysis of FHN model is a further simplified model, noticing that the cubic nullcline could be approximated by a piecewise linear one. Without concern for the details of different ionic models, Panfilov and Keener adopted a piece-wise-linear FHN model [67] to describe the local dynamics.
Figure 2.5: Phase plane for the generalized FHN model, from Ref. [66].

The red solid line is the nullcline for \( f(u,v) = 0 \) and the red dotted line is the nullcline for \( g(u,v) = 0 \). The point \( F \) is where the two nullclines intersect. \( F \) denotes static state and in this setting, \( F \) is on the middle branch of cubic nullcline and is not stable. There exists a stable periodic orbit \( A \to B \to C \to D \to A \).
2.3 Cardiac Electrophysiology Modeling

\[ f(u, v) = -\phi(u) - v, \quad (2.24) \]
\[ \frac{\partial v}{\partial t} = \epsilon(u)(ku - v) \quad (2.25) \]

with

\[ \phi(u) = \begin{cases} 
C_1 \times u & \text{when } u \leq e_1 \\
-C_2 \times u + a & \text{when } e_1 < u < e_2 \\
C_3 \times (u - 1) & \text{when } u \geq e_2 
\end{cases} \]

\[ \epsilon(u) = \begin{cases} 
\epsilon_1 & \text{when } u \leq e_1 \\
\epsilon_2 & \text{when } e_1 < u < e_2 \\
\epsilon_3 & \text{when } u \geq e_2 
\end{cases} \]

where the parameters of function \( \phi(u) \) are \( C_1 = 20, C_2 = 3, C_3 = 15, a = 0.15, k = 3, \) and parameters \( \epsilon_1 = 0.0065, \epsilon_2 = 0.841 \) are chosen to insure the continuity of the function \( \phi(u) \).

These parameters specify the fast processes such as initiation of the action potential. The refactoriness of the model is determined by the function \( \epsilon(u) \). In \( \epsilon(u) \), the parameter \( \epsilon_1 \) determines the duration of the refractory tail, and \( \epsilon_3 \) determines the duration of the excited state. Decreasing \( \epsilon_1 \) will extend the refractory period. However, a decrease in \( \epsilon_1 \) also increases the period of reentry and therefore the computational time. Panfilov and Keener chose the values \( \epsilon_1 = 0.14, \epsilon_2 = 0.0589, \) and \( \epsilon_3 = 2.5 \) in their study.

2.3.4.2 Barkley Model

Barkley model was first developed by Barkley in 1991 for studying the wave propagation in excitable media. It is also a two-variable model FHN-liked model [26]. It is based on reaction-diffusion equations and has the virtue of providing particularly
Figure 2.6: The local dynamic of the Panfilov-Keener piecewise linear model, with nullclines. The backward "N" shaped nullcline is \( f(u, v) = 0 \) and the straight line is \( g(u, v) = 0 \).
fast numerical simulations of spiral waves which is very important when comes to exploring parameter space and classifying spiral wave dynamics.

The two variables $u$ and $v$ can be thought of as membrane potential and recovery variable in a hypothetical physiological medium, respectively. They obey the reaction-diffusion equations

$$\frac{\partial u}{\partial t} = f(u, v) + \nabla^2 u, \quad (2.26)$$
$$\frac{\partial v}{\partial t} = g(u, v), \quad (2.27)$$

The Laplacian term accounts for diffusion in space and the local reaction kinetics are given by

$$f(u, v) = \frac{1}{\epsilon} u (1 - u) \left( u - \frac{v + b}{a} \right), \quad (2.28)$$
$$g(u, v) = u - v \quad (2.29)$$

where $\epsilon$, $a$ and $b$ are parameters. The parameter $\epsilon$ is typically small. The time scale of $u$ could be very fast due to the small $\epsilon$, much faster than the time scale of $v$. $\frac{v + b}{a}$ sets the excitability threshold for the fixed point which is defined as the intersect of the nullclines in the absence of spatial derivatives, see Figure 2.7. If the initial condition is set near the fixed point and to the left of the threshold, $u$ will decay quickly back to the origin. Initial conditions to the right of the threshold undergo a large excursion starting to the right of the threshold before returning to the fixed point. The boundary conditions are taken to be no-flux, i.e. zero normal derivative, on the boundary of the domain of interest.

For some values of the system control parameters, several typical spiral wave states can be represented through paths traced out by tips. The bottom of Figure 2.8
Figure 2.7: Shown is the nullclines of local reaction kinetics, from Scholarpedia (Barkley model). The $v$ nullcline, $g(u, v) = 0$, is the line $v = u$, and the $u$ nullcline, $f(u, v) = 0$, consists of three lines, $u = 0$, $u = 1$, and $u = (v + b)/a$. The nullclines intersect is an excitable fixed point.
shows a sequence of spiral states obtained as a function of the parameter $a$ and $b$ in the Equation 2.27 (barkleys model) with the parameters $b = 00.5, \epsilon = 0.02$. Each state is represented by a segment of the path of the spiral tip as it evolves in time. If one looks a how spiral states in the model system are organized as a function of control parameters $a$ and $b$, the landscape of the spiral wave trajectories can be summarized in the top portion of Figure 2.8. Diagrams such as this are common for spiral waves in excitable media. There are three main parameter regions containing: no spiral waves (white region), periodically rotating spirals (yellow region) and meandering spiral waves (cyan region). The meander region is itself separated into regions whose flowers have inward petals (left of the dashed curve) and outward petals (right of dashed curve). On the dashed curve separating the two flower types, there are "infinite" flowers whose petals lie along straight lines.

Figure 2.8 captures the essence of spiral dynamics in almost all homogeneous, isotropic two-dimensional excitable media. All the dynamics seen in these figures are intrinsic dynamics of isolated spiral waves. The states shown are also observed in a variety of laboratory experiments ( [68], [69], [70], [71]) and numerical simultions ( [69], [72], [73], [74], [75], [76]). Barkley’s model will be extended in later chapter and its dynamics is investigated in the excitable medium with rotating anisotropy.
Figure 2.8: Phase diagram for spiral wave states, from Scholarpedia (Barkley Model). Top: White region denotes no spirals. Yellow region denotes periodically rotating spirals. Cyan denotes meandering spirals. The dashed curve separates the meandering region into left-half region whose tip trajectory patterns have inward petals and outward petals in the other side of the curve. Along the dashed curve are the "infinite" flower patterns whose petals lie along straight lines. Bottom: Spiral states in the reaction-diffusion model as a function of the control parameter $a$ with the other parameters fixed: $b = 0.05$, $\epsilon = 0.02$. It corresponds to a one-parameter cut through the phase diagram.
Chapter 3

Introduction to Numerical Methods

Three basic approaches or methods have been used to study the dynamics of cardiac wave propagation. These methods are:

1. Experimental
2. Theoretical
3. Numerical

The mathematical models describing cardiac electrophysiology and potential propagation in tissue can easily become intractable from the standpoint of obtaining exact solutions analytically. Approximate perturbative approaches have been successfully employed to study the dynamics of nonlinear waves in excitable tissue (see for example, [77]). Numerical methods are used extensively to obtain solutions, providing a “bridge” between analytical and experimental approaches. In many cases, numerical solutions complement experimental results, bypassing limitations such as measur-
3.1 Basics of Finite Difference Methods

Many important cardiac electrophysiological mechanisms are governed by partial differential equations (PDEs). For the regular domains on which the cardiac dynamics problems are generally solved, finite difference schemes are relatively easy to implement and provide adequate resolution. The remainder of this study deals exclusively with the finite difference approach to spatial discretization.

3.1.1 Finite Difference

The Finite difference method (FDM), also called the grid method, is one of the most commonly used numerical methods for solving differential equations. The basic idea of FDM is:

1. Replace the continuous domain on which the problem is defined with a mesh consisting of a finite number of grid points. These discrete points are usually denoted as nodes.

2. Properly define the continuous functions and variables on the grid.
3. Replace a continuous operator, for instance, the partial differential operator with a finite difference operator. The integration can be approximated through summation.

4. Solve the discrete equations and use the solution as a approximation of the desired continuous solution.

Due to its easy implementation, FDM has been popular for years and is especially convenient and powerful when taking the advantages of the development of the modern computer. There are a few questions we need to answer when we apply FDM: how do we project the problem onto the grid? How to discretize the equations? And which numerical algorithm is suitable for the discrete equation system?

We will use the two-dimensional Poisson equation as an example to illustrate the application of FDM:

\[
\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} = f(x, y),
\]

where \(u(x, y)\) is the dependent variable in the square domain \(0 \leq x \leq 1, 0 \leq y \leq 1\). The boundary conditions are assumed to be \(u(0, y) = u(x, 0) = u(1, y) = u(x, 1) = 0\).

The continuous variables \(x\) and \(y\) are now discretized as \((i \Delta x, j \Delta y)\) and \(u(x, y)\) is replaced by \(u(i \Delta x, j \Delta y)\). Assuming the mesh is uniform and the mesh size is \(h\), we can now denote \(x = x_i = ih, y = y_j = jh\).

The next step is to approximate the partial differential operator. Recall the definition of the derivative for \(u(x, y)\) at \(x = x_0, y = y_0\):

\[
\frac{\partial u}{\partial t} = \lim_{\Delta x \to 0} \frac{u(x_0 + \Delta x, y_0) - u(x_0, y_0)}{\Delta x},
\]

For a sufficiently small \(\Delta x\) and a continuous \(u\), \([u(x_0 + \Delta x, y_0) - u(x_0, y_0)]/\Delta x\) will be a good approximation to \(\partial u/\partial x\). If we write down the Taylor expansion for \(u(x_0 + \Delta x, y_0)\) around \((x_0, y_0)\):

\[
u(x_0 + \Delta x, y_0) = u(x_0, y_0) + \left(\frac{\partial u}{\partial x}\right)_0 \Delta x + \left(\frac{\partial^2 u}{\partial x^2}\right)_0 \frac{(\Delta x)^2}{2!} + \cdots
\]
Figure 3.1: A typical finite-difference grid. The space step along horizontal direction is $\Delta x$, and the space step along the vertical direction of the grid is $\Delta y$. The indexing of the adjacent points of $u$ are shown in the zoom-in plot on the right.

\[ + \left( \frac{\partial^{n-1} u}{\partial x^{n-1}} \right) \frac{(\Delta x)^{n-1}}{(n-1)!} + \frac{\partial^n u}{\partial x^n} \frac{(\Delta x)^n}{n!} \xi \leq x_0 \leq (x_0 + \Delta x) \]  

Rearranging and switching now to the $i,j$ notation, we now have

\[ \frac{\partial u}{\partial x} = \frac{u_{i+1,j} - u_{i,j}}{h} + \text{Truncation error}, \]  

where $(u_{i+1,j} - u_{i,j})/h$ is the finite-difference representation for $\frac{\partial u}{\partial x_{i,j}}$. The difference between the partial derivative and its finite difference representation is called the \textit{Truncation error}. We characterize the truncation error by using the big “order-of” notation $O$:

\[ \frac{\partial u}{\partial x} = \frac{u_{i+1,j} - u_{i,j}}{h} + O(h) \]  

More details on the $O$ notation can be found in Ref. [78].
If we recursively apply the finite difference of first order derivatives, we can deduce one of the discrete representations of the second order derivative:

\[
\frac{\partial^2 u}{\partial x^2} = \frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{h^2} + O(h^2) \quad (3.6)
\]

\[
\frac{\partial^2 u}{\partial y^2} = \frac{u_{i,j+1} - 2u_{i,j} + u_{i,j+1}}{h^2} + O(h^2) \quad (3.7)
\]

So the Poisson equation could be discretized as

\[
\frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{h^2} + \frac{u_{i,j+1} - 2u_{i,j} + u_{i,j+1}}{h^2} = f(i,j). \quad (3.8)
\]

Another quick example is the one-dimensional heat equation \( \frac{\partial u}{\partial x} = \frac{\partial^2 u}{\partial x^2} \), which involves discretization of time:

\[
\frac{u_{j}^{n+1} - u_{j}^{n}}{\tau} = \frac{u_{j-1}^{n} - u_{j}^{n} + u_{j+1}^{n}}{h^2}, \quad (3.9)
\]

where \( \tau \) is the time step, equaling \( 1/T \). \( T \) is the total simulation time.

### 3.1.2 Error, Consistency, Stability and Convergence

Solving equations is not the whole story of numerical simulation. There are some important factors we need to understand before we can fully trust the results from simulation. Numerical approximation always comes with errors. While it may be possible to avoid outright errors in the simulation, there is necessarily error that we cannot fully eliminate but only reduce. To ensure that the numerical solution is a reliable approximation, convergence of the simulation needs to be demonstrated.

#### 3.1.2.1 Error

As mentioned in the preceding section, truncation error originates from the finite-difference representation of the partial differential equation. We can implement different representations to reduce the truncation error. However, truncation error would
persist even on a hypothetically perfect computer which had the ability to accurately represent any numerical value. We can’t completely eliminate it because it is intrinsic to the program or algorithm used, in our case, the finite-difference scheme.

There is another kind of error that is a characteristic of computer hardware called roundoff error. Computers store numbers not with infinite precision but rather in some approximation that can be represented through a fixed number of bits or bytes. A number in integer representation and the arithmetic between integers are represented exactly. However arithmetic among numbers in floating-point representation is not exact, even if the operands are exactly represented. The smallest floating-point number which, when added to the floating-point number 1.0, produces a floating-point result different from 1.0 is termed the machine accuracy $\epsilon_m$. Roughly speaking, the machine accuracy $\epsilon_m$ is the fractional accuracy to which floating-point numbers are represented. Pretty much any arithmetic operation among floating numbers should be thought of as introducing an additional error of at least $\epsilon_m$.

With the presence of truncation error and roundoff error, how do we know that our representation is acceptable and the solution obtained from finite difference scheme is a reasonable approximation to the PDE? To answer this question, our difference representation needs to meet the conditions of consistency and stability.

### 3.1.2.2 Consistency

Consistency deals with the extent to which the finite-difference equations approximate the partial differential equations. The difference between the PDE and the finite-difference equation (FDE) approximation has already been defined as the truncation error of the difference representation. A finite-difference representation of a PDE is said to be consistent if we can show that the difference between the PDE and its difference representation vanishes as the mesh is refined, i.e., $\lim_{\text{mesh} \to 0} (\text{PDE} - \text{FDE})$
= \lim_{\text{mesh} \to 0}(\text{TruncationError}) = 0. \text{ That is to say, truncation error can always be}
\text{made arbitrarily small by refining the grid if the discretized FDE is consistent.}

3.1.2.3 Stability

Numerical stability is a concept applicable in the strict sense only to marching problems. A stable numerical scheme is one for which errors from any source (truncation, round-off) are not permitted to grow in the sequence of numerical procedures as the calculation proceeds from one marching step to the next. Sometimes, however, any round-off error that becomes “mixed into” the calculation at an early stage is successively magnified until it comes to swamp the true answer, in which case this method is \textit{unstable}. Generally, concern over stability occupies much more of our time and energy than does concern over consistency. Consistency is relatively easy to check and most schemes which are conceived will be consistent just due to the methodology employed in their development. Stability is much more subtle and usually a bit of hard work is required in order to establish analytically that a scheme is stable.

3.1.2.4 Convergence

Generally, we find that a consistent, stable scheme is convergent. Convergence here means that the solution to the finite-difference equation approaches the true solution to the PDE having the same initial and boundary conditions as the mesh is refined. A proof of this is available for initial value problems governed by linear PDE’s. The theorem, due to Lax \cite{79} is stated here without proof.

\textbf{Lax’s Equivalence Theorem.} Given a properly posed initial value problem and a finite-difference approximation to it that satisfies the consistency condition, stability is the necessary and sufficient condition for convergence.

To summarize Lax’s theorem, we could safely say that
Consistency + stability $\iff$ convergence

We might add that most computational work proceeds as though this theorem applies also to nonlinear PDE’s although the theorem has never been proven for this more general category of equations.

3.2 Numerical Methods for Partial Differential Equation

3.2.1 Parabolic Equations

In this section we are concerned with the numerical solution of parabolic equations. We begin with the simplest explicit difference method, and the analysis of its error is easily accomplished by the use of a maximum principle. However, the numerical solution becomes unstable unless the time step is severely restricted. So we shall go on to consider other, more elaborate, numerical methods which can avoid such a restriction.

Most of the parabolic partial equations we encounter in scientific and engineering researches are in the form of

$$u_t = L(u) \quad (3.10)$$

where $L(u)$ is a second-order elliptic partial differential operator.

To explain the basic ideas and to illustrate the process of developing improved difference equations for a given problem, we will use the one-dimensional heat equation as an initial model.

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + f(x), \quad 0 < t \leq T, \quad 0 < x \leq l \quad (3.11)$$

with initial condition $u(x, 0) = g(x)$ and boundary conditions $u(0, t) = u(l, t) = 0$
3.2 Numerical Methods for Partial Differential Equation

During the following discussion explicit (Forward Euler), implicit methods and Crank-Nicholson will be introduced. The explicit scheme is a non-iterative "marching" process to obtain the solution at the present point in terms of the known preceding point and boundary values. Stability questions are critical in these situations. Implicit procedures generally involve simultaneous calculations of the present values in terms of known preceding and boundary values. Implicit methods are usually considered stable. The Crank-Nicholson method has a higher order of accuracy in the mean time it retains the implicit method’s stability feature.

3.2.1.1 Explicit (Forward Euler) Scheme

There are multiple ways to apply the finite-difference method to Equation 3.11. We choose to discretize as below:

\[
\frac{u^{k+1}_j - u^k_j}{\tau} = \frac{u^{k+1}_{j+1} - 2u^k_j + u^{k}_{j-1}}{h^2} + f_j, \quad (3.12)
\]

\[
u^0_j = g(x_j), \quad 1 \leq j \leq N - 1 \quad (3.13)
\]

\[
u^k_0 = \nu^k_N, \quad 0 \leq k \leq M - 1, \quad (3.14)
\]

where we have \(Nh = l\) and \(M\tau = T\). The parameters \(k\) and \(h\) represent the time and space steps, respectively, while \(N\) and \(M\) are the numbers of grid points along both axes.

If we denote \(r = \frac{\tau}{h^2}\), we can rearrange Equation 3.12 as

\[
u^{k+1}_j = ru^k_{j-1} + (1 - 2r)u^k_j + ru^k_{j+1} + \tau f_j. \quad (3.16)
\]

Equation 3.16 utilizes the explicit scheme. If we treat the solution at each time node as a layer structure, then the forward Euler calculation is by layer. The solution
on the current layer depends on the solution for the previous layer. Starting with \( k = 0 \), we have

\[
u_j^1 = ru_{j-1}^0 + (1 - 2r)u_j^0 + ru_{j+1}^0 + \tau f_j. \quad (3.17)
\]

Given the initial condition \( u_j^0 = g(x_j) \) and the boundary condition \( u_0^0 = u_N^0 \), we can calculate \( u_j^1 \) at all the mesh points. It is worth pointing out that each node on layer 1 solely rely on the points on layer 0. Once we carry on the calculation to next layer based on Equation 3.16, we will have \( u_j^2 \), so on and so forth ...

We then have solutions \( u_j^k \) for all the time nodes \( k, k = 0, 1, \ldots, M - 1, \; j = 1, 2, \ldots, N - 1 \)

Due to the layer structure of the explicit scheme, we can schematically represent the computational molecule for Equation 3.16 in Figure 3.2

![Figure 3.2: The computational molecule for Equation 3.16. \( r = \frac{\tau}{n^2} \)](image)

A vector representation of explicit Equation 3.16 could be written as

\[
u^{k+1} = Au^k + f, \quad (3.18)
\]
where

\[
A = \begin{bmatrix}
  1 - 2r & r & 0 & \cdots & 0 \\
  r & 1 - 2r & r & \ddots & \vdots \\
  0 & \ddots & \ddots & \ddots & 0 \\
  \vdots & \ddots & r & 1 - 2r & r \\
  0 & \cdots & 0 & r & 1 - 2r \\
\end{bmatrix}
\] (3.19)

Here we use the forward Euler scheme for the one-dimensional heat equation as an example to demonstrate that this finite difference approximation is indeed consistent. That is to say, as the mesh is refined, the solution of the finite difference equation converges to the true solution. As we pointed out at the beginning of the section, the explicit scheme also has stability concerns. We will also show the stability condition for the explicit scheme to be stable. For illustration purposes, we set the source term \( f(x) = 0 \). The maximum principle can be applied to analyzing the difference between \( u \) and \( U \), which are the approximate result and the exact solution, respectively. This method has evolved from the works of several authors, including [80], [81], and [82].

First of all, let’s look at the stability condition for the explicit method as applied to the one-dimensional heat equation. Noting that Equation 3.12 are written in matrix form as Equation 3.18 without the source term,

\[
u^{k+1} = Au^k
\] (3.20)

The iteration matrix \( A \), also called amplification factor has \( 1 - 2r \) on its diagonal and \( r \) on its off-diagonal. There are solution \( u^k \)s for all the time steps \( k \), \( k = 1, 2, \ldots, M - 1 \). Error is generated at each time step. The stability condition requires that the error generated in \( u^k \) is not magnified in \( u^{k+1} \). The stability condition requires the spectral radius \( \rho(A) < 1 + M\tau \), where \( M \) is a constant value. The eigenvalues \( \mu_j \) of \( A \) is

\[
\mu_j^A = (1 - 2r) + 2r \cos(j\pi h) = 1 - 4r \sin^2 \frac{j\pi h}{2}
\] (3.21)
To satisfy $\left| 1 - 4r \sin^2 \frac{j\pi h}{2} \right|$, we need $4r \sin^2 \frac{j\pi h}{2} \leq 2 + M\tau$. Therefore, we have $4r \leq 2$, which is

$$0 < r \leq \frac{1}{2}.$$  \hfill (3.22)

In fact it is

$$0 < r = \frac{\tau}{h^2} \leq \frac{1}{2}.$$  \hfill (3.23)

This shows the restriction on $\tau$ and $h$ for the explicit method approach to the one-dimensional heat equation.

Next we will show that the explicit method is consistent, in difference equation form:

$$U_j^{k+1} = rU_{j-1}^k + (1 - 2r)U_j^k + rU_{j+1}^k + O[\tau^2 + \tau h^2],$$

$$k = 1, 2, \ldots, M - 1 \hfill (3.24)$$

Here we reintroduce the truncation error, which we would like to capture while we do the stability analysis. Since $u$ is only defined at a finite number of points, there is no continuous differential equation defined for $u$. However, if we subtract Equation 3.16 and Equation 3.24, we obtain $e_j^k = U_j^k - u_j^k$, and

$$e_j^{k+1} = re_{j-1}^k + (1 - 2r)e_j^k + re_{j+1}^k + O[\tau^2 + \tau h^2],$$

$$j = 1, 2, \ldots, M - 1 \hfill (3.25)$$

$U$ and $u$ share the same initial condition and boundary values at time 0, therefore

$$e_j^0 = 0, \quad j = 0, \ldots, M \hfill (3.26)$$

$$e_0^k = e_M^k = 0, \quad k = 0, \ldots, N. \hfill (3.27)$$

The three coefficients on the right-hand side of Equation 3.25 sum to one for all values of $r$. From the stability condition Equation 3.23, we also learn that $1 - 2r$ is
non-negative. Applying the norm on Equation 3.25, we can achieve

\[ |e_j^{k+1}| \leq r|e_j^{k-1}| + (1 - 2r)|e_j^k| + r|e_{j+1}^k| + A[\tau^2 + \tau h^2] \]

\[ \leq \|e^k\| + A[\tau^2 + \tau h^2], \quad j = 1, \ldots, M - 1 \] (3.28)

where \(\|e^k\| = \max_{j=0,\ldots,M} |e_j^k|\), \(A\) is a constant which defines the ceiling of the truncation error function. Since \(\|e^0\| = 0\), we can calculate the \(\|e^{k+1}\| \leq \|e^k\| + A[k^2 + kh^2]\) as

\[ \|e^k\| \leq Ak[\tau^2 + \tau h^2] \]

\[ \leq AT[\tau + h^2] \] (3.29)

The error \(e_j^k\) tends to zero as \(h\) and \(\tau\) tend to zero. Thus the discrete solution of the finite difference equation converges to the solution of the differential equation as \(h\) and \(\tau\) approach zero. This means that the finite-difference approximation is indeed consistent. As we have shown in Section 3.1.2, based on Lax’s equivalence theorem, the explicit method here satisfies the condition of convergence.

### 3.2.1.2 Implicit Methods

We have derived the stability condition Equation 3.23 for the explicit scheme. By examining this condition, we found it places a severe restriction on the size of the time step if we would like to solve our equation on a fine grid. This in turn results in increasing computing time. The simple explicit scheme could be very inefficient if high resolution of the domain is required.

We will apply the same layer concept introduced in Section 3.2.1.1 when we analyse the implicit methods. Recall that each \(u_j^{k+1}\) on layer \(k+1\) is associated with multiple \(u\) on layer \(k\). It is an \(m \Rightarrow 1\) relationship and since all values on layer \(k\) are known, each \(u\) on layer \(k+1\) could be calculated independently. For the implicit
method, multiple \( u \)’s on \( k+1 \) layer are now "mapped" to a single \( u \) on layer \( k \), see (Reference Figure). Since \( u_{j}^{k+1} \) are unknown, we can not obtain one \( u \) on layer \( k+1 \) without knowing some other \( us \). Therefore, we end up solving a group of equations simultaneously.

First introduced by O’Brien et al. \[83\], the implicit scheme for the heat equation 3.11 is written in the form of Equation 3.30:

\[
\frac{u_{j}^{k+1} - u_{j}^{k}}{\tau} = \frac{u_{j-1}^{k+1} - 2u_{j}^{k+1} + u_{j+1}^{k+1}}{h^2} + f_{j} \quad (3.30)
\]

\[
u_{0}^{j} = g(x_{j}), \quad 1 \leq j \leq N - 1 \quad (3.31)
\]

\[
u_{0}^{k} = \nu_{N}^{k}, \quad 0 \leq k \leq M - 1 \quad (3.32)
\]

with \( f_{j} = f(x_{j}), \quad r = \frac{\tau}{h^2} \). Notice that on the right-hand-side of the equation, all \( u \)’s are now on layer \( k+1 \), in contrast with the explicit method where all \( u \)’s on the right-hand-side of the equation were known and on layer \( k \).

Rearranging Equation 3.30, we obtain

\[- ru_{j-1}^{k+1} + (1 + 2r)u_{j}^{k+1} - ru_{j+1}^{k+1} = u_{j}^{k} + \tau f_{j} \quad (3.33)\]

Figure 3.3: The computational molecule for Equation 3.33. \( r = \frac{\tau}{h^2} \)
Looping through \( k = 0, 1, \ldots, M - 1 \), we have a group of equations that need to be solved simultaneously:

\[
\begin{align*}
-ru^1_{j-1} + (1 + 2r)u^1_j - ru^1_{j+1} &= u^0_j + \tau f_j \\
-ru^2_{j-1} + (1 + 2r)u^2_j - ru^2_{j+1} &= u^1_j + \tau f_j \\
&\quad \vdots \quad \vdots \\
-ru^{k+1}_{j-1} + (1 + 2r)u^{k+1}_j - ru^{k+1}_{j+1} &= u^k_j + \tau f_j \\
&\quad \vdots \quad \vdots \\
-ru^{M-1}_{j-1} + (1 + 2r)u^{M-1}_j - ru^{M-1}_{j+1} &= u^{M-2}_j + \tau f_j
\end{align*}
\]

(3.34)

The corresponding vector form of the implicit method is

\[
Bu^{k+1} = u^k + \mathbf{f}
\]

(3.35)

where

\[
B = \begin{bmatrix}
1 + 2r & -r & 0 & \cdots & 0 \\
-r & 1 + 2r & -r & \ddots & \vdots \\
0 & \ddots & -r & \ddots & 0 \\
\vdots & \ddots & -r & 1 + 2r & -r \\
0 & \cdots & 0 & -r & 1 + 2r
\end{bmatrix}
\]

(3.36)

The stability requirement for the implicit method is \( \rho(B) < 1 + M\tau \). We have the eigenvalues of \( B \)

\[
\mu_j^B = [(1 + 2r) - 2r \cos j\pi h]^{-1} = [1 + 2r(1 - \cos j\pi h)]^{-1} \leq 1
\]

(3.37)

Therefore, for any value of \( r \) the implicit method is stable.

The solution of a system of equations such as Equation ?? is another topic of numerical methods. The numerical methods introduced in Section 3.2.2 for elliptic equation could in general be applied. The difference is that for parabolic equations,
we have a choice to avoid solving a system of equations by properly choosing a discretization method; while for elliptic equations, solving a system of equations cannot be avoided.

### 3.2.1.3 The Crank-Nicholson Method

Crank and Nicholson \[84\] proposed a method that takes the average of Equation 3.12 and Equation 3.30.

\[
\frac{u_{j}^{k+1} - u_{j}^{k}}{\tau} = \frac{1}{2} \left( \frac{u_{j}^{k} - 2u_{j}^{k} + u_{j+1}^{k}}{h^2} \right) + \frac{u_{j}^{k+1} - 2u_{j}^{k+1} + u_{j+1}^{k+1}}{h^2} + f_{j} \quad (3.38)
\]

\[
u_{j}^{0} = g(x_{j}), \quad 1 \leq j \leq N - 1 \quad (3.39)
\]

\[
u_{0}^{k} = \nu_{j}^{k}, \quad 0 \leq k \leq M - 1 \quad (3.40)
\]

Reorganizing Equation 3.38, we have

\[-\frac{r}{2}u_{j-1}^{k+1} + (1 + r)u_{j}^{k+1} - \frac{r}{2}u_{j+1}^{k+1} = -\frac{r}{2}u_{j-1}^{k} + (1 + r)u_{j}^{k} - \frac{r}{2}u_{j+1}^{k} + \tau f_{j} \quad (3.42)
\]

There are multiple \(u\) on layer \(k + 1\) at the left-hand-side of the equation, which means that we again need to solve a system of equations.

The vector form of Equation 3.42 could be written as

\[
\frac{I + B}{2}u^{k+1} = \frac{I + A}{2}u^{k} + f \quad (3.43)
\]

Noticing that the amplification factor of Crank-Nicholson is \(C = (\frac{I + A}{2})(\frac{I + B}{2})^{-1}\), and its eigenvalues are

\[
\mu_{j}^{C} = \frac{(1 - 2r) + r \cos j\pi h}{(1 - 2r) - r \cos j\pi h} = \frac{1 - 2r \sin^2 \frac{j\pi h}{2}}{1 + 2r \sin^2 \frac{j\pi h}{2}} \leq 1 \quad (3.44)
\]

Therefore, the Crank-Nicholson scheme is also unconditionally stable.
3.2 Numerical Methods for Partial Differential Equation

Figure 3.4: Crank-Nicholson finite difference approximation for Equation 3.42. \( r = \frac{k}{h^2} \)

What is the advantage of using the Crank-Nicholson scheme over an implicit scheme if both of them involve solving a group of equations? The answer is that Crank-Nicholson can have second order accuracy for both \( \tau \) and \( h \). Notice that

\[
\left( \frac{\partial u}{\partial t} \right)_{j}^{k+1/2} = \frac{u(x_j, t_{k+1}) - u(x_j, t_k)}{\tau} + O(\tau^2) \quad (3.45)
\]

and

\[
\left\{ \frac{\partial^2 u}{\partial x^2} \right\}_j^{k+1} = \left\{ \frac{\partial^2 u}{\partial x^2} \right\}_j^{k+1/2} + \frac{\tau}{2} \left\{ \frac{\partial^3 u}{\partial x^2 \partial t} \right\}_j^{k+1/2} + \frac{1}{2!} \left\{ \frac{\partial^4 u}{\partial x^2 \partial t^2} \right\}_j^{k+1/2} + O(\tau^3) \quad (3.46)
\]

\[
\left\{ \frac{\partial^2 u}{\partial x^2} \right\}_j^{k} = \left\{ \frac{\partial^2 u}{\partial x^2} \right\}_j^{k+1/2} + \frac{\tau}{2} \left\{ \frac{\partial^3 u}{\partial x^2 \partial t} \right\}_j^{k+1/2} + \frac{1}{2!} \left\{ \frac{\partial^4 u}{\partial x^2 \partial t^2} \right\}_j^{k+1/2} + O(\tau^3) \quad (3.47)
\]

Taking the average of Equation 3.47 and applying

\[
\left( \frac{\partial u}{\partial t} \right)_{j}^{k+1/2} = \left( \frac{\partial^2 u}{\partial x^2} \right)_{j}^{k+1/2} + f_j, \quad (3.48)
\]

we can achieve

\[
\frac{u(x_j, t_{k+1}) - u(x_j, t_k)}{\tau} = \frac{1}{2} \left( \frac{u(x_{j+1}, t_{k+1}) - 2u(x_j, t_{k+1}) + u(x_{j-1}, t_{k+1})}{h^2} + \frac{u(x_{j+1}, t_k) - 2u(x_j, t_k) + u(x_{j-1}, t_k)}{h^2} \right) + O(\tau^2 + h^4) \quad (3.49)
\]

Therefore, Crank-Nicholson has higher order of accuracy than the explicit and implicit method.
3.2.2 Elliptic Equations

Earlier in Section 3.1.1 when we introduced the FDM, we used the Poisson equation as an example for discretization. The solution for elliptic equations like the Poisson equation is usually challenging.

\[
\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} = f(x, y),
\]

(3.50)

where \( \rho \) is known.

The finite-difference representation of Equation 3.50 is re-written here:

\[
\frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{h^2} + \frac{u_{i,j+1} - 2u_{i,j} + u_{i,j-1}}{h^2} = f(i, j),
\]

(3.51)

assuming that the domain of the problem is uniform and the Poisson equation is discretized with mesh size \( h \). Through rearranging the equation, we obtain

\[
u_{i+1,j} + u_{i-1,j} + u_{i,j+1} + u_{i,j-1} - 4u_{i,j} = h^2 f_{i,j}
\]

(3.52)

If the dimension of the domain \( x - y \) is \( Mh \times Nh \) and the values on the boundaries are defined, we will have a size of \( (M - 1)(N - 1) \times (M - 1)(N - 1) \) linear equation system to solve. Using two indices \( i \) and \( j \) to list all the linear equation of the system would not be an efficient method. It is recommended to relabel the points, Ref. [85].

\[
l \equiv i(N + 1) + j \quad \text{for} \quad i = 0, 1, \ldots, M, \quad j = 0, 1, \ldots, N
\]

(3.53)

This labelling method counts the points consecutively from left to right and top to bottom. One of the advantages of mapping the two-dimensional indices to one-dimensional index is that the resulting matrix for the linear system is a banded matrix with band with at most \( 2n - 1 \). A banded matrix is relatively easier to solve than a full matrix system or a sparse matrix. Now Equation 3.52 becomes

\[
u_{l+(N+1)} + u_{l-(N+1)} + u_{l+1} + u_{l-1} - 4u_l = h^2 f_l
\]

(3.54)
The linear equation system can be represented in a matrix equation.

\[ Au = b \quad (3.55) \]

where \( A \) has the form shown in Figure 3.5. The matrix \( A \) is a special case of a band diagonal matrix.

Two commonly adapted numerical methods for solving linear systems such as that illustrated in Figure 3.5 are *direct matrix methods* and *relaxation methods*, which we will briefly introduce in the following sections. We will also introduce the *multigrid algorithm* which is proven to be the most efficient way to obtain the solution for elliptic equations.

### 3.2.2.1 Direct Matrix Methods

Direct Matrix methods attempt to solve Equation 3.55 directly, which means the result is obtained at each step without iterative calculation. The degree to which this is practical depends very strongly on the exact structure of the matrix \( A \). That’s why we always want to investigate the possible ways of labelling the discretized equation, in order to obtain an optimized form of the matrix to facilitate the direct methods; Otherwise the matrix problem may be prohibitively large. For example, the simplest problem on a \( 100 \times 100 \) spatial grid would involve 10000 unknown \( u'_{i,j} \)s, implying a \( 10000 \times 10000 \) matrix \( A \), containing \( 10^8 \) elements. One of these matrices takes roughly 800 MB of the system memory, which easily becomes exhausted.

If a square matrix can be written as a product of two matrices

\[ LU = A, \quad (3.56) \]

where \( L \) is *lower triangular* (has elements only on the diagonal and below) and \( U \) is *upper triangular*, the Equation 3.55 can be first solved for a vector \( y \) such that

\[ Ly = b, \quad (3.57) \]
Figure 3.5: Matrix structure for the discretized Poisson equation, adapted from Ref. [86]. All elements not shown are zero.
and then solving
\[ \mathbf{U} \mathbf{x} = \mathbf{y}. \] (3.58)

The forward substitution method could be used to solve a linear system with triangular matrix very efficiently, which is the reason why we would like to find a way to decompose a matrix into two triangular matrices. The decomposition step could be very expensive in terms of the load of computing, however, we only need to do it once. Of course, not all the matrices could be decomposed and even if it is feasible to perform the decomposition, there are limitations that imposed by computer hardware and software, for instance, the ability of the compiler to allocate a large trunk of memory to host the resulting matrices.

Two special linear systems are tridiagonal and band diagonal. Tridiagonal system have nonzero elements only on the diagonal plus or minus one. A problem discretized into the form of Equation 3.55 could be solved very effectively since the LU decomposition of the triadiagonal matrix \( \mathbf{A} \) could be done with forward substitution in one sweep of all the points on the mesh. On the other hand, band diagonal systems have \( m_1 \geq 0 \) non-zero elements immediately to the left of the diagonal and \( m_2 \geq 0 \) nonzero elements immediately to its right, and require \( m_1 \) and \( m_2 \) are both \( \ll N \) to be meaningful. Band diagonal matrices can still be decomposed, however the resulting matrices are not compact and usually double the storage space. This will eventually make the direct method obsolete since as the dimensions of the domain grow, the size of band diagonal matrix increases dramatically and there might not be enough space to host the resulting matrices.

Generally speaking, when there is storage available to implement these methods — not nearly as much as \( 10^8 \) above, but usually much more than is required by relaxation methods — then we should consider doing so. Only multigrid relaxation methods are competitive with the best matrix methods. This is one of the famous
dilemmas in computer science: storage space has to be sacrificed in order to gain speed. That is to say, when we are optimizing an algorithm, we usually need to allocate more memory in order to speed up the program. The numerical methods we will introduce in the next section have a minimum requirement of memory usage but in general they are slower than the direct methods.

### 3.2.2.2 Iterative Methods

Several iterative (relaxation) methods for solving equation Equation 3.55 are built around a partition of $A$ into the form

$$A = L + D + U,$$  \hspace{1cm} (3.59)

where $L$ and $U$ have same elements of the lower and upper parts of $A$, respectively. $D$ is a diagonal matrix.

\[ L = \begin{bmatrix}
0 & 0 & \cdots & 0 \\
0 & a_{21} & \cdots & 0 \\
\vdots & \ddots & \ddots & \vdots \\
a_{n1} & a_{n2} & \cdots & a_{n,n-1} & 0
\end{bmatrix} \]  \hspace{1cm} (3.60)

\[ D = \begin{bmatrix}
0 & \cdots & 0 \\
\vdots & \ddots & \vdots \\
a_{11} & \cdots & a_{n,n}
\end{bmatrix} \]  \hspace{1cm} (3.61)

\[ U = \begin{bmatrix}
0 & a_{12} & \cdots & a_{1n} \\
0 & \cdots & a_{2n} \\
\vdots & \ddots & \vdots \\
0 & \cdots & 0
\end{bmatrix} \]  \hspace{1cm} (3.62)

The iterative methods below are based on different arrangements of $L$, $D$ and $U$. 

56
Jacobi method  This method was introduced by Jacobi [87] in 1844. Owing to its comparatively slow convergence it is little used today. Nevertheless its simplicity will serve to describe the general concepts.

First of all, we denote \( w \) as an approximation of the true solution \( u \), and the error is now \( e = u - w \). The way the iterative methods solve for the solution is to first assume an initial solution \( w^0 \), next calculate \( w^1, \ldots \), after a series of iteration steps until the solution converges.

Substituting \( w \) into Equation 3.59, we write it as

\[
Dw^{k+1} + (L + U)w^k = f. \tag{3.63}
\]

Through reordering we have
\[
w^{k+1} = -D^{-1}(L + U)w^k + D^{-1}f. \tag{3.64}
\]

Note that \( r^k = f - Au^k = f - (L + D + U)w^k \).

Equation 3.64 can be expressed as
\[
w^{k+1} = -D^{-1}(L + U)w^k + D^{-1}(r^k + Au^k) \tag{3.65}
\]
\[
= w^k + D^{-1}r^k. \tag{3.66}
\]

The iterative matrix of Jacobi method is
\[
R_J = I - D^{-1}A = -D^{-1}(L + U), \tag{3.67}
\]
and the algebraic form of Equation 3.66 is
\[
x_i^{(k+1)} = \frac{1}{a_{ii}}(f_i - \sum_{j=1, j \neq i}^{N} a_{ij}x_j^{(k)}), \tag{3.68}
\]
where the \( x_i \) denote the elements of \( x \).
**Gauss-Seidel method**  This iteration was used by Gauss in his calculation \[88\] and was independently discovered by Seidel \[89\] in 1874. The scheme is based upon immediate use of the improved values. It is actually derivable from Equation 3.68 by employing the improved values when available. To derive the algebraic form of Gauss-Seidel method, we first look at

\[(L + D)w^{k+1} + Uw^k = f, \quad (3.69)\]

and again through reordering we have

\[w^{k+1} = - (L + D)^{-1}Uw^k + (L + D)^{-1}f. \quad (3.70)\]

Using \(r^k = f - Aw^k\), we have

\[w^{k+1} = -(L + D)Uw^k + (L + D)^{-1}[r^k + Aw^k] \quad (3.71)\]

\[= w^k + (L + D)^{-1}r^k. \quad (3.72)\]

The iterative matrix of Gauss-Seidel method is \(R_{GS} = -(L + D)^{-1}U\). Similar to the deduction we used for the Jacobi method, the algebraic form is

\[x_{i}^{(k+1)} = \frac{1}{a_{ii}}(f_i - \sum_{j=1}^{i-1} a_{ij}x_{j}^{k+1} - \sum_{j=i+1}^{N} a_{ij}x_{j}^{k}). \quad (3.73)\]

The Gauss-Seidel method is a linear stationary iterative scheme. The matrix \((L + D)^{-1}\) exists since the determinant of \(L + D\) is nonzero.

**Successive over-relaxation (SOR)** SOR introduces a positive parameter \(\omega\) to accelerate the convergence of the Gauss-Seidel method. It was first introduced by Frankel \[90\] and Yound \[91\]. This work has later been expanded by Friedman \[92\] and Arms, Gates, and Zondek \[93\]. Given a pre-determined \(\lambda\), one uses the Gauss-Seidel method to obtain a temporary solution \(\tilde{w}^{k+1}\), and then uses this temporary solution to “over-relax” the previous solution \(w^k\)

\[w^{k+1} = w^k + \lambda(w^{k+1} - w^k). \quad (3.74)\]
3.2 Numerical Methods for Partial Differential Equation

We repeat this for every new $w^{k+1}$ until certain criteria is reached. The iterative process of SOR is

$$Dw^{k+1} + Lw^{k+1} + Uw^k = f$$  \hspace{1cm} (3.75)

$$w^{k+1} = w^k + \lambda(w^{k+1} - w^k)$$ \hspace{1cm} (3.76)

$$= \lambda w^{k+1} + (1 - \omega)w^k$$ \hspace{1cm} (3.77)

Eliminating $w^{k+1}$ through Equation 3.75 and Equation 3.77,

$$w^{k+1} = (D + \lambda L)^{-1}[(1 - \lambda)D - \lambda U]w^k + \lambda(D + \lambda L)^{-1}f,$$ \hspace{1cm} (3.78)

or in a concise form

$$w^{k+1} = w^k + \lambda(D + \lambda L)^{-1}r^k$$ \hspace{1cm} (3.79)

The iterative matrix for SOR can be deduced $R_{SOR} = (D + \lambda L)^{-1}[(1 - \lambda)D - \lambda U]$. When $\lambda = 1$, the SOR method reduces to Gauss-Seidel method.

The algebraic format of the SOR method can be written as

$$x_i^{(k+1)} = (1 - \lambda)x_i^k + \frac{\lambda}{a_{ii}}(f_i - \sum_{j=1}^{i-1}a_{ij}x_j^{k+1} - \sum_{j=i+1}^{N}a_{ij}x_j^k).$$ \hspace{1cm} (3.80)

**Stopping Criterion and Rate of convergence**  The iteration to solve for the solution can not run forever, so we need a criterion to decide when it should stop. Again we denote $e^k = u - w^k$ as the error vector resulting from the true solution $u$ and the approximation solution $w^k$ at step $k$. We usually require a sequence $e_i^{k=1}$ of vectors that converge to 0 with respect to the norm $\| \cdot \|$. The most commonly chosen norm is the $\| \cdot \|_\infty$, which results in the stopping criterion,

$$\|e^k\| < \epsilon, \text{ for all } k \geq N(\epsilon).$$ \hspace{1cm} (3.81)

The definition of the infinity norm is

$$\|x\|_\infty = max|x_i|, \ i = 1, 2, \ldots, n.$$ \hspace{1cm} (3.82)
Assuming one uses the same stopping criterion, the convergence speed for the iterative methods vary. We now briefly introduce how we can measure the rate of convergence of iterative methods. The error of the iterative methods is denoted as \( e \) and has the relation
\[
Ae = f - Aw = r. \tag{3.83}
\]

If we know \( e \), we can use it to correct the approximate solution \( w \) to obtain the true solution \( u \), like
\[
u = w + e = A^{-1}r. \tag{3.84}
\]

Inspired by Equation 3.83, a way to solve for \( u \) is to solve for \( r \). We define the general form of the iterative equation, which summarizes the iterative equations introduced for the Jacobi method, Gauss-Seidel method and SOR method.
\[
w^{k+1} = w^k + Br^k, \tag{3.85}
\]
where \( r^k = f - Aw^k \), \( B \) is an approximation of \( A^{-1} \).

Denoting \( w^0 \) as initial guess of the solution and applying the iterative equation 3.85, we can obtain a list of \( w^k \). Replacing \( r \) in Equation 3.85,
\[
w^{k+1} = w^k + Br^k = w^k + BAe^k, \tag{3.86}
\]
where \( e^k = u - w^k \). We can now obtain the iterative equation for \( e^{k+1} \)
\[
e^{k+1} = e^k - BAe^k = (I - BA)e^k. \tag{3.87}
\]

Let \( R = I - BA \), \( R \) represent the iterative matrices we introduced for Jacobi method, Gauss-Seidel method and SOR method.
\[
\|e^{k+1}\| \leq \|I - BA\|\|e^k\| \leq \cdots \leq \|I - BA\|^k = \|R\|^k\|e^0\|. \tag{3.88}
\]

The notation \( \|R\| \) is called the *convergence factor*. It is obvious that in order for the approximation \( w \) to converge to \( u \), \( e^{k+1} \) will tend to be zero after a certain
number of iteration \( l \). In other words, \( \| R \| < 1 \) is required, which implies that the spectral radius of \( \| R \| < 1 \), a.k.a., \( \rho(R) < 1 \).

We can substitute \( R \) with the iterative matrix Equation 3.67 of Jacobi method and obtain the convergence rate of Jacobi iterative method as \( h^2/2 \).

For the Gauss-Seidel iterative method, the convergent rate is of order \( h^2 \), which is twice as fast as the Jacobi iterative method. The SOR iterative method has a convergent rate around of \( 2h \). A detailed derivation can be found in Reference [94].

**Alternating direction methods** Alternating-direction implicit (ADI) method is another finite difference method for solving parabolic and elliptic partial differential equations. The advantage of the ADI method is that the equations which to be solved in every iteration have a simpler structure and are thus easier to solve.

The SOR method proceeds by taking all the lines in the same direction. As in Figure 3.6, for example, we first solve for the values at 1, 2, 3, then for 4, 5, 6, and finally for 7, 8, 9. A complete iteration in ADI method consists of a first half in the row direction followed by a second half in the column direction. The first ADI method, developed by Peaceman and Rachford [95]( PRADI for short), is related to a procedure for solving the equation \( u_t = u_{xx} + u_{yy} \). Douglas and Rachford [96] present a method similar to that of PRADI characterized by its ease of generalization to three dimensions.

The PRADI scheme for Laplace’s equation approximated by a five-point molecule in a rectangular domain with equal mesh size \( h \) is

\[
\begin{align*}
\frac{u_{i+1,j} + u_{i-1,j} + u_{i,j+1} + u_{i,j-1} - 4u_{i,j}}{h^2} = 0
\end{align*}
\] (3.89)

The iteration proceeds from \( u_{i,j}^k \) to the determination of
by a single row iteration followed by a single column iteration determined from

\[ u_{i,j}^{k+1/2} = u_{i,j}^k + \rho_k [u_{i+1,j}^{k+1/2} + u_{i-1,j}^{k+1/2} - 2u_{i,j}^{k+1/2}] + \rho_k [u_{i,j+1}^k + u_{i,j-1}^k - 2u_{i,j}^k] \] (3.90)

Equation 3.90 and Equation 3.91, with \( \rho_k = \frac{1}{4} \), defines a method which is similar to but is not the same as, the Jacobi row iteration. The quantities \( \rho_k \), called iteration parameters, may depend upon \( k \). In any event it is important that the same values be employed for both parts of the iterative step.

3.2.2.3 Geometric Multigrid Methods

Owing to the strict resolution requirement by electrical wave propagation problems, and the increased focus on large-scale three-dimensional simulation, the linear system from equations Equation 2.10 and Equation 2.11 are potentially huge, and it is crucial to employ methods that scale well as the size of the problem increases. Traditional
linear solvers, such as direct methods and simple iterative methods mentioned above, will not be efficient.

Multigrid solvers are the only group of linear solvers that can be shown to give order-optimal behavior for linear systems that arise from the discretization of PDEs. The multigrid idea was first introduced by Fedorenko in 1964 [97] and various components of multigrid process had been introduced. Later the multigrid method was implemented by Brandt in 1977 [98] as a means of constructing fast solvers for general elliptic problems. The multigrid method provides significant improvements over the traditional iterative schemes on solving the elliptic PDEs. Multigrid method exploits

![Figure 3.7: ADI calculation procedure](image-url)
the structure of the domain on which the question is defined and is used in conjunction with traditional linear solver to yield better convergence rate. Therefore the multigrid solver is problem-dependent. There isn’t an universal implementation of multigrid method that can suit all the elliptic equations. We need to first analyze the elliptic equation and define it under the multigrid framework. Then at least the core components of the algorithm, for instance, the solver for coarsest grid, the prolongation and restriction methods, etc, need to be modified accordingly in order to apply the multigrid technique to our specific problem.

Multigrid methods are classified into two branches:

- Algebraic Multigrid.
- Full Geometric Multigrid.

The Algebraic Multigrid defines the coarse grids using a coefficient matrix only (hence the name algebraic), therefore, no actual grid definition is needed. While the other approach, termed the full geometric multigrid method (FMG) is a method to solve the problems that can be finely discretized, by using several levels of coarser discretizations for that same problem. Since our model is a rectangular grid and the problem we are solving can be defined on all sizes of the grid by simply down-sampling of the nodes. In our study, we would use the FMG as an elliptic equation solver.

Before introducing the FMG, we will first start with a subset of it: multigrid method. Actually the FMG is developed through multigrid method, which was first used as a way to speed up the convergence of a traditional relaxation method. In the following sections, we first studied the multigrid method, then use the concepts developed to introduce the FMG method.

**Multigrid method** The basic idea behind multigrid methods relies on the fact that simple iterative methods are very efficient at reducing high frequency components of
3.2 Numerical Methods for Partial Differential Equation

the residual, but are very inefficient with respect to the low frequency components. In other words, simple iterative methods remove abrupt spatial changes in the solution with a few iterations, but require many iterations to change the baseline level of the solution.

The solution for the low efficiency of simple iterative methods is that the multigrid method projects the residual onto a smaller space, a coarser grid of the problem, where the lower spatial frequency components can be handled more efficiently. By ”projection”, it means a solution or residual is obtained on a particular grid and then interpolated or extrapolated to a grid of lower or higher resolution, respectively. Usually, iterative methods are applied at all grid levels but the coarsest, which is usually solved directly. The simple multigrid method being introduced employs a basic process call ”V-cycle” where one starts with the finest level, works to the coarsest, and then works back to the finest. Let’s start understanding the basic of multigrid method by considering the simplest case of a two-grid method. The general form of elliptic equation can be written as

\[ \mathcal{L} u = f \]  

(3.92)

where we assume \( \mathcal{L} \) is an elliptic operator and \( f \) is specified, \( u \) is the unknown. In most of the discussion we assume for simplicity that \( \mathcal{L} \) is linear. We first discretize the elliptic equation defined in Equation 3.92 on a uniform grid with space-step size \( h \).

\[ \mathcal{L}^h u^h = f^h \]  

(3.93)

After the application of a few pre-smoothing sweeps, we obtain an approximation \( \tilde{u}^h \), whose error \( \tilde{e}^h = u^h - \tilde{u}^h \) is smooth. Then \( \tilde{e}^h \) can be approximated on a coarser space. We need to express this smooth error as solution of a coarse problem. For this
purpose notice that $L$ is a linear difference operator and the residual $r^h = f^h - \tilde{L}h$ is a smooth function if $\tilde{e}^h$ is smooth. Obviously the original equation $\tilde{L}^h u^h = f^h$ and the residual equation $\tilde{L}^h e^h = r^h$ are equivalent. Therefore we can think of representing them on a coarser grid with mesh size $H = 2h$. We define $r^H$ as the restriction of the fine-grid residual to the coarse grid, that is $r^H = R^H_h r^h$, where $R^H_h$ is a suitable restriction operator. This defines the right-hand-side of the coarse problem. Since $\tilde{e}^h$ is the solution of a difference operator which can be represented analogously on the coarse discretization level, we define the following coarse problem

$$L^H \tilde{e}^H = r^H \quad (3.94)$$

Here $L$ represents the same discrete operator but relative to the grid with mesh size $H$. We can reasonably assume that $\tilde{e}^H$ is an approximation to $\tilde{e}^h$ on the finer grid.

Next step, we apply a prolongation operator $P^h_H$ to transfer $\tilde{e}^H$ to the finer grid. By definition, $u^h = \tilde{u}^h + \tilde{e}^h$, we now can update the function $\tilde{u}^h$ by applying the coarse grid correction step

$$\tilde{u}^h_{\text{new}} = \tilde{u}^h + P^h_H \tilde{e}^H \quad (3.95)$$

In practice, to reduce the errors that introduced by the interpolation procedure, it is convenient to complete the two-grid process by applying a few numbers of post-smoothing sweeps after the coarse-grid correction. Now we summarize the steps we described above.

*The two-grid method for solving $L^h u^h = f^h$*

- Pre-smoothing step on the fine grid for an approximation $\tilde{u}^h$
- Computation of the residual on the fine grid: $r^h = f^h - L^h \tilde{u}^h$
3.2 Numerical Methods for Partial Differential Equation

- Restriction of the residual: \( r^H = R^H_h r^h \)
- Solution of coarse-grid problem: \( e^H = (L^H)^{-1}r^H \)
- Coarse-grid correction, including the prolongation: \( \tilde{u}^{\text{new}}_h = \tilde{u}^h + P^h_H e^H \)
- Post-smoothing step of the fine grid.

As mentioned at the beginning of the section. The iterative method and changing the size of the grid could help reduce two kinds of errors. At each grid level, a few simple iteration steps (smoothing) are applied to reduce the high frequency error. When the grid is reduced to be a coarser grid, the remaining low frequency error that is not capture by the simple iterative solver now becomes high frequency error, which can be “smooth” again through the iteration steps on the coarser grid level. The two-grid method and later the multigrid method take advantages of this technique to achieve fast convergent rate.

The two-grid method starts at the fine level with pre-smoothing, performs a coarse-grid-correction and ends with post-smoothing. A representation of the process where fine grid is at a high level and coarse grid is at a low level looks like a "V" workflow. So we call the whole process a V-cycle.

In the two-grid scheme, there are only two levels and the coarser grid could still be too large to solve efficiently. We can introduce an even coarser grid and apply the two-grid iteration method on it. This process can be repeated recursively until a coarsest grid is reached where the corresponding residual equation is inexpensive to solve. This is the qualitative description of the multigrid method.

The multigrid method, extended from two-grid iteration method, starts from the finest grid to coarsest grid and back to finest grid again. We could still describe the process pictorially as V-cycle but the multigrid method could be 3 or more grids depending on the complexity of the problem it solves.
Multigrid method introduces a new parameter (cycle index) called $\gamma$, which is the number of times the multigrid grid procedure is applied to the coarse level problem. For the V-cycle, $\gamma = 1$. When $\gamma = 2$, we usually call it W-cycle, see Figure 3.8. For most of the practical usage of the multigrid method, the V-cycle does not solve the coarse-grid equations sufficiently well. While with a large $\gamma$, the coarse problem could be solved almost exactly. However, increasing $\gamma$ will result in lots of recursive steps which will hurt the efficiency instead. So in most of the practical usage, $\gamma$ is chosen to be 2.
**Full multigrid algorithm**  Multigrid method starts with one initial guess on the finest grid and carries out enough cycles to achieve convergence. However, it is sometimes important to start the iterative procedure from a good initial approximation. The multigrid setting suggests a natural way of how to get this approximation cheaply. The idea of using a coarse-grid approximation as a first guess for the solution process on a finer grid is known as *nested iteration*. The algorithm obtained by combining the multigrid scheme with nested iteration is the *Full Multigrid Algorithm* (FMG).

It is essentially the same as multigrid method but instead of starting with an arbitrary approximation on the finest grid, the FMG solves the discretized equation at the coarsest grid exactly at minimum cost due to the small grid numbers. Then it progresses up to the next finer grid and goes through one or two cycles, then moves up to the next finer level until the finest level is reached, see Figure 3.9. Because of the improvement on the initial solution at each starting level, the FMG scheme results to be cheaper than the iterative application of the multigrid cycle without FMG initialization.

Using Figure 3.9, we now illustrate the FMG process. It starts from the coarsest grid at level 1 from the left corner where the discrete approximation is exactly solved. The resulting solution is interpolated to the next finer grid at level 2. It then goes through a V-cycle multigrid process and a converged result at level 2 is obtained. The solution at level 2 is then interpolated to serve as initial guess for the next V-cycle. This process is repeated until the solution on the finest grid is obtained. Although FMG still utilizes the multigrid cycle in its process, it now has a better initial guess for each level of the cycle. Therefore it achieves better convergence rate than the multigrid method. The Figure 3.9 shows just the simplest V-cycle, we can replace it with any multigrid cycle.

*The full multigrid scheme*
1. Compute $u^H$ exactly at the coarsest grid level $n$;

2. If $n < N$, where $N$ is the finest level, interpolate $u^H_n$ to $u^{2H}_{n+1}$ for the next finer grid;

3. Perform multigrid method;

4. if $n + 1 < N$, increment $n$ and go to step 2.

Figure 3.9: Workflows for full multigrid (FMG) method. There are total 4 level of the grids and the mesh sizes double as the grid gets coarser. The "E" denotes exact solution and the red highlighted "E" is the starting point of FMG. The "S" denote relaxation steps and the yellow "S" denote the converged result at each finer level. The arrow pointing up means prolongation operation and the arrow point down means restriction operation. The elements in the parentheses represent a V-cycle.

**Boundary Conditions** Boundary conditions should not affect the efficient of the multigrid method. The boundary contains fewer grid points than the main body the grid. Therefore even if there may be some complicated boundary conditions, the extra work for the boundary will not increase the computing time by much.
For Dirichlet boundary condition, the implementation is straight forward. Each time a converged result is obtained, the boundary points are just inserted directly. While during the coarse-grid-correction, only the finest grid will use the specified value on the boundary and zeros for the coarser grids.

Neumann boundary condition is more complicated. Now boundary conditions are equations so they will be relaxed. The residual on the boundaries will be transferred to coarse grids. It is worth pointing out that relaxing on the boundary is not to impose boundary conditions but to smooth the error along the boundary on the intermediate grid levels.

Smoothing, Restriction, and Prolongation

Smoothing, restriction and prolongation are considered key components in the multigrid framework. A proper choice of these components could greatly improve the efficiency.

The heart of a multigrid method is the relaxation scheme used on each grid to smooth the error, i.e. as we mentioned before, to reduce the high frequency error components. Even the restriction operator serves to provide an environment (coarser grid) so as to improve the relaxation efficiency. The simplest relaxation schemes are the successive schemes (Gauss-Seidel) introduced in Section 3.2.2.2. They are appropriate for most of the elliptic problems and in general have better convergent rate than the Jacobi method.

The common Gauss-Seidel scheme is not directly vectorizable and hence do not exploit the full potential of parallel computing. Jacobi relaxation scheme seems preferable since it updates all the new values in a single sweep. A better approach will be to use red-black Gauss-Seidel scheme with the grid point and lines taken in a different order. The first sweep will relax all the "red" point and the second sweep updates the "black" point. Each of these schemes is fully vectorizable so they are more suitable for parallelization.
The prolongation is used to transfer the computed error from a coarse grid to upper finer grid. It is a coarse-to-fine process. One of the common choice for two-dimensional prolongation is \textit{bilinear interpolation}. It is often used to interpolate 2D gridded data between similar data grids starting from corners of a rectangular grid to the centers. It is an simple extension from one-dimensional linear interpolation. It requires rectangular grid and we can choose either start with the horizontal direction then the vertical direction, or the other way around. The result doesn’t affect by the order of the 1D interpolation. This symbol for bilinear interpolation operator is Equation 3.2.2.3

\[
\begin{bmatrix}
\frac{1}{4} & \frac{1}{2} & \frac{1}{4} \\
\frac{1}{2} & 1 & \frac{1}{2} \\
\frac{1}{4} & \frac{1}{2} & \frac{1}{4}
\end{bmatrix}
\]

The extension of the bilinear 2D prolongation operator to 3D is straight forward and now it becomes trilinear interpolation between the grids. It approximates the value of an intermediate point within the local axial rectangular prism linearly, using data on the lattice points. Figure 3.10 shows the structure of the operator.

Restriction is used to transfer the value of the residual from a finer grid to coarse grid. It is then a finer-to-coarse process. The most simple method is \textit{injection}, which means that simply copying the values to the coarser grid at the points common to both grids. In some cases if the residuals are not smooth, the injection method doesn’t give adequate approximation to the residual. A more common choice is called the \textit{full weighting} restriction operator. Using this operator, the residuals transferred to a coarse-grid point is a weighted average of residual values at surrounding fine-grid points, with the weights chosen to preserve the integral of the residual over the problem domain. For example, 9-point full weighting in two dimensions is given in Equation 3.2.2.3
In our implementation of the multigrid algorithm, we used full weighted 27-point scheme for the 3D restriction operator in our multigrid scheme. The weights of the adjacent grid points can be found in Figure 3.11.

In summary, the multigrid method stands out as particularly attractive for effective elliptic equation integration, which in turn is an important component of bidomain system. We have implemented full multigrid scheme for our bidomain simulation on large-scale three-dimensional simulations.
3.2 Numerical Methods for Partial Differential Equation

Figure 3.11: The 3D restriction operator matrix, from Ref. [99]. The solid dark node denotes the coarse grid point. The gray nodes denote the finer grid points to be used for restriction. The numbers attached to the grid nodes denote their weights in the operator.
Chapter 4

Numerical Implementation and Verification

In this chapter, we summarize the main features of the numerical implementation of our models. First, in Section 4.1 we will reiterate the anatomy of the heart walls and develop a numerical model based on its architecture. Next in Section 4.2, we present the details of our numerical implementation, and the algorithm we used to capture the phase singularities. To ensure that our numerical observations are fundamental and not due to numerical artifacts, we conduct rigorous tests of the numerical convergence of our models in the Section 4.2.3.

4.1 Model Development

4.1.1 Cardiac Tissue Anatomy and Mathematical Model

The actual cardiac muscle structure is complicated; Densely packed, elongated cells are arranged into cardiac tissue’s fiber bundle-like structure with the longer axes of the cells are parallel. This inhomogeneity of tissue structure continues at a larger
scale, further arranged into layered sheets, each having a common fiber orientation. These sheets then form a laminar structure of varying orientation of fiber directions.

To simplify and facilitate the implementation of the rotating anisotropy, especially the complexity introduced by bidomain description, the cardiac tissue is modelled as an idealized geometry: a three-dimensional rectangular slab with anisotropy and fiber rotation incorporated.

4.1.1.1 Conductivity tensor and diffusion terms

As briefly introduced in Chapter 2, myocardial cells can be viewed as roughly rod-shaped with elliptical cross section. As a consequence of this rod-like shape and fibrous bundle structure of the cells, the propagation speed of electrical waves is about $2 \sim 3$ times faster along the fibre axis than perpendicular to it. Individual cells are interconnected via gap junctions, and clusters of interconnected cells are partially isolated from other clusters by vessels, fluid filled space.

The most common representations of cardiac tissue treat the fine details of the cellular structure in some average sense. For example, the resistance to current flow associated with the intracellular region of a single cell and the additional resistance of the gap junction are lumped and spread uniformly over a region of interest. In two or three dimensions, this leads to a region with uniformly anisotropic resistivities.

Monodomain description usually assume tissues in contact with an extensive homogeneous isotropic bathing fluid, the extracellular resistance is small, and the entire extracellular region can be treated as being grounded (i.e., isopotential). Bidomain model is regarded as a more accurate model that accounts for current flow in both the intracellular and extracellular spaces. The quantities associated with the intracellular and extracellular spaces are considered as space averages. In bidomain, the transmembrane current is also volume averaged and is defined at each point. Bidomain assumes
different conductivity tensors in the intracellular and extracellular spaces, except that if the two sensors are simply related by a multiplicative constant, then the bidomain model reduces to a monodomain formulation (see Section 2.3.3).

A mathematical description of this anisotropy of cardiac tissue is to use a conductivity tensor \( \tilde{D} \). \( \tilde{D} \) is a \( 3 \times 3 \) matrix which reflects the different propagation speeds along and transverse to the fiber orientation. In monodomain model it can be written as

\[
\tilde{D} = \begin{bmatrix}
D_1 & 0 & 0 \\
0 & D_2 & 0 \\
0 & 0 & D_3 
\end{bmatrix}
\] (4.1)

For bidomain model, we will need two sensors, for both intra- and extra-cellular spaces.

\[
\tilde{D}_i = \begin{bmatrix}
D^i_1 & 0 & 0 \\
0 & D^i_2 & 0 \\
0 & 0 & D^i_3 
\end{bmatrix}
\] (4.2)

\[
\tilde{D}_e = \begin{bmatrix}
D^e_1 & 0 & 0 \\
0 & D^e_2 & 0 \\
0 & 0 & D^e_3 
\end{bmatrix}
\] (4.3)

Here, \( D_1 \) is the diffusion constant for propagation parallel to the fiber direction, \( D_2 \) is the diffusion constant for perpendicular propagation and \( D_3 \) is diffusion constant for propagation transmurally to the fiber axis. \( i \) denotes intracellular space and \( e \) denotes extracellular space. This is a conductivity tensor that only shows the anisotropic property of a three dimensional rectangular model. The absence of off-diagonal terms reflects the fact that all layers are horizontal and the fibre orientation of all layers are the same.
4.1.1.2 Fiber Rotation

Streeter et al [100], [32] have shown that the myocardial wall can be regarded as a well-ordered continuum of interconnecting muscle fibers. The wall is characterized by smoothly changes of fiber angle from about 60° endocardium to about −60° epicardium.

An example of the change of fiber angle through the wall at a single sampling point in the left ventricle myocardial wall of canine is shown in Figure 4.1 below, by a representative sequence of photomicrographs of the sections cut by the microtome. This dissection results indicate that cardiac fibers are arranged in surfaces, where fibers are approximately parallel in each surface while the mean fiber angle rotates around 120° from the inner to outer wall.

An idealized parallelepipedal slab of cardiac muscle is shown schematically in Figure 4.2. It shows the change in fiber orientation with depth (z) in the schematic model slab. Within each layer the fiber orientation was uniform and was characterized by a fiber angle $\theta$ which was defined with respect to the $x$-axis.

The fiber rotation was simulated by continuously varying the angle $\theta$ from layer to layer according to the formula

$$\theta(z) = \theta_0 + \eta z,$$

(4.4)

where $\theta_0$ is the fiber angle at the bottom face of the slab and $\eta$ is a constant characterizing the rate of twist.

To incorporate the fiber rotation as illustrated in Figure 4.2, the diffusion tensor now have the form

For monodomain:
4.1 Model Development

\[
\tilde{D} = \begin{bmatrix}
D_{11} & D_{12} & 0 \\
D_{21} & D_{22} & 0 \\
0 & 0 & D_{33}
\end{bmatrix}
\] (4.5)

For bidomain:

Figure 4.1: Typical sequence of photomicrographs showing fiber angles in successive sections taken from a heart in systole at region Tc, adapted from Ref. [32]. Fiber angle is +90° at the endocardium, running through 0° at the midwall to −90° at the epicardium.
4.1 Model Development

\[
\tilde{D}_i = \begin{bmatrix}
D_{i1} & D_{i2} & 0 \\
D_{i1} & D_{i2} & 0 \\
0 & 0 & D_{i3}
\end{bmatrix}
\]  
(4.6)

\[
\tilde{D}_e = \begin{bmatrix}
D_{e1} & D_{e2} & 0 \\
D_{e1} & D_{e2} & 0 \\
0 & 0 & D_{e3}
\end{bmatrix}
\]  
(4.7)

where the matrix elements

\[
D_{i1}^{i,e} = D_{1}^{i,e} \cos(\theta(z)) + D_{2}^{i,e} \sin(\theta(z))
\]
(4.8)

\[
D_{i2}^{i,e} = D_{1}^{i,e} \sin(\theta(z)) + D_{2}^{i,e} \cos(\theta(z))
\]
(4.9)

\[
D_{i2}^{i,e} = D_{1}^{i,e} = (D_{1}^{i,e} - D_{2}^{i,e}) \cos(\theta(z)) \sin(\theta(z))
\]
(4.10)

\[
D_{i3}^{i,e} = D_{3}^{i,e}
\]
(4.11)

The absence of \(D_{13}, D_{23}, D_{31} \) and \(D_{32} \) reflects the fact that all layers are horizontal

Figure 4.2: Schematic view of a slab of cardiac tissue with intramural fiber rotation from epicardium to endocardium.
in the x-y plane.

The model accounts for the effect of the strong anisotropic property of cardiac tissue in the intracellular and extracellular spaces, and the gradually rotation of the mean fiber angles from endocardium to epicardium. It is this fiber architecture and the difference of the conductivities along and perpendicular to the fibre direction give rise to the rotating anisotropy.

### 4.1.2 Mathematical Model

Here we first reintroduce the models we use to describe the cardiac tissue with rotational anisotropy. The monodomain equations that govern the transmembrane potential are

\[
\frac{\partial u}{\partial t} = \nabla \cdot (\tilde{D} \nabla u) + f(u, v), \quad (4.12)
\]

\[
\frac{\partial v}{\partial t} = g(u, v), \quad (4.13)
\]

where \( u \) denotes transmembrane potential and \( v \) is cellular state variable. \( f(u, v) \) and \( g(u, v) \) describe local dynamics.

For bidomain model, the problem is commonly formulated in terms of the variable \( u, u_e \) and \( v \), which represent the transmembrane potential, the extracellular potential and the cellular state variables, respectively. The bidomain equations are given by:

\[
\frac{\partial u}{\partial t} = \nabla \cdot (\tilde{D}^* \nabla u^e) + f(u, v), \quad (4.14)
\]

\[
0 = \nabla \cdot (\tilde{D}^i \nabla u) + \nabla \cdot ((\tilde{D}^i + \tilde{D}^e) \nabla u^e), \quad (4.15)
\]

\[
\frac{\partial v}{\partial t} = g(u, v), \quad (4.16)
\]

The ionic current models we studied is Barkley’s model
4.2 Model Implementation and Verification

\[ f(u, v) = \frac{1}{\epsilon} u(1 - u) \left( u - \frac{v + b}{a} \right), \quad (4.17) \]
\[ g(u, v) = u - v \quad (4.18) \]

We assume no current flux at the boundaries of the intracellular and interstitial domains, namely:

\[ (\nabla u^i) \cdot \tilde{n} = 0, \quad (4.19) \]
\[ (\nabla u^e) \cdot \tilde{n} = 0, \quad (4.20) \]

where \( \tilde{n} \) is the normal vector to the domain boundary. \( u^i \) is the potential of intracellular space, \( u = u^i - u^e \). This prevents current flow across the boundary and sometimes corresponds to the boundary being a line of symmetry in the solution on some larger domain. This is a standard assumption when considering a heart tissue surrounded by a conductive bath or a conductive body.

4.2 Model Implementation and Verification

4.2.1 Numerical Simulation

The monodomain model (Section 4.1.2) is a coupled system of ordinary differential equation (ODE) and partial differential equation (PDE) with parabolic type. The bidomain model constitutes a more complex system of nonlinear ODE, parabolic PDE and elliptic PDE, for which it is difficult to derive efficient numerical methods. In this section, we describe approaches that we used to discretize the system.

A variety of methods can be applied to transform the continuous operators in Equation 4.13 and Equation 4.16 into the discrete matrix forms like finite-difference
method (FDM) and the finite-element method (FEM). We applied FDM for discretization in our simulation. Suppose vectors \( u_n, u^e_n \) and \( v_n \) are discretizations of \( u, u^e \) and \( v \) respectively at time \( n \delta t \), and that the spatial operators \( \nabla \cdot \tilde{D}^e, \nabla \cdot \tilde{D}^i \) and \( \nabla \cdot \tilde{D} \) are approximated by the finite difference matrix operators \( D^e, D^i \) and \( D \) respectively. \( h = \delta x = \delta y = \delta z \) is a measure of the spatial discretization. We will use bidomain model to demonstrate our numerical method. The numerical implementation of monodomain model is essentially part of the bidomain model implementation.

The numerical scheme to solve the parabolic PDE are introduced in Section 3.2.1. The forward Euler (explicit) scheme with five-node approximation of the Laplacian is used to solve the parabolic PDE.

\[
    u_{n+1} = u_n + \delta t[D^e u^e_n + f(u_n, v_n)] \quad (4.21)
\]

Given \( u_n, u^e_n \) and \( v_n \), transmembrane potentials \( u_{n+1} \) at next time step are computed directly. Here we didn’t adopt semi-implicit or Crank-Nicolson methods because although the diffusion operator has no time step restrictions for stability, the local dynamic term \( f(u_n, v_n) \) often does.

The transmembrane potential \( u_n \) can be obtained through solving only the parabolic PDE in monodomain model. While for bidomain model, this is the first step. The next step is to discretize the elliptic equation.

\[
    (D^i_n + D^e_n)u^e_n = -D^i_n u_n \quad (4.22)
\]

Once we have the solution for the transmembrane potential \( u_n \) of current time step through solving the parabolic PDE equation 4.21, next is to prepare the extracellular potential \( u^e_n \) for the simulation of next time step. This was done by solving elliptic equation 4.22 using full multigrid algorithm introduced in Section 3.2.2.3. The outline of the steps of simulation are:
4.2 Model Implementation and Verification

• Calculate the source term \(-D_n^i u_n\) based on the known \(u_n\);

• Restrict the grid to coarsest level and exactly solve the restricted elliptic equation;

• Interpolate the grid to one finer level above, perform "W" cycles on the finer grid. A total 200 relaxation steps were applied on the finer level of the grid.

• The previous multigrid cycles were calculated recursively on level 3, and then level 4 and so on, until the finest grid level was reached. The smoothing was also done on each finer grid through relaxations;

• The \(u_n^i\) at the finest level is the solution at the current time step, which will be used to calculated \(u_{n+1}\)

The local dynamic \(\frac{\partial v}{\partial t} = g(u, v)\) was treated explicitly.

\[
v_{n+1}^i = v_n^i + \delta t[g(u_n, v_n)]
\] (4.23)

Most of our simulations are performed on a 127 \times 127 \times 7 ventricular free wall slab with a fiber twist of 120° from endocardium to epicardium. We have also used domain size 127 \times 127 \times 15 and 127 \times 127 \times 31 when we studied the effect of tissue thickness on the scroll wave behavior. The multigrid method imposes a restriction on the dimension of the domain. The length of any edge of the rectangular slab must be of the form \(2^j + 1\) for some integer \(j\). Since all the coarse grids are obtained through dividing a factor 2 from their finer parent grids. We used a "ghost-layer" to deal with the discretization and the calculation of boundary condition, therefore, the actual nodes of the model are 129 \times 129 \times 9 which complies with the requirement of multigrid method. The space discretization step are \(dx = 0.25\), \(dy = 0.25\) and \(dz = 0.25\) space unit. The
time step is 0.0005 time unit. The minimum total simulation time is 100 time units for all of our numerical results.

In later section (Section 4.2.3.1), we will prove that our numerical treatment of the model is stable and converged.

### 4.2.2 Tips and Filament Finding Algorithm

In order to thoroughly study the spiral/scroll wave dynamics, it is crucial to investigate the singularities in two-dimensional and three-dimensional spaces, tips and filament, respectively.

Spiral wave tips were identified as where the excitation wavefront meets the repolarization wave back of the action potential, or equivalently the point having zero normal velocity, as described in Ref. [24]. Mathematically this point is intersection point of the lines $V(\vec{r}, t) = V_{iso}$ and $\partial_t V(\vec{r}, t) = 0$. $V(\vec{r}, t)$ is an arbitrarily chosen isopotential line of constant membrane potential $V_{iso}$. The position vector $\vec{R} = x_{tip}\vec{x} + y_{tip}\vec{y}$ of tip coordinate $(x_{tip}, y_{tip})$ satisfies,

$$V(\vec{R}, t) - V_{iso} = \partial_t V(\vec{R}, t) = 0,$$

Equation 4.24 also defines the instantaneous vortex line (filament) in 3D as the intersection of two surfaces. We here followed the algorithm in Ref. [66] to locate the organization centers in 3D.

We first applied the tip-finding algorithm for each layer in x-y plane. By randomly picking a tip, the filament-finding algorithm searches the closest tip on the same layer or adjacent layers. The distance of these two tips is compared with a pre-defined constant threshold. If the threshold is not reached, the connection between the tips is established. And the exact same search will start on the newly connected tip point, until no tips satisfy the criterion. If the initial search can’t find a tip to connect with,
it will reverse the search and repeat the routine described above. All the tip points were not connected as part of the filament in the previous search will all be selected as start point for filament formation until all points were either connected or selected.

The threshold as an input value is determined empirically through visually inspecting the contour plots of transmembrane potentials. It is roughly equal to the 2D spiral core size.

4.2.3 Convergence Test and Numerical Result Verification

4.2.3.1 Convergence Test

Rigorous convergence tests have been performed to ensure that the numerical results we present here are valid, especially those observed instabilities are fundamental and not due to numerical artifacts.

We employed two methods to verify the bidomain model. The first step is to test its convergence. There are multiple factors can affect the convergence of the numerical methods we implemented for bidomain model, among which the multigrid algorithm is the most important and complicated. We can always ensure convergence of forward Euler scheme by using a small time step, however, this along is not sufficient for multigrid scheme. There are several factors associated with multigrid scheme that play a role in its effectiveness of the convergence, for example, the restriction and prolongation methods, the exact solver for the coarsest grid, the relaxation algorithm for each intermediate layer, the relaxation times and the cycles. Once the algorithm is implemented, the cycles and the relaxation number can be easily varied through input parameters. These two factors are also the most effective elements to improve the convergence. Typically two cycles (W-cycle) are chosen for multigrid algorithm.

Increasing the relaxation number will improve the convergent speed. By fixing the cycle as 2, we gradually changed the relaxation number on each intermediate grid with
different coarseness. Our first method to verify the convergence is to examined the transmembrane potentials of selected points in the snapshot of last frame captured at the end of each simulation. We have selected two typical points on the middle layer ($N_z = 4$). One is close to the center of the region ($x = 76, y = 71$) and the other is near the boundary ($x = 53, y = 10$). The Figure 4.3 shows that a reasonable convergence has been obtained when the relaxation number is above 200.
Figure 4.3: Convergence test of multigrid scheme for three-dimensional bidomain model. Transmembrane potential versus relaxation numbers of each grid level. The relaxation numbers that are tested are 10, 20, 40, 50, 60, 80, 100, 150, 200, 300, 400, 500 and 600. Red dotted line denotes the transmembrane potential of point \((x = 76, y = 75)\) at the center of the domain. Blue triangle line denotes the transmembrane potential of boundary point \((x = 53, y = 10)\). Two curves converge as more relaxations for each grid level are performed.

Next we demonstrate an alternative method to verify the convergence of multigrid algorithm. We use Gauss-Seidel relaxation method on each level to smooth the residuals. For testing purpose, the code is slightly modified so that the minimum change(residual) was tracked for various relaxation steps. A smaller residual means
better convergence of the numerical result. For each selected number of relaxation, we recorded the residual of the finest grid at the end of each simulation. The logarithm of the residual is plotted against the number of relaxation, as shown in Figure 4.4.

![Log Residual vs Relaxation](image)

Figure 4.4: Alternative convergence test of multigrid scheme for three-dimensional bidomain model. The plot is logarithmic of residuals versus the number of relaxations for each grid level. The smaller the residual, the higher accuracy of each relaxation. The residuals decrease as the relaxations step increases. The residuals converge when the relaxation steps are 200 or larger.

As we can see from Figure 4.4, the residual starts converging at 200 relaxations. Our bidomain simulations are based on 2 cycles and 200 relaxations per grid level in
order to ensure the convergence, meanwhile optimize the computing time.

4.2.3.2 Bidomain Results Verification

We have shown in last section (Section 4.2.3.1) that the result converges. In Chapter 2 we have shown that the bidomain can be reduced to monodomain model by setting the same anisotropy ratios for intra- and extra-cellular spaces. Based on this observation, in this section, we compared the results of reduced bidomain model with the results of monodomain model as a way of numerical verification.

The comparison was done in two scenarios: in homogeneous space and in space with rotating anisotropy.

Medium 1: Homogeneous Space  The Barkley parameters \(a, b\) are set to 1.10, 0.16, respectively. This corresponds to a rigid rotating tip trajectory in the phase diagram Figure 5.1. The space is assumed isotropic and without fiber rotation. We first look at how the transmembrane potential evolves with time in both models. We selected a point \((x = 60, y = 60)\) close to the center of the domain and another point \((x = 120, y = 120)\) at the boundary for demonstration. In homogeneous space, the spiral dynamics is invariant across transmural layers. We use the mid-layer spiral dynamics to demonstrate the results of comparison. In Figure 4.5, the transmembrane potential \(u\) was plotted over time for both points. The subplots (a) and (b) were obtained from boundary point, where subplot (b) is the zoom-in plot for subplot (a). The subplots for center point were presented in (c) and (d), where subplot (d) is a zoom-in plot for subplot (c). The black dash line is from bidomain model. The red triangles dots denote the results from monodomain model. We can see from the graph that two curve agree well.
4.2 Model Implementation and Verification

Figure 4.5: $u$ vs Time plots for homogeneous monodomain and reduced bidomain models. The domain size for both models are $127 \times 127 \times 7$. In all subplots, the black dash lines were plotted from reduced bidomain results, the red triangles are data points from monodomain model. (a) boundary point ($x = 120, y = 120$) transmembrane potential $u$ vs time plot; (b) zoom-in plot of $u$ vs time for boundary point; (c) center point ($x = 60, y = 60$) transmembrane potential $u$ vs time plot; (d) zoom-in plot of $u$ vs time for center point.

Moving to another perspective, we presented in Figure 4.6 the density plots for the differences of transmembrane potential $u$ between two models, captured by the middle layer of the domain, during early stage and late fully developed stage.
In the case of isotropic space, the two models agree very well except minor difference of propagation speed developed over time. The propagation of activation was faster in the bidomain model than in the monodomain model.

**Medium 2: Space With Rotating Anisotropy** Rotating anisotropy was incorporated into the domain for this comparison. The reduced bidomain model is in theoretical a monodomain model with rotating anisotropy. The Barkley’s control parameters $a$ and $b$ are 0.96 and 0.16, respectively. This point is located inside the break-up region yet close to the quasi-stable boundary in phase diagram Figure 5.1. The conductivity coefficients are $D_1 = 1.0$, $D_2 = 0.1$, $D_3 = 0.1$ for both spaces in bidomain model, and for monodomain model, the values were multiplied by 1/2 according to section 2.3.3. Now with presence of rotating anisotropy, the spiral wave
dynamics varies by layers. We again selected points at the center and at the boundary of the domain, while in each case, there are three points chosen from top, middle and bottom layers of the models.

We first look at the group of points at the center of the model \((x = 60, y = 60)\), with \(y = 1, 4\) and 7. The transmembrane potential \(u\) vs time plots for points at three different layers are shown in Figure 4.7.
Figure 4.7: $u$ vs time plots for center points ($x = 60, y = 60$) in monodomain and reduced bidomain model with rotating anisotropy. The domain size for both models are $127 \times 127 \times 7$. In all subplots, the black dash lines were plotted from reduced bidomain results, the red triangles are data points from monodomain model. Subplots (a), (c) and (e) are $u$ vs time plots of full simulation period for top, middle, and bottom layers, respectively. Subplots (b), (d) and (f) are zoom-in plots for (a), (c) and (e) respectively.

While for the points close to the boundary, their $u$ vs time plots are in Figure 4.8.
4.2 Model Implementation and Verification

Figure 4.8: $u$ vs time plots for boundary points $(x = 120, y = 120)$ in monodomain and reduced bidomain model with rotating anisotropy. The domain size for both models are $127 \times 127 \times 7$. In all subplots, the black dash lines were plotted from reduced bidomain results, the red triangles are data points from monodomain model. Subplots (a), (c) and (e) are $u$ vs time plots of full simulation period for top, middle, and bottom layers, respectively. Subplots (b), (d) and (f) are zoom-in plots for (a), (c) and (e) respectively.

The scroll breakup always starts at the center of the domain, where the core filament resides. Therefore, the $u$ vs time plots around the center of the region differ greatly by layers compared to those of boundary points. Meanwhile, we observed a slightly greater differences between curves of monodomain and bidomain models, with the monodomain curves lag further behind bidomain curves.

The corresponding density plots of differences of transmembrane potentials $u$ be-
Figure 4.9: Density plots for the differences between monodomain model and reduced bidomain model with rotating anisotropy at layer 1. (a) absolute differences between results from monodomain model and reduced bidomain model at 10 time units; (b) absolute differences between models at 50 time units.
Figure 4.10: Density plots for the differences between monodomain model and reduced bidomain model with rotating anisotropy at layer 4. (a) absolute differences between results from monodomain model and reduced bidomain model at 10 time units; (b) absolute differences between models at 50 time units.
Once we turned on rotating anisotropy, more factors came to exist and their impacts on the results become more complicated. The spiral waves in monodomain model start lagging slightly behind the spiral waves in bidomain model as time goes by. In general the results from two models agree reasonably well.

**Conclusion** For comparisons in both mediums, the general scroll wave behaviors are the same. The core characteristics of the scroll waves are preserved in both models. For example, both scroll waves are rigid rotating in homogeneous medium, and both scroll waves break up in the space with rotating anisotropy. Moreover, the shapes of the spiral wave/spiral wave fragments in all layers at all time are similar. They are not laid right on top of each other because of the difference in propagation speeds but they are reasonably close, which we believe it is as expected. Multiple
factors may lead to the difference, one of which is the difference between the underlying numerical algorithms. Although analytically the reduced bidomain model is equivalent to monodomain model, the multigrid method is far more sophisticated than the method in monodomain and we are still solving two PDEs simultaneously in bidomain model. The theoretical equivalence of the two models governs the general scroll wave behaviors. That’s why we observe similar spiral wave patterns but not exactly the same results and the differences only happen at the edges of the wave front.
Chapter 5

Numerical Results

Numerical experiments suggest that spiral waves (in two dimensions) and scroll waves (in three dimensions) are a major cause of reentrant cardiac arrhythmias (Ref. [14, 37, 47, 101, 102]). In particular, ventricular fibrillation, the leading cause of sudden cardiac death, has been identified with spiral or scroll wave breakup, in which wavelets are continually being created and destroyed (see references [14, 21, 103]), and electrical wave propagation is no longer under control of the heart’s pacemaker. Thus, understanding the fundamental determinants of scroll wave instability from simulation becomes extremely important, as a complement to experiments. Previous studies (see references [23, 24]) have proposed that the rotating anisotropy of cardiac tissue can lead to further breakup of scroll waves once they are formed. In this chapter, we extend the work noted above by exploring additional perspectives on the role of fiber rotation.

While the monodomain model, is most amenable to numerical and analytical computation given its relative simplicity, we aim to address whether it is necessary to conduct studies with the more realistic bidomain model. For this we carry out a systematic comparison of results from monodomain and bidomain simulations on
scroll wave instability. To help provide a calibration for this comparison, we first compare results from monodomain simulations in two and three dimensions for isotropic media; we then introduce rotating anisotropy into the monodomain code and compare with the isotropic 3D simulation results. Finally, we compare results from the monodomain and bidomain descriptions with rotating anisotropy.

In Section 5.1 we first examine spiral wave dynamics with the monodomain model in two dimensions and summarize various types of spiral wave tip trajectories in the form of a phase diagram. Next we extend the model to three dimensions and perform a similar analysis of the scroll wave dynamics in Section 5.2, again using the monodomain model. In Section 5.3, we introduce the rotating anisotropy into the monodomain model. The role of rotating anisotropy in the monodomain model is characterized by looking separately at effects of the transmural diffusion constant and tissue thickness for a fixed fiber rotation angle. In Section 5.4, we present the corresponding results from our bidomain study, organized as a direct comparison with the results of monodomain model simulations in Section 5.3.

5.1 Spiral Wave Dynamics in Homogeneous Monodomain 2D Tissue

The spiral waves found in excitable media often do not rotate rigidly about stationary centers. Winfree was the first to carefully examine and point out that the tips of spiral waves could in fact trace out complex pattern as they rotate [104]. He coined the term “meander” for such non-periodic spiral dynamics. Through subsequent years of experimentation [68, 69, 70] and numerical studies [69, 72, 73, 74, 75, 76], it has been established that spiral waves in excitable media can execute either periodic rotations or a fascinating variety of other deterministic dynamics depending on parameters of
In this section, we explore the phase diagram for spiral-wave dynamics using the Barkley model \([73], [76]\):

\[
\begin{align*}
\frac{\partial u}{\partial t} &= \nabla^2 u + \frac{1}{\epsilon} u(1 - u) \left( u - \frac{v + b}{a} \right), \\
\frac{\partial v}{\partial t} &= u - v.
\end{align*}
\] (5.1) (5.2)

We begin by describing the dynamics typical of a single, isolated spiral wave in an excitable medium. The phase diagram for spiral wave behavior is plotted in terms of the control parameters \(a\) and \(b\) in Figure 5.1 with \(\epsilon = 2 \times 10^{-2}\). The parameter plane is composed of three main regions. The dynamics of each region is illustrated with segments of the path taken by the tip of the spiral as it evolves in time. There is a region in which spiral waves (i) cannot be formed, (ii) rotate rigidly, and (iii) meander. The meandering region can be further subdivided into a region in which the paths have inward-pointing petals and a region in which paths have outward-pointing petals. On the curve that divides these two regions, the petals formed by the tip paths travel along straight lines. The tip paths of spiral waves that rotate rigidly form circles, while the paths for the meandering states are not closed curves in general.

With this characterization of two-dimensional spiral wave behavior as a benchmark, our goal is to determine how the third dimension and rotating anisotropy affect spiral wave stability.
Figure 5.1: Phase diagram of two-dimensional monodomain model as a function of two control parameters $a$ and $b$ using the Barkley model. There are three main parameter regions: no spiral wave, meander and rigid rotation. Spiral waves do not form in no-spiral-wave region. The tip trajectories of spiral waves in the rigid-rotation region form circles. The meander region is itself separated into regions where tip paths have inward petal (left of red dash-dot curve) and outward petal (right of red-dash-dot curve). On the boundary (dash-dot curve), there are “infinite” flowers whose petals lie along straight lines.
In the phase diagram where a spiral wave exists, it is either rigidly rotating or meandering. There is only one spiral wave in the domain and no break-up occurs. We next studied the corresponding scroll wave phenotypes in homogeneous 3D tissue using Barkley’s model to see how the third dimension affects the corresponding scroll wave behavior when these spiral waves are placed in 3D tissue.

5.2 Scroll Wave Dynamics in Homogeneous Monodomain 3D Tissue Slab: Does tissue thickness matter?

Previous work on scroll wave propagation in homogeneous excitable media (see Refs. [105, 106]) have emphasized that for certain ionic electrophysiological models, an instability can occur when the tissue thickness exceeds a certain critical value. This “3D-
induced” instability has been related to a “negative” filament tension in some ionic models [107], where a small deformation of the filament in three dimensions can lead to further bending and collision of the filament with boundaries, resulting in multiple filaments. Here, we investigate whether the stability properties of the Barkley model are different in two and three dimensions.

We again applied forward-Euler explicit scheme for the diffusion term and semi-implicit scheme for the local dynamic in our 3D model. We have tested various slab thicknesses in the third dimension: 7, 15, 31 and 63 layers. We found a straight scroll filament throughout all simulations. We extract the tip trajectory from the middle layer of all the tested 3D models and aggregated the paths of the tip based on control parameters $a$ and $b$. The choice of the control parameters ensure the coverage of all regions on the phase diagram in Figure 5.1. We conclude that the thickness of the model does not affect the phase diagram for 3D monodomain model; it is the same as the phase diagram in 2D. Figure 5.3 is a snapshot of a typical scroll wave in homogeneous 3D monodomain model.
5.2 Scroll Wave Dynamics in Homogeneous Monodomain 3D Tissue Slab: Does tissue thickness matter?

Figure 5.3: Density plot of scroll wave in the monodomain model of homogeneous cardiac tissue, with Barkley parameters $a = 0.96$ and $b = 0.16$ at 100 time units.

As we can see from the 3D density plot, there is one scroll wave in the domain. No break-up is developed even with a long simulation period. In fact, each layer shares the same spiral wave plot. We can think of the 3D scroll wave dynamic as a number of 2D spiral waves plots stacked along the transmural direction to form a vertically straight scroll wave.

In summary, in the regions where scroll waves exist straight filaments were all stable and no scroll break-up was found. Thus our findings indicate that a conversion from 2D no-breakup spiral wave behavior to 3D break-up behavior, caused by tissue thickness only, does not occur within the Barkley model.
5.3 Scroll Wave Dynamics in Monodomain 3D Tissue Slab with Rotating Anisotropy

As previously described, in real cardiac tissue, conduction is anisotropic, being faster parallel to the fiber direction and slower transversely. The fiber direction also rotates from epicardium to endocardium through the ventricular wall, leading to the so-called rotating anisotropy of tissue as a conducting medium. Numerically, this is achieved with different diffusion coefficients along and transverse to the local fiber direction. By convention, the parallel axis defines the fiber direction. The fiber direction was then rotated at a uniform rate along the z axis between the top (“epicardial”) and bottom (“endocardial”) surfaces. The combination of anisotropy and fiber rotation gives rise to rotating anisotropy, which was incorporated into 3D monodomain model.

We take equal discretization steps in all three directions. To introduce the anisotropy, we denote $D_1$ as the conductance along the fiber axis, while $D_2$ measures the in-plane conductance transverse to the fiber axis and $D_3$ measures the out-of-plane conductance transverse to the fiber. We take $D_1 = 1$, and to achieve a typical experimentally measured 1/3 ratio for the velocity of wave propagation in the transverse and longitudinal directions, we have $D_2 = D_3 = (1/3)^2 = 0.1111$.

As illustrated in Section 4.1.1.2, the fibers are arranged in layered sheets, which correspond to the $x−y$ plane in the Cartesian coordinates adopted here. Dissection results show that the fiber orientation in these layers varies by as much as 120° across the thickness of the ventricular wall ($z$–axis). We thus define the total rotation of the fiber between the top and bottom layers as 120° in our model.

In the presence of rotating anisotropy, the rigid circles and petals previously observed in the 2D (and 3D) simulations of the isotropic medium are no longer tractable. However as we sweep through the control parameters $a$ and $b$ across the phase di-
agram of the isotropic 2D and 3D domains, we observe irregular wave activity for certain combinations of $a$ and $b$. Figures 5.4 and 5.5 respectively show the density plots and filament maps illustrating this irregular behavior, characterizing break-up for control parameters $a = 0.96, b = 0.16$.

![Diagram](image)

**Figure 5.4:** Density plots illustrating scroll wave behavior in a rectangular tissue slab with rotating anisotropy $D_1 : D_2 : D_3 = 1 : 0.1111 : 0.1111$, and total fiber rotation angle $120^\circ$. The Barkley parameters are set to $a = 0.96, b = 0.16$ in the simulation depicted. Three stages of scroll wave dynamics are shown. Note that only the scroll waves on top and bottom surfaces can be seen in three-dimensional plotting mode employed here.
At early stages, there is one scroll wave in the medium, as observed in these figures. The spiral wave is “squeezed” in the $x - y$ plane due to the anisotropy. As a result of the fiber rotation in the $z$-direction, we note that the spiral waves in successive layers are not stacked up as in the case of simulations in the isotropic medium. The scroll wave exhibits irregular behavior in the initial stage. Although the spiral wave in the bottom layer barely maintains its shape, the spiral wave in the top layer broke up into wavelets. When breakup is fully developed, the computational domain is comprised of multiple wave breaks of various sizes.

We can compare the density plots at these times with the filament evolution. A single scroll wave is represented by a single filament within the domain. The scroll wave is twisted as a result of rotating anisotropy during the early stage. More filaments appear as the single scroll wave breaks up into multiple fragments. When fully developed, the filament bending and breaking leads to a complex scroll breakup pattern (Figure 5.4).
5.3 Scroll Wave Dynamics in Monodomain 3D Tissue Slab with Rotating Anisotropy

Figure 5.5: The three-dimensional filament dynamic plot with rotating anisotropy $D_1 : D_2 : D_3 = 1 : 0.1111 : 0.1111$, fiber rotational angle $120^\circ$. The Barkley parameters are set to $a = 0.96$, $b = 0.16$ in the simulation depicted. The times correspond to the density plots in Figure 5.4.

Comparing the three-stage density plot of Figure 5.4 with the homogeneous 3D density plot of Figure 5.3, they share most model parameters: same domain size
127 × 127 × 15, same computational cell size \( \Delta x = \Delta y = \Delta z = 0.25 \), and same control parameters \( a = 0.96, b = 0.16 \). The only difference is rotating anisotropy. We conclude that for these control parameters, rotating anisotropy induces scroll wave break-up.

We know that for \( a = 0.96, b = 0.16 \), rotating anisotropy induces break-up of the scroll wave. What about in other regions of \((a, b)\) parameter space? In Figure 5.6, we chose values \( a = 0.92, b = 0.16 \). The filament exhibits different dynamics. Most of the time there was a single filament in the domain; however, sometimes due to the twist induced by rotating anisotropy, the filament deforms as in Figure 5.6b, leading to filament break. The break formed a new, shorter, less twisted filament fragment. The newly formed fragment is just a cut out segment of the original filament. The fragment finally shrank and disappeared, leaving only one filament in the space. Unlike the previous case, with parameters \( a = 0.96, b = 0.16 \), where the initial break further developed into a fully “turbulent” state, this filament fragment, however, is usually short lived, disappearing on a time scale much shorter than the period. We define such kind of scroll wave dynamic as quasi-stable.
5.3 Scroll Wave Dynamics in Monodomain 3D Tissue Slab with Rotating Anisotropy

Figure 5.6: Three-dimensional snapshots of filaments for quasi-stable scroll wave dynamic with Barkley parameters $a = 0.92$, $b = 0.16$. Most of the time there is single filament in the computational domain. But sometimes the filament becomes highly deformed and breaks up, producing a small filament fragment. The filament fragment shrinks and finally disappears. The single filament state is then recovered.

Figure 5.7 shows simulation results for control parameters $(a = 0.92, b = 0.16)$. It is a snapshot of slices of top, middle and bottom layers. In the top and bottom layers, there are single scroll waves. There is a wave break in the middle layer. It corresponds to part of the newly form filament section in Figure 5.6.
Figure 5.7: Density plots of top, middle and bottom layers for Barkley model with parameters $a = 0.92, b = 0.16$. This set of slice plots demonstrates a snapshot of scroll wave dynamics when the highly deformed single filament breaks up, generating a small filament fragment as shown in the middle slice plot.

Next, we choose parameter values $a = 1.13, b = 0.16$. The results of these simulations are shown in Figure 5.8: density plot and filament number/length plots. While the spiral waves rotate in orientation from bottom to top layer due to fiber
rotation, there is a single spiral in each of the layers. The filament number is one through out the simulation and the filament length fluctuates around $N = 17$ but does not increase over time. The single scroll remained intact and stable for the chosen parameters, $a = 1.13$, $b = 0.16$.

Figure 5.8: Scroll wave and filament dynamics for the stable state, with Barkley model parameters $a = 1.13$, $b = 0.16$. (a) Snapshot of density plot of scroll wave dynamics. The scroll wave is distorted and twisted due to rotating anisotropy but only one scroll wave exists in the domain. (b) Filament number plot. (c) Filament length plot for stable state. The filament length fluctuates but does not grow with time.
Above we have identified three states of the scroll wave dynamics in different regions of \((a, b)\) parameter space where scrolls exits. Therefore, we can summarize scroll wave behavior in the 3D monodomain model with rotating anisotropy as follows: There are regions in parameter space in which scroll waves (i) do not exist, (ii) are quasi-stable, (iii) break up and (iv) are stable. Having categorized these different behaviors, in Figure 5.9 we generate a phase diagram in the full \((a, b)\) parameter space.
Figure 5.9: Three-dimensional monodomain phase diagram with rotating anisotropy. There are four regions in the diagram. The no-spiral-wave region overlaps with the phase diagram in the isotropic medium. There is a quasi-stable region in which scroll wave breaks up transiently. The newly formed filament fragment is short-lived, and disappears and leaving a single filament. There is a break-up region in which the scroll wave breaks into a “turbulent” state and further develops into chaos state. The final region is a stable region in which there is no break-up.

Next we focus on the break-up region. With the control parameters \((a,b)\) charac-
terizing the electrophysiological properties of the medium fixed, we examine the role of the parameters $D_3$ and tissue thickness on the scroll dynamics.

5.3.1 The effect of transmural diffusion constant $D_3$ in monodomain model with rotating anisotropy

Based on the observation that spiral waves in 2D model are stable, we conjecture that the diffusion coefficient along transmural direction ($z$–direction) plays an important role in the instabilities of the scroll waves in 3D with rotating anisotropy. Our numerical framework allows $D_3$ to be varied independently while keeping the ratio of in-plane conductivity tenors unchanged ($D_2/D_1 = 0.1111$). We gradually increase the diffusion coefficient $D_3$ from 0.1111 to 1.0. The effect of $D_3$ on filament stability is demonstrated using a series filament number plots Figure 5.10.

As $D_3$ approaches 1.0, the scroll wave is stabilized. When $D_3$ equals 0.1111 and 0.3, we observe that the filament number increases steadily. For $D_3 = 0.5$, the filament number did not increasing rapidly and fluctuated between 3 and 6 once fully developed, signalling a transition from the breakup state to the quasi-stable state. The scroll wave became quasi-stable for $D_3 = 0.7$, and was stable at $D_3 = 0.9$ and $D_3 = 1.0$. 
Figure 5.10: Filament number plots at different values of $D_3$. The model size is $127 \times 127 \times 15$. While keeping all other parameters unchanged, $D_3$ is gradually increased. The filament number plots demonstrate the change in scroll wave behavior from break-up to quasi-stable, then to stable. When $D_3 < 0.7$, scroll waves break up. It is quasi-stable when $D_3 = 0.7$ and stable for larger values of $D_3$. 
5.3.2 The role of tissue thickness in monodomain model with rotating anisotropy

We have verified that the tissue thickness alone does not trigger filament break-up in the isotropic 3D monodomain model in Section 5.2. Here we would like to re-examine its role in the presence of rotational anisotropy. We fixed all the parameters of the model except the tissue thickness $N_z$, with Barkley model parameters ($a = 0.96, b = 0.16$) and $D_3 = 0.7$. The choice of these parameter values is dictated by the fact that we would like to start with a model with thinner tissue and without scroll wave break-up, and monitor any change in scroll behavior as the thickness is increased. We have shown in the previous section that a scroll wave is quasi-stable when $D_3 = 0.7$ with $N_z = 15$. Now we start in the stable region with $N_z = 7$, and monitor the scroll wave dynamics as we increase $N_z$. The result is shown in Figure 5.11.

The filament number and filament length evolving with time are plotted for various model thicknesses. At $N_z = 7$, the scroll wave is stable with the characteristics of a single filament. As $N_z$ was doubled, it became quasi-stable. The steep increases of the filament length correspond to brief breakup intervals of the filament. Starting at $N_z = 31$, the scroll wave broke up, with increasing filament number and filament length.
Figure 5.11: Filament number and filament length plots for different slab thicknesses, fixed Barkley model parameter values ($a = 0.96, b = 0.16$) and $D_3 = 0.7$. At different thicknesses, the scroll wave behavior varies. As $N_z$ is increased, the scroll wave becomes more unstable. At $N_z = 15$, it is quasi-stable. For $N_z > 31$, breakup occurs.
Table 5.1: This table summarizes the combined role of $D_3$ and $N_z$ on monodomain scroll wave dynamics. “Y” denotes scroll wave break-up; “N” denotes no break-up (stable scroll) and “Q” means the scroll wave is quasi-stable.

### 5.3.3 The effects of $D_3$ and $N_z$ in the monodomain model with rotating anisotropy

We have examined the isolated impact of both $D_3$ and $N_z$ on the scroll wave dynamics in monodomain 3D model. This is summarized in Table 5.1. This table shows that scroll wave dynamics can be stabilized by increasing $D_3$ and reducing $N_z$. Indeed, defining a dimensionless transverse length

$$\hat{L}_z \equiv \Delta z N_z / \sqrt{D_3/\omega_0}$$

where $\omega_0$ is the scroll wave period. As $\hat{L}_z$ decreases, the scroll wave dynamics becomes more stable. This is achieved through decreasing $N_z$ and increasing $D_3$. From Table 5.1, there does not appear to be a single value of this dimensionless control parameter that characterizes the stable/unstable transition, although for thinner slab thicknesses, the values of $\hat{L}_z$ at the transition are comparable.
5.4 Scroll Wave Dynamics in Bidomain 3D Tissue Slab with Rotating Anisotropy

The bidomain models require solution of an implicit equation to obtain $u_e$ at every simulated time instant. It is a more accurate description of cardiac tissue and more challenging to implement computationally. Therefore its use has been limited to relatively small preparations. Previous work has suggested the bidomain model to be necessary for the realistic simulation of transmembrane potential propagation in cardiac tissue [4], in particular in studies of current flow through the extracellular and extracardiac domains [108, 109, 110], for example during defibrillation or pacing. The goal of this section is to examine whether and to what extent the qualitative behavior of scroll waves (stable, unstable, quasi-stable) changes in going from the monodomain to the more accurate bidomain description of tissue.

To make direct comparison, all the parameters used in the bidomain model were inherited from monodomain model described. To maintain unequal anisotropy ratio, the diagonal components of the conductivity tensor in the extracellular space are $D_{e1} = 1.0, D_{e2} = 0.4, D_{e3} = 0.4$, and $D_{i1} = 1.0, D_{i2} = 0.1111, D_{i3} = 0.1111$ for all simulations. Due to computational constraints, bidomain simulations were performed on a group of pre-selected parameters $(a, b)$, setting $b = 0.04, 0.10$ and $0.16$. This represents three horizontal lines in the phase diagram of the monodomain model with rotating anisotropy, Figure 5.9. It covers all the four regions represented in the phase diagram.

First, we investigate the role of the Barkley model control parameters. The bidomain results of sweeping through a horizontal line on the phase diagram are presented in Figure 5.12, allowing direct comparison with monodomain results.
Figure 5.12: Comparison of the ranges of the regions corresponding to different scroll wave behavior between monodomain and bidomain. For \( b = 0.04, 0.10 \) and 0.16, in the bidomain model, the break-up region is wider than that in the monodomain model.
5.4.1 The effect of transmural diffusion constant $D_3^i$ on bidomain model

Similar to the analysis carried out in Section 5.3.1, we varied the value of coefficient of conductivity along $z$ axis in the intra-cellular space $D_3^i$ and tried to isolate its effect on the scroll wave dynamics. To facilitate the comparison with the results of monodomain model, we started with model size $127 \times 127 \times 15$. The result is shown in Figure 5.13. For all the $D_3^i$'s we tested, the scroll waves broke up except at $D_3^i = 1.0$, for which the scroll wave is quasi-stable. This indicates a different dynamic landscape than the monodomain model, in which the scroll wave gradually transitioned from break-up to stability with varying $D_3$. 
Figure 5.13: Filament number plots in the bidomain model for various $D_3^i$. The model size is $127 \times 127 \times 15$, and $D_3^i$ is increased from 0.1111 to 1.0. The scroll waves break up for most values of $D_3^i$ except at 1.0, where the scroll wave is quasi-stable.

When the model thickness is reduced to $127 \times 127 \times 7$, the results of bidomain also differ from those of monodomain in that the transition from break-up to stable
behavior for increasing $D^i_3$ is not as steep as in monodomain model. It starts with a relatively moderate break-up pattern at $D^i_3 = 0.1111$ then moves into the quasi-stable region. The scroll waves are quasi-stable at $D^i_3 = 0.2$ and $D^i_3 = 0.3$, with the behavior being more volatile for the smaller diffusion constant. The scroll waves are stable when $D^i_3$ equals 0.4 or larger. This observation supports the result in Section 5.4 that scroll waves are more unstable in bidomain model.

In the next section, we will examine the isolated effect of the model thickness.
5.4 Scroll Wave Dynamics in Bidomain 3D Tissue Slab with Rotating Anisotropy

Figure 5.14: Filament number plots using the bidomain model, \( N_z = 7 \). While keeping all parameters unchanged, \( D_3^j \) is increased from 0.1111 to 0.4. The filament number increases over time for \( D_3^j = 0.1111 \); the scroll wave is clearly in the break-up region. For \( D_3^j = 0.2 \) and 0.3, the filament number fluctuates but does not increase over time, which means the scroll wave is quasi-stable. For \( D_3^j = 0.4 \), there exists a single stable scroll.

5.4.2 The role of tissue thickness, \( N_z \), in bidomain model

In the case of monodomain, increasing the thickness of the model results in instability (Section 5.3.2). Here, we varied \( N_z \) to similarly study its role in bidomain model, where we present the results for \( N_z = 7, 15 \) and 31. We chose \( D_3^j = 0.7 \), as in the
monodomain model in these simulations.

As shown in Figure 5.15, the scroll wave is stable when $N_z = 7$. It broke up starting at $N_z = 15$. More wavelets developed when $N_z$ was further increased to 31. We note that the boundary of the transition is shifted compared to monodomain model. The scroll wave is quasi-stable when $N_z = 15$ in monodomain while it breaks up in bidomain. Increasing the model thickness has stronger effect on the scroll wave instability, and we again observed that the scroll waves are less stable in bidomain model.
5.4 Scroll Wave Dynamics in Bidomain 3D Tissue Slab with Rotating Anisotropy

![Diagram showing filament number and filament length plots for various slab thicknesses.](image)

Figure 5.15: Filament number and filament length plots in the bidomain model for various slab thicknesses. The scroll wave is stable when $N_z = 7$. It breaks up for $N_z \geq 15$.

5.4.3 The role of $D_3^i$ and $N_z$ in the bidomain model

To summarize, in Section 5.4, we have studied the effects of both $D_3^i$ and $N_z$ on the stability of scroll waves in bidomain model. In general, we find scroll waves to be
more unstable compared to monodomain model. The transition from break-up to
the stable scroll wave state lagged behind the monodomain as \( D_3^i \) is increased. We
justify this in the following way: while varying, \( D_3^i \), the extracellular conductivity
tensor remained unchanged, in particular with \( D_3^e = 0.4 \) Hence, the transmural layer-
to-layer coupling likely remained reduced with respect to the monodomain model,
even with \( D_3^i = 1 \). While we increase \( D_3^e \) to 1.0 and the layers become less coupling.
The scroll waves show sign of increasing stability when we compare Table 5.2 and
Table 5.3. Finally, the impact of increasing model thickness in the bidomain, leading
to scroll instability, is consistent with the monodomain results.

Table 5.2: The table summarizes the role of \( D_3^i \) and \( N_z \) on bidomain
scroll wave dynamic for \( D_3^e = 0.4 \). “Y” denotes scroll wave break-up.
“N” means no break-up (stable state) and “Q” means the scroll wave is
quasi-stable.

<table>
<thead>
<tr>
<th></th>
<th>( D_3^i = 0.1111 )</th>
<th>( D_3^i = 0.3 )</th>
<th>( D_3^i = 0.5 )</th>
<th>( D_3^i = 0.7 )</th>
<th>( D_3^i = 0.9 )</th>
<th>( D_3^i = 1.0 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N_z = 7 )</td>
<td>Y</td>
<td>Q</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>( N_z = 15 )</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Q</td>
</tr>
<tr>
<td>( N_z = 31 )</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>
### Table 5.3

The table summarizes the role of $D_3^i$ and $N_z$ on bidomain scroll wave dynamics for $D_3^e = 1.0$. “Y” denotes scroll wave break-up. “N” means no break-up (stable state) and “Q” means the scroll wave is quasi-stable.

<table>
<thead>
<tr>
<th>$N_z$</th>
<th>$D_3^i = 0.1111$</th>
<th>$D_3^i = 0.3$</th>
<th>$D_3^i = 0.5$</th>
<th>$D_3^i = 0.7$</th>
<th>$D_3^i = 0.9$</th>
<th>$D_3^i = 1.0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>15</td>
<td>Y</td>
<td>Y</td>
<td>Q</td>
<td>Q</td>
<td>Q</td>
<td>Q</td>
</tr>
<tr>
<td>31</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Q</td>
</tr>
</tbody>
</table>
Chapter 6

Discussion and Conclusion

The bidomain model is widely recognized as providing an accurate description of the conducting properties of cardiac tissue for the purposes of theoretical and numerical investigation of macroscopic electrical wave phenomena. In particular, in studies of electrical current injection in the heart - for example during pacing and defibrillation - the bidomain model leads to predictions, supported by experiment, that differ substantially from those obtained with the monodomain model.

In this thesis we have investigated rotational anisotropy as a possible cause for the breakdown of a single scroll in to the fibrillatory state using both the monodomain and bidomain descriptions of cardiac tissue. Tissue rotational anisotropy is inherently present in mammalian hearts and has been shown to play an important role in the breakup of three dimensional scroll waves in previous numerical work in the monodomain [23], [24]. The aim of this study has been a systematic investigation of the role of tissue anisotropy using both monodomain and bidomain descriptions of cardiac tissue, namely whether and to what extent the bidomain model differs from monodomain model in the stability of the scroll wave dynamics.

To conclude, in this chapter we discuss relevant previous works, and then summa-
rize our main findings, limitations of the present work and possible future research directions (Section ??).

6.1 Previous Works

The bidomain model has long been regarded as a more realistic description of the conducting properties of cardiac tissue; however, due to its numerical complexity, most of previous studies have relied on the monodomain representation of cardiac tissue structure. Panfilov and Keener first suggested the rotating anisotropy of myocardium as a possible cause for scroll wave instability [23]. In their study, the spiral/scroll wave dynamics are described by the monodomain model with rotating anisotropy. They found that while the spiral wave in two-dimensional space (2D) is stable, the scroll wave could break up in three dimensional space (3D) when the tissue thickness and total rotational fiber angle exceed certain values. Later, Fenton and Karma also studied the role of fiber rotation on scroll wave stabilities in the monodomain model [24] using a reduced ionic model. The main finding of their work was that rotating anisotropy generates localized regions of large twist, known as “twistons”, that destabilize the scroll filament.

Previous works [27, 28, 29] have emphasized the bidomain model as a more accurate description of cardiac tissue, especially with the presence of external current injection. For example, Roth and Wikswo explored the impact of unequal anisotropy ratios of intra- and extracellular spaces of cardiac tissue on the response of cardiac muscle to stimulation by electrical current [27]. Their numerical study confirmed the experiment observation that the action potentials originated from a cathodal stimulus has a “dog-bone” shape which is the result of the differing intracellular and extracellular anisotropies. None of these earlier works have explicitly treated the role of the rotating anisotropy on the stability of scrolls in the bidomain model.
6.1 Previous Works

The work presented in this thesis is distinguished from previous studies in that we study the role of rotating anisotropy on scroll wave instability in a tissue slab described by bidomain model and carry out a systematic comparison with monodomain model. We use Barkley model for the dynamics of ion channels, since it has been successfully previously used and extensively benchmarked. While Barkley has conducted a systematic study of the spiral meandering and corresponding parameter phase space \cite{111} in two-dimensional space, and Dowle \textit{et al.} extended the numerical scheme for fast two-dimensional simulation \cite{26} into three dimensional space \cite{112}, ours is the first systematic study in 3D using the Barkley model with rotating anisotropy.

Our findings confirm that rotating anisotropy is a destabilizing factor of the heart as a conducting medium. First, we observed no break-up in spiral wave dynamics in two-dimensional and three-dimensional homogeneous media. Going from two-dimensions to three-dimensions did not introduce an instability, as demonstrated by the fact that in the homogeneous monodomain model, the 2D and 3D simulations have the same phase diagram. Second, when we turned on rotating anisotropy we observed instabilities of scroll wave. For some control parameters, the scroll waves become quasi-stable while for other control parameters we observed scroll wave break-up in both monodomain and bidomain models.

With the presence of fiber rotation, we demonstrated direct comparisons between monodomain and bidomain descriptions of scroll wave dynamics. We first thoroughly studied the scroll wave states as a function of control parameters of Barkley’s model when we extended to 3D model with rotating anisotropy. We obtained a new dynamics landscape, or phase diagram as opposed to the phase diagram in homogeneous monodomain 3D model. We have examined briefly the scroll wave behaviors described by bidomain model with selected Barkley’s control parameters. We have found a boundary shift of the regions we discovered in the case of monodomain model. The scroll waves under bidomain description tend to be more unstable. While the quasi-stable
region remains unchanged. The break-up region extends into the stable region in bidomain model.

Next we have studied the effects of tissue thickness and transmural diffusion coefficient in both models. In both monodomain and bidomain models, increasing tissue thickness and reducing transmural diffusion destabilizes the scroll waves. These results support the conclusions from previous works that tissue thickness is critical for scroll wave break-up [55], [47]. Both monodomain and bidomain models demonstrated the same trend but they differ in the boundaries of quasi-stable to break-up and break-up to stable regions. In general, we find the bidomain model to be more unstable. For example, for the same Barkley parameter values, at \( N_z = 15 \), varying the transmural diffusion constant, \( D_3 \), the scroll wave is quasi-stable at \( D_3 = 0.7 \) and stabilizes for larger values of \( D_3 \) in the monodomain model, while it is not until \( D_3^b = 0.9 \) that the scroll wave becomes stable in the bidomain model. We note that while the intracellular transmural diffusion constant is increased in these studies, diffusion in the extracellular space remained unchanged in the bidomain model. We speculate that the fixed, small transmural diffusion constant in the extracellular space delays the transition from break-up to stability in the bidomain model.

At this point some limitations should be mentioned. First, we have used a simplified Fitzhugh-Nagumo-like ionic model. It accurately reproduces most of the basic properties of cardiac tissue, include the depolarization and repolarization phases of the action potential, restitution properties, dynamical changes in ionic concentration, etc. It is suitable for modeling solitary myocytes, myocardiac fibers and even synthytium, which may consist of up to tens of thousands of myocardiac cells. However this model has been found to lack many important properties, including separate time scales for depolarization and repolarization and rate dependence of action potential duration and conduction velocity. It does not account for a non-zero minimum diastolic interval following an action potential before a new action potential can be produced, which
is a key characteristic of cardiac cells. Second, we implement our simulations in an idealized rectangular slab, which lacks the complexity of the left-ventricular anatomy. Finally, our multigrid algorithm for bidomain model is still computationally intensive and it limits the layers of the model we can run our simulations. We are lacked of full phase diagram using bidomain model.

Despite these limitations, the findings of the present study are nevertheless encouraging. Reproducing propagation in biophysically realistic left ventricle is possible, but a systematic investigation is in practice at the limits of available computing resources using bidomain model. The idealized rectangular slab using simplified Fitzhugh-Nagumo dynamic described in this study gives great insight into the roles of rotating anisotropy on scroll wave break-up, and provides direct comparisons between monodomain and bidomain description of the transmembrane potential dynamics in the cardiac tissue. It lends hope to the concept that rotating anisotropy may be a crucial parameter regulating dynamical instability, which promotes scroll wave break-up.

The work presented here not only introduced the role of rotating anisotropy on the scroll wave breakup, but also carefully studied the two possible contributing factors: $D_3$ and $N_z$. Our main result is the bidomain description of the scroll wave dynamics and its paralleled comparison with monodomain results: while previous works either only demonstrated the bidomain model implementation [61] or only restricted the study in monodomain model [23], our work separates the role of transmural diffusion coefficient from the conductivity tensor, systematically studied the effect of the model thickness and their combined impact on the scroll wave dynamics. Our comparison results between the two model descriptions indicate that although the scroll wave dynamics in bidomain model in general is affected by the same factors as in monodomain model, it differs in the boundaries of the scroll wave prototypes. In bidomain model, the scroll waves are more unstable while we varying the $D_3$ and $N_z$ due to the effect of anisotropy in extra-cellular domain.
Future extension of the work presented here is to go beyond the idealized slab geometry and to conduct these studies using a minimally realistic fiber architecture model of the heart. Recent work has shown that the nested fiber surfaces and resulting fast conduction pathway between the two sides of the midwall provided by fibers on these surfaces has a stabilizing role by effectively enhancing the transverse diffusion, which is not captured in idealized geometries. On the numerical front, parallelization of the multigrid scheme will increase efficiency of simulations and facilitate systematic studies. Finally, electrical activity in heart tissue has been mostly studied with mechanical function suppressed, especially when utilizing the bidomain model due to its complexity. An ultimate goal is to include excitation-contraction coupling using the bidomain model of tissue in a minimally realistic fiber architecture model of the left ventricle in numerically resolved, systematic simulations to investigate the mechanisms underlying the generation and sustainance of phase singularities.
Appendix

A.1 Rotating Anisotropy on Fitzhugh-Nagumo-type Dynamics

Panfilov and Keener were the first to systematically study the role of rotating anisotropy in the dynamics of scroll wave propagation in a three-dimensional monodomain model of myocardial tissue, with the ionic current is described by the Fitzhugh-Nagumo-type model we introduced in Section 2.3.4.1 (see reference [23]). Their numerical study suggests that rotating anisotropy can induce break-up of the scroll wave when the tissue thickness and fiber rotation are large, confirmed by further experimental and numerical studies. Their results indicate that the scroll wave is stable when the total fiber rotation angle is less than 60° or the total thickness of the tissue is less than 1.375 space units.

We replicated their numerical model and used the same set of parameters except that we use a smaller space step. Our simulation indicates that on a finer grid, the scroll waves have a different dynamics than those observed by Panfilov and Keener. In fact, we found no break-up using all the fiber rotation angles and tissue thickness suggested in the paper.

In Panfilov and Keener’s computations, space step is 0.5 space units and time step
Table A1: The table summarizes the comparison between Panfilov and Keener’s study and our simulations on a small grid for different parameters of the tissue. “Y” means scroll wave break-up is observed; “N” means the scroll wave is stable.

<table>
<thead>
<tr>
<th>$D_2/D_1$</th>
<th>Rotation angle</th>
<th>Thickness(layer)</th>
<th>Panfilov Keener</th>
<th>Finer grid</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>120°</td>
<td>9</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>0.1111</td>
<td>120°</td>
<td>9</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>0.06</td>
<td>120°</td>
<td>9</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>0.1111</td>
<td>60°</td>
<td>9</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>0.1111</td>
<td>40°</td>
<td>9</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>0.1111</td>
<td>60°</td>
<td>5</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>0.1111</td>
<td>40°</td>
<td>3</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

is 0.01 time units. Their domain size is $60 \times 60$ grid points for x-y plane with thickness of 3, 5, and 9 grid points. We conducted similar study using 0.25 as space step and 0.001 as time step. In order to maintain similar domain size, our model has $120 \times 120$ grid points for x-y plane and the thickness are 5, 9 and 17 layers accordingly. We present the result of comparison in table A1.

We have looked at the iso-surface plot of the scroll wave in our result and compare with the figure presented by Panfilov and Keener. Figure A1(a) is taken from their work. It shows the shape of scroll wave pattern in the monodomain model with anisotropy $D_2/D_1 = 0.1111$ at 189.4 time units. The scroll in their figure broke into two halves, the upper and the lower. We first reproduced their work using the same parameter set, we observed the same irregular scroll wave behavior in our simulation, as shown in Figure A1(b). We then plot our result on the finer grid in Figure A1(c)
with rotational angle $120^\circ$ and the same anisotropy at 250 time units. In a model with smaller space step, the scroll wave does not break apart. The “squeezed” spiral waves in each layer rotate smoothly from bottom to top and form a twisted scroll wave.

Figure A1: Three dimensional iso-surface plots of scroll wave from Panfilov and Keener’s work, and our numerical result on a model with smaller grid size. (a) the shape of the scroll wave with space step $h = 0.5$, anisotropy $D_2/D_1 = 0.1111$ at 189.4 time units from Ref. [23]; (b) The iso-surfaces plot based on the same parameters as in (a) from our simulation; (c) Similar scroll wave iso-surfaces plot with space step $h = 0.25$, rotating anisotropy $D_2/D_1 = 0.1111$, angle = $120^\circ$ at 250 time units.

In Figure A2, we present the filament number and length plots for our simulation.
in Figure A1(b) to verify the scroll wave dynamics. The filament number is one throughout the simulation and the filament length is stable and fluctuates around the value 24 due to rotating anisotropy. These results indicate that when the grid size is reduced, the scroll wave is indeed stable and no break-up is observed.

Figure A2: The filament number and filament length plot for scroll wave in monodomain model using the same ionic current model from Panfilov and Keener’s work, Ref. [23], with space step $h = 0.25$, rotating anisotropy $D_2/D_1 = 0.1111$, angle = 120°, model size 120 × 120 × 7. (a) the filament number plot over time; (b) the filament length evolves over time.
Bibliography


JIANFENG LV

1615 Park Towne Ct NE Apt N11 812-340-4753
Cedar Rapids, IA, 52402 jilv@indiana.edu

Education

Aug. 2003 - Present  Physics Department, Indiana University, Bloomington
Degree Expected: Ph.D. (Feb. 2012)
Major: Physics  Minor: Scientific Computing

Sep. 1999 - Jul. 2003  Materials Sciences and Engineering,
University of Sciences and Technology of China
Degree: B.S, B.E  Major: Material Physics

Experience

1. Equity Derivatives Analyst, Transamerica Capital Management, Mar. 2011 to Present

2. Research Assistant, Physics Department, Indiana University, Aug. 2004 to Present  Advisor: Sima Setayeshgar, Physics Department, Indiana University

3. Associate Instructor, Physics Department, Indiana University, Aug. 2003 to July 2004

Skills

1. Computer Skills: C/C++, Python, C#, SQL, VBA, Matlab, Mathematica, NumeriX
2. **Quantitative Skills**: Computer Simulation, Numerical Modeling, Partial differential equation, Monte Carlo simulation, Mathematical finance, Stochastic differential equation

**Projects**

1. **“The Role of Bidomain Model of Cardiac Tissue in the Dynamics of Phase Singularities”**, Jianfeng Lv and Sima Setayeshgar

   We study the nonlinear wave propagation in excitable system. We focus on systematically study of bidomain and monodomain descriptions of cardiac tissue in the generation of rotating-anisotropy-induced scroll wave instability. We have studied the effects of tissue thickness and transmural diffusion coefficient on both models. We conclude that rotating-anisotropy induces scroll wave breakup in both bidomain and monodomain models. We have established phase diagrams denoting the stable/unstable regions for each model and identified shifts in the boundaries among these regions between the two models. Overall, we find that bidomain model is more susceptible to rotating-anisotropy induced instability than the monodomain model.

**Seminars and Conference**

1. **“The Role of Bidomain Model of Cardiac Tissue in the Dynamics of Phase Singularities”**, Jianfeng Lv and Sima Setayeshgar, Poster, May 2007, Snowbird, UT

2. **“Boulder School for Condensed Matter and Materials Physics (Biophysics)”**, Boulder, Colorado