



Faculty of Computer Science and Information Technology

**A Generic Model for Transmission of Mosquito-Borne Diseases Based On
Reaction-Diffusion Equations**

Cynthia Kon Mui Lian

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A Generic Model for Transmission of Mosquito-Borne Diseases Based On
Reaction-Diffusion Equations

Cynthia Kon Mui Lian

A thesis submitted

In fulfilment of the requirements for the degree of Doctor of Philosophy

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DECLARATION

I hereby declare that the thesis is based on my original work except for quotations and citation, which have been duly acknowledged. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.

Name of the Student: Cynthia Kon Mui Lian

Matric No: 11011594

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ABSTRACT

Simple epidemic models are disease-specific and assume individuals interact in homogeneous environment. In reality, individuals move around in space and they engage with each other and the environment. Geographical spread of infectious diseases is related to movement of individuals and spatial heterogeneity in environment. Mosquito-borne diseases are infections transmitted by the bite of an infectious mosquito, such as malaria, West Nile virus, chikungunya, dengue and Zika virus. One way to incorporate the random movement of mosquito and human population through space in disease modeling is to assume a large-scale form of Brownian motion, leading to reaction-diffusion equations. To address this issue, a spatio-temporal model based on reaction-diffusion equations for transmission of different types of mosquito-borne epidemics is formulated. The intention of this study is to explore the ability of the reaction-diffusion generic model to reproduce literature and published secondary data of actual cases of some mosquito-borne diseases. A system of partial differential equations is formulated. It is discretized and solved using finite-difference method. The generic model is found to be able to reproduce numerical results from literature reaction-diffusion malaria and dengue model. In order to gain general insights, threshold dynamics, basic reproduction number R_0 , endemic and disease free equilibrium points of the spatio-temporal generic model are analysed and defined. From numerical analysis, it is established that increment in human random movement lowers the disease risk and urbanization aggravates disease risk. In addition, the spatio-temporal generic model can be transformed to a temporal model by setting diffusion rates as zero. The temporal generic model is found to be able to reproduce numerical results from literature deterministic ordinary differential equations malaria and dengue model. Furthermore, the existence of traveling wave solution is explored numerically and the minimum spread speed

for a simulation is determined. In numerical analysis of the generic model, spatial heterogeneity in disease transmission is found to heighten the spread of infection. Moreover, the recruitment rate of mosquito is determined to be a vital parameter because when it is low enough, disease will cease to exist in the population. Finally, the temporal and spatio-temporal generic model is validated by examining its reliability to reproduce actual observed data for malaria, dengue and Zika virus. The performance measure used in this study is Root Mean Square Error (RMSE) and Mean Absolute Percentage Error (MAPE). In malaria validation, for the temporal model, the best fit values for mosquito death rate d_M in the four locations differ suggesting that mosquito longevity is distinct in different locations. In dengue cases validation, it is reported that the recovery rate is different in the studied locations indicating different genotypes. In the Zika virus cases validation, it is determined from the best fit curve that the period an infectious person is capable of transmitting the virus is 1.2 weeks. The overall percentage accuracy of the generic model for all the validation comparison cases is 88%. To conclude, the proposed reaction-diffusion generic model for mosquito-borne diseases can be a platform for software developers to create a useful predictive tool for policymakers, public health and medical officials.

Keywords: Reaction-diffusion model, transmission, mosquito-borne, generic

Model Generik Tindakbalas-Resapan untuk Penyebaran Penyakit Nyamuk

ABSTRAK

Model wabak ringkas adalah khusus untuk penyakit spesifik dan menganggap individu berinteraksi dalam persekitaran homogen. Pada hakikatnya, individu bergerak di persekitaran dan mereka berinteraksi dengan satu sama lain dan alam sekitar. Penyebaran penyakit berjangkit berkaitan dengan pergerakan individu dan perbezaan di alam sekitar. Penyakit nyamuk adalah jangkitan yang disebarkan oleh gigitan nyamuk berjangkit, seperti malaria, virus West Nile, chikungunya, virus denggi dan Zika. Salah satu cara untuk menggabungkan pergerakan rawak nyamuk dan populasi manusia melalui ruang dalam pemodelan penyakit adalah untuk mengambil gerakan Brownian yang luas, yang membawa kepada persamaan tindakbalas-resapan. Untuk menangani isu ini, model spatio-temporal berdasarkan persamaan tindakbalas-resapan untuk penyebaran pelbagai jenis wabak yang ditularkan oleh nyamuk diformulasikan. Tujuan kajian ini adalah untuk meneroka keupayaan model generik tindakbalas-resapan untuk menghasilkan keputusan literatur dan data terbitan sekunder kes-kes sebenar beberapa penyakit yang disebarkan nyamuk. Satu sistem persamaan pembezaan separa dibentuk dan diselesaikan menggunakan kaedah perbezaan terhingga. Ia didapati mampu menghasilkan simulasi dari model tindakbalas-resapan literatur malaria dan denggi. Untuk mendapatkan penyelidikan am, dinamik ambang, nombor pembiakan asas R_0 , titik endemik dan penyakit bebas keseimbangan dari model generik spatio-temporal dianalisis dan ditakrifkan secara teori. Dari analisis berangka, didapati bahawa peningkatan dalam pergerakan rawak manusia merendahkan risiko penyakit dan urbanisasi menimbulkan risiko penyakit. Di samping itu, model generik spatio-temporal boleh diubah kepada model temporal dengan menetapkan kadar resapan

sebagai sifar. Model generik temporal didapati dapat menghasilkan semula keputusan dari model temporal literatur biasa model malaria dan denggi. Selain itu, kewujudan penyelesaian gelombang perjalanan dieksplorasi secara numerik dan kelajuan penyebaran minimum untuk simulasi ditentukan. Dalam analisis berangka model generik, perbezaan spatial dalam penularan penyakit didapati meningkatkan jangkitan sebaran jangkitan. Selain itu, kadar pemakanan nyamuk ditentukan sebagai parameter penting kerana apabila ia cukup rendah, penyakit akan pupus dalam populasi. Akhir sekali, model generik temporal dan spatio-temporal disahkan dengan memeriksa kebolehannya untuk menghasilkan keputusan untuk data sebenar malaria, denggi dan Zika. Langkah prestasi yang digunakan dalam kajian ini ialah Ralat Kesilapan Maksimum Root (RMSE) dan Kesilapan Peratusan Mutlak Maksimum (MAPE). Dalam pengesahan malaria, untuk model temporal, nilai terbaik untuk kadar kematian nyamuk d_M di empat lokasi berbeza-beza menunjukkan jangka hayat nyamuk berbeza di lokasi yang berbeza. Dalam kes pengesahan kes denggi, dilaporkan bahawa kadar pemulihan adalah berbeza di lokasi yang dikaji yang menunjukkan genotip yang berbeza. Di dalam kes pengesahan virus Zika, ia ditentukan dari lengkung sesuai terbaik bahawa tempoh orang yang berjangkit mampu menyebarkan virus itu adalah 1.2 minggu. Ketepatan keseluruhan peratusan model generik untuk kes perbandingan pengesahan ialah 88%. Kesimpulannya, model generik penyebaran tindakbalas-resapan yang dicadangkan untuk penyakit penularan nyamuk boleh menjadi platform bagi pemaju perisian untuk mencipta alat ramalan yang berguna untuk penggubal dasar, pegawai kesihatan dan perubatan awam.

Kata kunci: Model tindakbalas-resapan, penyebaran, nyamuk, generik

TABLE OF CONTENTS

	Page
DECLARATION	i
ACKNOWLEDGEMENT	ii
ABSTRACT	iv
<i>ABSTRAK</i>	vi
TABLE OF CONTENTS	viii
LIST OF TABLES	xii
LIST OF FIGURES	xiv
CHAPTER 1: INTRODUCTION	1
1.0 Background	1
1.1 Research Problem	4
1.2 Hypothesis	5
1.3 Research Question	6
1.4 Research Objectives	6
1.5 Research Scope	7
1.6 Research Significance	8
1.7 Thesis Outline	8

CHAPTER 2: LITERATURE REVIEW	10
2.0 Introduction	10
2.1 Motivation of Modeling Mosquito-Borne Infectious Diseases	10
2.2 Spatio-Temporal Models	14
2.3 Generic Models	19
2.4 Discussion	20
 CHAPTER 3: REACTION-DIFFUSION GENERIC MODEL	 23
3.0 Introduction	23
3.1 Formulation of the Initial Model	23
3.2 Methodology for Numerical Analysis and Validation	35
3.3 Model Implementation	39
3.4 Numerical Analysis of the Initial Model	57
3.5 Formulation of the Generic Model	62
3.6 Discussion	65
 CHAPTER 4: THEORETICAL AND NUMERICAL ANALYSIS OF THE GENERIC MODEL	 68
4.0 Introduction	68

4.1	Theoretical Analysis of the Generic Model	68
4.1.1	Krein-Rutman Theorem	69
4.1.2	The Principal Eigenvalue	70
4.1.3	The Basic Reproduction Number	72
4.1.4	Threshold Dynamics	74
4.1.5	Basic Reproduction Number of the Generic Model	77
4.1.6	Equilibrium points of the Generic Model	84
4.2	Numerical Analysis of the Generic Model	87
4.3	Discussion	116
 CHAPTER 5: VALIDATION OF REACTION-DIFFUSION GENERIC MODEL		118
5.0	Introduction	118
5.1	Results of Simulation with Actual Malaria Cases	120
5.2	Results of Simulation with Actual Dengue Cases	135
5.3	Results of Simulation with Actual Zika Cases	147
5.4	Discussion	156
 CHAPTER 6: CONCLUSION		158
6.0	Research Summary	158

6.1	Contribution of Research	161
6.2	Limitations of Research	164
6.3	Future Studies	165
REFERENCES		167

LIST OF TABLES

		Page
Table 3.1	Parameters for the Initial Model	34
Table 3.2	Values of parameters used for comparison with Lou and Zhao (2011)	43
Table 3.3	Values of parameters used for comparison with Wang and Zhao (2011)	60
Table 3.4	Comparison among initial generic model, Lou & Zhao (2011) and Wang & Zhao (2011)	67
Table 4.1	Values of parameters used for comparison with Esteva and Vargas (1998)	102
Table 4.2	Values of parameters used for comparison with Chitnis (2005)	105
Table 5.1	Summary of properties for actual data for malaria, dengue and Zika virus	119
Table 5.2	Values of parameters used for Kapit, Song, Marudi and Belaga for simulation of model	122
Table 5.3	New parameter values used for Kapit, Song, Marudi and Belaga for simulation of model	128

Table 5.4	Values of parameters used for Kuching, Sibuluan, Bintulu and Miri for simulation of model	145
Table 5.5	New parameter values used for Kuching, Sibuluan, Bintulu and Miri for simulation of model	146
Table 5.6	Values of parameters used for Rio de Janeiro, Brazil for simulation of temporal generic model	152
Table 5.7	New parameter values used for Guaratiba, Santa Cruz, Campo Grande and Bangu for simulation of model	153

LIST OF FIGURES

	Page
Figure 3.1 Schematic diagram of susceptible human (S_H) compartment	28
Figure 3.2 Schematic diagram of infectious human (I_H) compartment	29
Figure 3.3 Schematic diagram of susceptible mosquito (S_M) compartment	31
Figure 3.4 Schematic diagram of infectious mosquito (I_M) compartment	32
Figure 3.5 The integrated initial generic reaction-diffusion model for mosquito-borne diseases	33
Figure 3.6 Methodology for Validation of the Generic Model	40
Figure 3.7 The density of infectious human(I_H) in time and space for the initial generic model using explicit finite difference scheme	44
Figure 3.8 The density of infectious mosquito (I_M) in time and space for the initial generic model using explicit finite difference scheme	45
Figure 3.9 The density of infectious human (I_H) in time and space for the initial generic model using Crank Nicolson scheme	56
Figure 3.10 The density of infectious mosquito (I_M) in time and space for the initial generic model using Crank Nicolson	

	scheme	56
Figure 3.11	R_0 is an decreasing function of D_H	58
Figure 3.12	R_0 is an increasing function of δ	59
Figure 3.13	The density of infectious human (I_H) in time and space for the initial generic model using parameter values from Wang and Zhao (2011)	61
Figure 3.14	The density of infectious mosquito (I_M) in time and space for the initial generic model using parameter values from Wang and Zhao (2011)	62
Figure 3.15	The compartmental model for the reaction-diffusion system of equations (3.55)-(3.58)	66
Figure 4.1	Flowchart of the MATLAB numerical procedure to solve the generic model	99
Figure 4.2	The density of infectious mosquitoes (I_M) in time and space for the generic model using parameter values from Wang and Zhao (2011)	101
Figure 4.3	The density of infectious humans (I_H) in time and space for the generic model using parameter values from Wang and Zhao (2011)	101
Figure 4.4	Comparison of numerical result of generic model with Esteva & Vargas (1998)	106

Figure 4.5	Comparison of numerical result of generic model when acquired immunity is added with Esteva & Vargas (1998)	106
Figure 4.6	Comparison of numerical result of generic model with Chitnis (2005)	107
Figure 4.7	Flowchart of the MATLAB numerical procedure to traveling wave solution	111
Figure 4.8	The existence of traveling wave front for infectious mosquito population when speed $\varsigma = 0.005\text{km/day}$	113
Figure 4.9	The existence of traveling wave front for infectious human population when speed $\varsigma = 0.005\text{km/day}$	114
Figure 4.10	R_0 is an increasing function of p	114
Figure 4.11	R_0 is an decreasing function of D_H	115
Figure 4.12	R_0 is an increasing function of p and the disease dies out when $\Lambda = 0.00385$	115
Figure 5.1	Weekly malaria cases in Kapit from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model	125
Figure 5.2	Weekly malaria cases in Song from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model	126

Figure 5.3	Weekly malaria cases in Marudi from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model	126
Figure 5.4	Weekly malaria cases in Belaga from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model	127
Figure 5.5	The actual density of infectious humans in time and space	132
Figure 5.6	The simulated density of infectious humans in time and space	132
Figure 5.7	Weekly actual malaria cases in Song from week 39 in 2012 to week 22 in 2013 and simulated cases from the spatio-temporal generic model	133
Figure 5.8	Weekly actual malaria cases in Kapit from week 39 in 2012 to week 22 in 2013 and simulated cases from the spatio-temporal generic model	133
Figure 5.9	Weekly actual malaria cases in Belaga from week 39 in 2012 to week 22 in 2013 and simulated cases from the spatio-temporal generic model	134
Figure 5.10	Weekly actual malaria cases in Marudi from week 39 in 2012 to week 22 in 2013 and simulated cases from the	

	spatio-temporal generic model	134
Figure 5.11	Weekly dengue cases in Kuching from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model	135
Figure 5.12	Weekly dengue cases in Sibu from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model	138
Figure 5.13	Weekly dengue cases in Bintulu from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model	139
Figure 5.14	Weekly dengue cases in Bintulu from week 39 to 47 in 2012 and predicted cases from temporal generic model	139
Figure 5.15	Weekly dengue cases in Miri from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model	140
Figure 5.16	Weekly dengue cases in Kuching from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model	140
Figure 5.17	Weekly dengue cases in Sibu from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model	143

Figure 5.18	Weekly dengue cases in Bintulu from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model	143
Figure 5.19	Weekly dengue cases in Miri from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model	144
Figure 5.20	Weekly Zika cases in Rio De Janeiro from week 52 in 2015 to week 24 in 2016 and predicted cases from the temporal generic model	144
Figure 5.21	Weekly Zika cases in Guaratiba from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model	151
Figure 5.22	Weekly Zika cases in Santa Cruz from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model	154
Figure 5.23	Weekly Zika cases in Campo Grande from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model	154
Figure 5.24	Weekly Zika cases in Bangu from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model	155

Figure 5.25 Weekly Zika cases in Bangu from week 52 in 2015

to week 24 in 2016 and predicted cases from the

spatio-temporal generic model

155

CHAPTER 1

INTRODUCTION

1.0 Background

Diseases can be categorized into two types, infectious and non-infectious. Infectious diseases are caused by microorganisms and can spread from one person to another, directly or indirectly. Non-infectious diseases, also known as non-communicable diseases are not passed from an individual to another. They are normally caused by unhealthy diets, environmental factors, physical inactivity or genetics. Infectious diseases can be further classified into two categories, direct transmission and indirect transmission. Direct transmission occurs when there is direct close physical contact with the infected individual. Examples of direct transmission include person-to-person contact, droplet spread and vertical transmission (spread of disease from mother to child which occurs: during pregnancy, labor or after birth through breast milk). Indirect transmission occurs when there is no direct contact between individuals. For instance, pathogens can be spread through airborne transmission, contaminated objects and vectors. Vectors transmit infectious diseases from human to human or animal to human. Most of these vectors are blood sucking arthropods such as mosquitoes, ticks and fleas.

Mosquitoes are the most common infectious disease vector. Chikungunya, dengue, yellow fever and Rift Valley fever are all spread by *Aedes* the genus of mosquitoes found in tropical zone. Furthermore, Japanese Encephalitis, lymphatic filariasis and West Nile Virus outbreaks have been attributed to mosquitoes of the genus *Culex* and malaria by *Anopheles*.

According to the World Health Organization (WHO) (2017b), vector-borne diseases account for more than 17% of all infectious diseases, causing more than 1 million deaths annually. The worldwide incidence of dengue has risen thirty-fold in the past 30 years. Besides that, more than 2.5 billion people in over 100 countries are at risk of contracting dengue alone. In addition, malaria causes more than 400 000 deaths every year globally, most of them children under 5 years of age. Control efforts to combat these diseases are for example: mosquito control by fogging and insecticide usage, personal use of repellent, improving public awareness by providing education and elimination of mosquito breeding sites. Apart from that, public health authorities can utilise disease models to determine the prevalence of the infections and the best combination of control measures to wipe out the diseases.

Disease models are imperative to enhance the understanding of the dynamics of the interacting populations. Mathematics can be used to describe biological phenomenon. Moreover, mathematical models can convert the mechanism of the transmission of diseases into prediction of the prevalence of diseases. The modeling of infectious diseases in this research is focused on indirectly transmitted infectious diseases, exclusively by the vector mosquito.

Disease models are developed to shed light on the introduction of infections and their transmission across populations. One of the prime reasons for modeling infectious diseases is to determine the best control measure to reduce and then eradicate a disease from a population. Mathematical models can be used to forecast the outcome of a disease even if there is limitation in available data. These models are able to elucidate the long term behaviour of the spread of diseases and also the impact of different types of control measures.

At critical time, these models are valuable as they are able to provide recommendation to public health authorities. Although predictions are not always perfect, they contribute insights to the spread of the infection. Besides, mathematical models allow experiments to be carried out without the necessity to attempt in real life as this might be unethical. By doing so, many what-if questions can be answered.

Ross (1910) first came up with a mathematical model for the transmission of malaria. MacDonald (1957) extended the model and utilized it in the Global Malaria Eradication Programme. Since then, the interest in mosquito-borne diseases transmission has multiplied. Deterministic models consisting of a system of ordinary differential equations are formulated to cater for specific mosquito-borne diseases such as malaria (Ngwa & Shu, 2000; Labadin et al., 2009), dengue (Pongsumpun et al., 2002; Derouich & Boutayeb, 2006) and West Nile Virus (Bowman et al., 2005; Cruz et al., 2009). Moreover, temporal models produce results in terms of population against time. In addition, since the introduction of Ross-MacDonald model more than a century ago, most general disease models resembles it and lack geographical variety and individual movement. The concept of spatial heterogeneity has been widely investigated but not fully utilised. Simple deterministic models make assumption that the environment is homogeneous. Therefore, the geographic spread of diseases is less understood compare to the temporal study on the spread of diseases.

Gause (1971) experimented with a predator-prey system in the laboratory using paramecium and didinium. His experiments indicated that space makes an impact as one or both species eventually extinct when they both can coexist in nature. Besides that, Huffaker (1958) showed that coexistence was possible. His experiment included an orange, herbivorous mite and carnivorous mite food. He considered environment as homogeneous

by arranging the orange closely and evenly, it is found that the predator mite overate its prey and eventually extinct. However, increasing the distance between the oranges increased the time to extinction. When made heterogeneous, the system stabilized. This contributed to the acknowledgment that space can bring about changes in the dynamics of populations. In reality, population stays in a heterogeneous environment therefore recognizing different locations is imperative. Moreover, mobility of population can also be taken into account, allowing the effect of movement of human and mosquito population on the spread of the disease to be analysed.

1.1 Research Problem

Most disease models consider the distinctive interaction between individuals and dynamics for one infection. These models are developed for a specific mosquito-borne disease and majority of them are temporal models as discussed in the previous section. From these disease models, software developers can develop a platform that can be utilized by those in public health. An application that can capture the trend of diseases can be a powerful tool. Normally, the issue that public health practitioners and policymakers encounter would be that they need to use a different application should they want to analyse the spread of different mosquito-borne infections. Apart from that, temporal models produce results of prevalence against time therefore users who are interested in disease cases in different districts or locations, would need to run the model to obtain results for a location each time. Utilizing different disease models and running them repeatedly would be a waste of time and resources. Reiner et al. (2013) developed a bibliography of mosquito-borne pathogen transmission models and a system to classify biological assumptions. They proposed that

spatial heterogeneity deserves more attention as it is under represented and is important based on empirical studies. Empirical studies are based on actual observation or experiences in the field and not from theory. Also, it has been addressed that spatial heterogeneity in mosquito density has been ignored. Furthermore, Murray (2003) stated that geographic spread is far less understood and studied than temporal development and control of diseases. To address these issues, the interest is to formulate a general disease model which can be used for different types of mosquito-borne diseases. In addition, time and space are taken into account therefore predictions would inform public health authorities where and when an outbreak may occur in a single run. The prediction tool could be used by medical officials and policymakers to predict outbreak and epidemic spread at district, state and national level. This study contributes to the knowledge needed to address these challenges by answering the research question in Section 1.3.

1.2 Hypothesis

The hypothesis of this study is:

A spatio-temporal generic model for transmission of mosquito-borne diseases based on reaction-diffusion equations can be formulated and it can reproduce temporal and spatio-temporal literature simulations and historical data of actual cases of various mosquito-borne cases in specified locations.

The research and analysis carried out in this study allow this hypothesis to be tested.

1.3 Research Question

The main research question is: Can a spatio-temporal generic model be formulated and can it reproduce ordinary and partial differential equations models' simulations from literature and historical data of actual cases of various mosquito-borne diseases?

1.4 Research Objectives

The following are the objectives of this study:

- (a) To formulate a system of partial differential equations (PDEs) incorporating the spatial aspect and diffusion of human and mosquito population, plus to analyse the dynamical system to gain general insights: threshold dynamics, basic reproduction number R_0 , endemic and disease free equilibrium points.
- (b) To numerically evaluate suitable numerical method and investigate the existence of traveling wave solution, the effect of model parameters, initial population data, and diffusion on the behaviour of the transmission of mosquito-borne diseases.
- (c) To explore the accuracy of the generic model by examining its ability to reproduce simulations from models for different types of mosquito-borne diseases taken from literature.
- (d) To validate the generic model by investigating its reliability to reproduce actual observed data for different types of mosquito-borne diseases in different locations at a regional to national spatial scale.

1.5 Research Scope

In this study, a reaction-diffusion generic model which considers the similarity in transmission of different mosquito-borne diseases, is formulated. As all mosquito-borne diseases are transmitted through mosquito bites, and not through human contact, this is the focal point where these diseases spread. Occam's razor is a principle which suggests that if there are two competing theories, the simplest is preferred to the more complex or if there are two explanations of an unknown phenomena, the one with less assumptions is always better. Adopting this principle, the generic model is kept as simple as possible. The human and mosquito population is divided into two compartments namely susceptible and infectious. Immunity is not considered in this study. Apart from that, only adult mosquitoes are included hence the aquatic stage of mosquito is disregarded. Environment factors such as temperature and weather, plus control measures are dismissed so as not to complicate matters. With the simplest possible model which takes into account, the transmission, movement, recruitment and death of both populations, it is studied if this model is able to reproduce numerical results from literature and historical data of a few mosquito-borne diseases. Since there are different kinds of mosquito-borne diseases, to validate the results from this generic model, three common mosquito-borne diseases are investigated, particularly malaria, dengue and Zika virus. The spatial aspect of the generic model is related to specific geographical location points by the latitude/longitude distance. As the spatial scale for this continuous model is large, the locations studied are districts in Sarawak, Borneo and neighbourhoods in Rio de Janeiro, Brazil.

1.6 Research Significance

This study designs a generic spatio-temporal model for mosquito-borne diseases that hopes to enhance the way medical and public health authorities track the spread of many types of mosquito-borne epidemics. One model which caters for many types of mosquito-borne diseases eliminates the need of a specific model for every mosquito-borne infection. The generic model can be a platform for software developers to produce a user friendly application. As spatial aspect is incorporated, this application can be used by public health authorities and policy makers to determine where and when an outbreak might occur. Normally, for a temporal model, different initial data and parameter values for different locations need to be input multiple times and the model needs to be run repeatedly. However, using a general spatio-temporal model, necessary data is required to be entered only once at the start and processed once. Another strength of a generic model is that generalized parameter values can be utilised across all locations and this is essential because data availability is scarce. Using the application, public health practice can determine the best control or preventive measure to carry out in different locations. In addition, it can be a guide to government in deciding allocation of money and resources for combating mosquito-borne diseases. This enables time, money and resources to be saved instead of spending on mass campaigns without having a focused area to work on. More detailed discussion on the contributions of this study is presented in Section 6.1.

1.7 Thesis Outline

In this thesis, a generic spatio-temporal model for mosquito-borne diseases which is made

up of reaction-diffusion equations is developed and investigated. Chapter 2 presents the development of mathematical models for mosquito-borne diseases and introduce the different types of spatial models used to explore the geographical spread of vector-borne diseases. In Chapter 3, the formulation of an initial nonlinear PDEs model for the transmission of mosquito-borne diseases is discussed. The model is then analysed numerically to study the impact of certain parameters on the spread of mosquito-borne diseases. Apart from that, the ability of the initial model to reproduce results of literature reaction-diffusion models for malaria and dengue is explored. The initial model is refined thus the generic model is presented. In Chapter 4, the generic model is analysed both theoretically and numerically. Moreover, the existence of traveling wave solution and the spread speed for a specific case is investigated numerically. The ability of the model to reproduce simulations from literature is explored. In Chapter 5, the model is validated by comparing numerical results with actual cases of malaria, dengue and Zika virus. Finally in Chapter 6, conclusion and possible future developments are discussed.

CHAPTER 2

LITERATURE REVIEW

2.0 Introduction

In the first chapter, the burden of mosquito-borne diseases and the roles of mathematical modeling in providing insights and forecast of the spread is discussed. The contribution of spatial heterogeneity to the transmission of diseases and the importance of capturing this in disease models is illustrated. Furthermore, the typical deterministic disease models are customized for a single disease therefore there is a need for a generalized model which can cater for most mosquito-borne diseases.

In this chapter, a review of the motivation of mathematical models for mosquito-borne diseases is presented. Temporal models formulated based on a system of ordinary differential equations (ODEs) to describe the transmission of various kinds of mosquito-borne diseases are discussed. Then, different kinds of spatial temporal models are presented, namely metapopulations, cellular automata, reaction-diffusion models and Geographic Information Systems (GIS).

2.1 Motivation of Modeling Mosquito-Borne Infectious Diseases

Many mathematical models had been constructed according to the epidemiology and factors contributing to the transmission of infectious diseases. These mathematical models are commonly based on the understanding of the dynamics of the host and pathogen. They

are to provide forecast of the prevalence of an infection in a population. Mathematical models are essential in the armoury of epidemiological devices as they can be utilized in spite of limitations in data. Factors which contribute to the spread of diseases can be analysed by integrating them in the models and studying the number of infectious cases as their intensity increases or decreases. A significant amount of models use mathematical equations to interpret the dynamics of diseases. Henceforth, experiments need not be carried out in real life. The effect of certain parameters on the spread of a disease can be manipulated for different scenarios.

The study of epidemic modeling first started in 1766 when a mathematical model was developed by Daniel Bernoulli to analyse the performance of inoculation on smallpox virus. This was the first published mathematical model to study infectious diseases. Bernoulli wanted to find out if the introduction of a small amount of virulent smallpox in an individual's body which protects a person from getting infected, should be promoted or otherwise. He concluded using his model that inoculation increases lifespan from birth by about three years. Lambert included age dependent parameters to Bernoulli's model in 1772. Hamer (1906) published a discrete time measles transmission model where the number of new cases depends on the product of susceptible and infectious.

Ronald Ross described the transmission dynamics of malaria mathematically. He formulated the first malaria model where he considered susceptible and infectious state for both human and mosquito population. However, he did not consider latent periods for both populations. Latent period is the interval between the exposure to pathogen and symptoms first appear. The model illustrated the relationship between the number of mosquitoes and incidence of malaria in humans. In 1927, Kermack and McKendrick studied mathematical

epidemiology more in depth and found out that a certain threshold value of susceptible needs to be exceeded for an outbreak to occur. The model considered that after susceptible humans get infected, they will recover and remain immune. MacDonald (1957) extended Ross' model and applied it to the Global Malaria Eradication Programme. By including the latent period of mosquitoes, the compartments for human is the SIS (Susceptible-Infectious-Susceptible) model and SEI (Susceptible-Exposed-Infectious) model for mosquito. Bailey (1975) linked deterministic and stochastic models to data. Anderson and May (1991) then introduced latent period for humans hence they developed SEIS (Susceptible-Exposed-Infectious-Susceptible) model for human population and SEI model for mosquito population. Dietz et al. (1974) further refined the Ross-MacDonald model and added two classes of humans, namely those with low recovery rate and high recovery rate.

Deterministic models consist of ODEs, for example malaria models by Ngwa and Shu (2000), Tumwiine et al. (2007), Labadin et al. (2009), and Syafruddin and Noorani (2012). In addition, there are temporal models for dengue (Feng & Velasco-Herna'ndez, 1997; Derouich & Boutayeb, 2006; Pinho et al., 2010; Kongnuy et al., 2011; Rodrigues et al., 2012) and chikugunya (Dumont et al., 2008; Moulay et al., 2011; Poletti et al., 2011). These compartmental mathematical models illustrate whether in time the disease will prevail or die out in a population. Deterministic models (Gao et al., 2016; Ondrej et al., 2017; Padmanabhan et al., 2017) consider both sexual and vector transmission for Zika Virus (ZIKV) concluded that sexual transmission plays a minor role in the spread of the disease. Agosto et al. (2017) took into account vertical transmission and asymptomatic individuals. From scenario-based exploration, it is decided that personal protection is more effective than mosquito-reduction. Kucharski et al. (2016) considered ZIKV to be only

vector-borne and using a mathematical model, studied the dynamics of infection in French Polynesia from 2013 to 2014. Their study suggests that ZIKV transmission in island population displays similar dynamics as dengue virus. Gourley, Liu and Wu (2007) developed a model for vector-borne diseases which has transmission dynamics similar to West Nile Virus. The spatial aspect is added to the temporal model which leads to a reaction-diffusion system. The populations are divided into susceptible and infected juvenile and adult reservoir population and the adult infected vector.

Bacaer and Guernaoui (2006) developed a mathematical model for vector-borne diseases which included the seasonality of the vector population and the distribution of the latent period from infection to symptomatic in humans. The human host is divided into SIR (Susceptible-Infectious-Recovered) compartments while vector sandflies, into SI compartments. Real data from a province in Morocco are compared with simulations from the model and some parameters values estimated. Supriatna, Serviana and Soewono (2008) presented a general host-vector SIR transmission model in a form of a system of partial differential equations which reduces to a system of ODEs. The reduced model is then applied to examine the medical treatment in controlling Flariasis disease in Jati Sampurna, West Java, Indonesia. They concluded that a combination of treatment will improve the effectiveness of the control program. A study on the global dynamics of a vector-borne diseases model which consists of SIR compartments for human host and SI compartments for vector population, by Yang, Wei and Li (2010) is found to be determined by the basic reproduction number, R_0 .

Blayneh, Cao and Kwon (2009) formulated a control model using Pontryagin's Maximum Principle and the model is applied to study the effects of prevention and

treatment controls on malaria. This principle is used to find the optimal control for taking a dynamical system from one state to another, especially in the presence of constraints. A System Dynamics model to study the diffusion of a disease transmitted by the *Aedes* mosquito in different locations has been built by Mecoli, Angelis and Brailsford (2010). The model took into account the movement of people between the regions and allows evaluation of different control strategies. The human host and adult vector population are represented by SEI compartments. The eggs and larvae are considered as susceptible and infectious (SI model).

Vector-borne disease systems made up of infectious host and vector populations on networks of patches were developed by Cosner et al. (2009). The models enabled the study of the effect of human movement in heterogeneous environments on transmission of vector-borne diseases. It is concluded that the movement of humans between patches is adequate to maintain disease persistence in patches with zero transmission. A review on mosquito-borne transmission mathematical models by Reiner et al. (2013) mentioned that one of the modelling deficiencies which deserve more attention is spatial heterogeneity. According to Sattenspiel and Lloyd (2009), epidemiologists have great interest in the spatial spread of infectious diseases. Consequently, there is growing attention in spatio-temporal models which are able to provide understanding on the effect of spatial heterogeneity.

2.2 Spatio-Temporal Models

Simple deterministic models make assumption that the environment is homogeneous. On the contrary, populations are distributed in space and individuals are mobile. Space can

bring about changes in the dynamics of populations. Spatial models remain an area of high interest to researchers. Transmission of infectious diseases occurs between individuals when there is an interaction. Movement of individuals has been known to influence the geographical spread of infectious diseases. Modeling spatial spread includes this aspect and enable the transmission speed of an infection to be determined. The spatial nature of the transmission also affects the persistence of the disease and the type of effective control measures. Moreover, researchers examined the geographic distribution of diseases by dividing populations according to their spatial locations.

There are a few approaches to modeling spatial spread. Metapopulation models divide an entire population into discrete groups based on their locations and are interconnected. The interaction is described by the way the infection transmit between the groups. A multigroup dengue disease transmission model was studied by Ding et al. (2012) where the populations are divided into n groups. The human population is represented by SIR model and mosquito population SI model. They showed that global dynamics are determined by the basic reproduction number, R_0 . Mecoli et al. (2010) produced a System Dynamics model to study the diffusion of diseases transmitted by the mosquito *Aedes albopictus*. In addition, they examined the effects of human travel among different geographical regions on the diffusion of the virus and different control strategies in the various regions. Simulation of the model are compared with a real case of Chikugunya epidemic which occurred in Italy in 2007. It is found that starting a control strategy earlier reduces the number of infectious cases. To include human movement and spatial heterogeneity, Prosper et al. (2012) studied a two patch malaria model and concluded that malaria persists in regions where it could have died out because of human mobility. They also found that single patch malaria model could mistakenly predict the elimination of the

disease. Moreover, it is concluded that mosquito death rate is more sensitive than biting rate from their elasticity analysis.

Another type of population level spatial model is the reaction-diffusion model. Reaction-diffusion models assume that population is distributed continuously across the environment and not in discrete form. The standard partial differential models assume that transmission happens locally, meaning interaction occurs at a given location depending on the individuals at that location. In 1951, Skellam (1951) developed a reaction-diffusion model of invasion biology. He established the relationship between random walks as movement of individual members of biological species and the diffusion equation as a description of dispersal of the population as a whole (Cantrell & Cosner, 2003). A reaction-diffusion system for chemical basis of morphogenesis was constructed by Turing (1952) and he discovered diffusion-driven instabilities. The spread of rabies among foxes were modeled and the progress of rabies if introduced near Southampton was carried out by Murray et al. (1986). The model suggests that vaccination is a much beneficial control strategy compare to culling. Eventually, Takahashi et al. (1995) took into account diffusion and advection of *Aedes aegypti* mosquito. They studied the existence of travelling wave in different situations and the minimum spread speed which corresponds to biological invasion. Lewis et al. (2006) mathematically evaluated the spread of West Nile virus by spatially extending the temporal deterministic model of Wonham et al. (2004) to include diffusive movement of birds and mosquitoes. The spread rate of the disease is found to be an increasing function of bird diffusion. Comparison of results showed that the spread rate of the simplified model may provide an upper bound for the spread rate of a more realistic and complex version of the model.

A model to study dengue propagation was proposed by Maidana and Yang (2007). They determined the minimum speed of the traveling waves which describes the propagation of dengue in an area previously colonized by the mosquito *A. aegypti*. Furthermore, the minimum traveling waves velocity as a function of the model's parameters was resolved, permitting control strategies to be studied in order to attain the eradication of dengue. A periodic Ross-Macdonald type model with diffusion and advection was presented by Lou and Zhao (2010) to study the effect of mobility on the spread of malaria. The effect of advection was studied numerically and it was found to increase the rightward spreading speed, whereas decrease the leftward spreading speed. As for human movement, the rightward and leftward spreading speeds increase with human diffusion coefficient, indicating that global traffic networks may deteriorate malaria situation. In the next year, Lou and Zhao (2011) modified Ross' model to include time-delay and diffusion of human and mosquito population. The intention is to include spatial heterogeneity and extrinsic incubation period in the study of the spread of malaria. Their numerical analysis suggested that spatial heterogeneity strongly affects the infection risk. In addition, it is shown that the model with spatially averaged parameters may underestimate the transmission intensity. Also, a nonlocal and time-delayed reaction-diffusion model of dengue fever was proposed by Wang and Zhao (2011). They found that time delay reduces the infection risk. It is concluded that population mobility decreases the values of the basic reproduction number in heterogeneous spatial infection. Similar to Lou and Zhao (2011), they concluded that the infection risk may be underestimated if the spatially averaged parameters are used to compute the basic reproduction number for spatially heterogeneous infections. Anița and Capasso (2012) considered an oversimplified two-component reaction-diffusion system which describes the spread of malaria. They

showed that it is possible to diminish the epidemic process, in the whole habitat, by focusing on the segregation rate between the population of infected mosquitoes and the susceptible human population in a sufficiently large subset of the spatial domain.

In a setting where it is not necessary to divide the entire population, a different spatial approach which is lattice-based model can be adopted. In this model, individuals within a grid site are grouped together. Cellular automata is where a grid site is occupied by one individual hence each site is either occupied or empty. Interactions are assumed to take place with the neighbouring grids. De Castro Medeiros et al. (2011) formulated a stochastic cellular automata model to represent the dynamics of dengue transmission in a community incorporating human mobility and human renewal. From the model, it is found that it is possible for dengue to persist in large cities with low infestation rates in a few neighbourhoods. Moreover it was concluded that better methods should be used to measure house index values (the proportion of mosquito-infested buildings). Using lattice-based epidemic models, Caraco et al. (2001) analyzed the effects of host spatial heterogeneity on the transmission of the disease spread by a vector. They deduced that increasing host spatial heterogeneity increases the physically separation between the host and vector, hence reducing the infection. The effect of host heterogeneity, however, apparently requires smaller neighbourhood sizes.

Geographic information systems (GIS) are used to secure, collect spatial data and when needed, regain and to depict the spatial facts. Hence, it can be utilized for data populations, disease prevalence, environmental data and to create a connection among them. Examples of application of GIS are carried out by Chaput et al. (2002) and Kitron (2000). Chaput et al. (2002) studied a newly recognized tick-borne disease, human

granulocytic ehrlichiosis (HGE), for nonrandom patterns and clusters in an area known to be endemic for tick-borne diseases. Analysis of confirmed cases of HGE identified in years 1997–2000 in a 12-town area around Lyme, Connecticut, showed that the distribution of HGE infections are not random. On the other hand, Kitron (2000) commented that the appearance and utility of risk maps depended on the purpose: whether to test a hypothesis, identify gaps in knowledge, provide a direction for control efforts, or investigate the actual or potential effectiveness of an intervention. Shirayama et al. (2009) study the impact of the intervention coverage and people's adherence to the intervention on malaria health outcome. Geographic information system (GIS) maps were developed using the data collected in Khammouane province, Laos. It was found based on the maps that malaria remained unevenly distributed within districts. Perez and Dragicevic (2009) integrated an agent-based model with GIS to mimic the spread of diseases. They observed that the dynamic spatial interactions within the population lead to high numbers of exposed individuals who perform stationary activities in areas after they have finished commuting, such as in schools and universities.

2.3 Generic Models

Belik et al. (2011a, 2011b) included regular bi-directional movements of the host between base locations and accessible destinations in a metapopulation model. Comparison between the model and ordinary diffusion and effective force of infection models are carried out. Effective force of infection model is short of explicit incorporation of host movements, a systematic analysis is complicated. It is found that the front velocity of the epidemic does not increase unboundedly but reaches a maximum level with increasing

global travel rate, which differs from reaction-diffusion approach. Apart from that, using a generic inverse variance model, Handel et al. (2010) calculated the relative risk of multiple sclerosis (MS) following infectious mononucleosis (IM). They concluded that IM is a dominant risk factor in development of MS considering a large MS patient sample size in comparison to previous meta-analysis. Saldana considered metapopulation of SIS model which takes into account that migration, transmission and recovery exists simultaneously. They found that if an epidemic spreads in nodes with low connectivity for generic networks, the infection spreads to all patches. In addition, should the density of individuals and/ or maximum connectivity be high enough, confirming the disease-free equilibrium to be unstable, the epidemic will spread. A SIS model is extended by Sahneh and Scoglio (2014) to a model of two competitive viruses over two network with generic structure where each virus has a distinct network of transmission. From their analysis, it is shown that competitive virus can coexist long term in a region where there is distinct nontrivial multilayer networks. It appears that none or little overlapping on the central nodes is the key of coexistence. When the effective infection rates are high, the central nodes are mostly those with the highest node degrees, however, when the effective infection rate is low, the central nodes are those with highest eigenvector centrality.

2.4 Discussion

As presented, modeling mosquito-borne diseases has expanded greatly since Ross model. Many compartmental models have been developed to shed light on the behavior of the spread of diseases such as malaria, chikugunya and dengue. Compartments such as susceptible, exposed, infectious and recovered can be combined according to the behavior

of the diseases to best depict the epidemiological process. Apart from that, there are several ways of modeling spatial spread of diseases. In general, few considerations come to mind when formulating a model. One of the main factors is the purpose of the development of the model. As the interest in this study is the effect of movement of human and mosquito population and spatial heterogeneity on the spread of the disease, spatial factor is incorporated. A beneficial model should be able to cater for different types of infection and geographical conditions. Moreover, a model which is easy to update when there are changes to environment or conditions is appropriate. As the purpose of this study is to formulate a generic model which is applicable for various mosquito-borne diseases, a compartmental model is appropriate.

Metapopulations are applicable for modeling dynamics where populations can be divided into different units according to their locations. This model can be used when the population can be separated into groups. The spread of diseases basically depends on the movement of individuals out of their home to a different location. Lattice based model is bounded by the size of the discrete grids. For example, for cellular automata, each grid contains an individual, hence it is appropriate for populations which has low density. Interaction between individuals is stochastic hence parameters are normally defined at individual level. Reaction-diffusion models in general assume local interaction and depends on diffusion of individuals to spread diseases. These models enable mathematical analysis to be possible. Theoretical analysis shed light on the general behavior of the spatial spread of a disease. Common queries such whether a disease persists or dies out in a population and where the disease will spread to, can be studied using the model. It is apt for cases where the population is compactly distributed across the environment hence it can be considered as continuous. Geographic Information Systems (GIS) are computer-

based tools used to store, visualize and interpret geographic data. Geographic data includes anything associated with a location on the globe, or anything that can be mapped. In public health, GIS can be used in the surveillance and monitoring of vector-borne diseases, water borne diseases and in environmental health. For example, where to target polio immunization campaigns in geographically isolated locations can be determined. Although it is a tool in the fight against infectious diseases and other public health problems; it is not always user friendly. Public health officers might find it difficult to use as it requires reorganizing the way data are collected and displayed.

The focus of this study is to formulate a generic model which can be utilised for different types of mosquito-borne diseases. Furthermore, the model should be applicable at a national or state scale, allowing public health authorities to use it as a guidance at critical moments when there is an epidemic. It can be used to predict the future spread of mosquito-borne diseases and to explore the effects of different parameters. Most populations can be accumulated by neighbourhoods and districts, hence combined population data are mostly available. Parameter values defined at a district or state level can be obtained with ease in comparison with individual level data. Taking these into account, a reaction-diffusion model is well suited for this study. As most health authorities monitor the spread and control of diseases at a district, state or national level, it is befitting to have a model which provides the mean trend of the behaviour of these diseases. Generalized parameter values and initial data are the input of a reaction-diffusion model making it a feasible choice for monitoring diseases at a large spatial scale. The well-known practise, Occam's razor, is adopted here, to develop the simplest model possible that is dependable to reproduce observed cases.

CHAPTER 3

REACTION-DIFFUSION GENERIC MODEL

3.0 Introduction

In Chapter 2, the introduction of deterministic disease model by Ross-MacDonald and the expansion of compartmental models for mosquito-borne diseases are discussed. The acknowledgment that human movement and spatial heterogeneity affects behaviour of the geographic spread of diseases led to the growing interest in spatial modeling. Then, the different approaches of spatio-temporal models are presented.

In this chapter, an initial spatio-temporal generic model for transmission of mosquito-borne diseases which incorporates the movement of human and mosquito population is formulated. From the comprehension of the behavior of mosquito-borne diseases, a schematic diagram of the transmission of the disease is being drawn and a system of nonlinear differential equations is formulated. After that, numerical results from the proposed model are explored by comparing them with simulations from literature. The initial model is refined to produce better replication of literature simulation hence the generic model is attained.

3.1 Formulation of the Initial Model

In the beginning, mosquito-borne and vector-borne diseases compartmental models presented by Lord, (1996), Bacaër and Guernaoui (2006), Gourley, Liu and Lou, (2007), Supriatna, Serviana and Soewono (2008), Blayneh, Cao and Kwon (2009), Cosner et al.

(2009), Lou and Zhao (2010), Mecoli, Brailford and Angelis (2010), Belik, Geisel and Brockmann (2011b), Lou and Zhao (2011), Wang and Zhao (2011), Gao and Ruan (2012) and Martcheva and Prosper (2012) were deliberated to identify the similarities among these models. The purpose is to formulate a generic model which is appropriate for multiple mosquito-borne diseases; the core is the manner of transmission of these diseases. Mosquito-borne diseases cannot be transferred between hosts (human to human) directly but only through an intermediary vector, the mosquito. The history of vector-borne diseases is known to adhere to a standard behavior (Keeling & Rohani, 2008). A mosquito takes a blood meal from an infected human host, and at a certain probability will acquire the disease. After a latent period, it will become infectious and when it takes another blood meal on a different person who is susceptible, the disease-causing agent will enter into the person's bloodstream making this person infected. According to Choisy, Guegan and Rohani (2007), "The transmission process is at the heart of any epidemiological model". The focal point here is the two major mechanism of transmission which is from human to mosquito and vice versa.

The common compartments used in mosquito and vector borne diseases models found in literature are determined. They are susceptible and infectious, for both host and vector population. In addition, the corresponding terms are birth rate for population, death rate, force of infection and recovery rate. The force of infection according to epidemiologists is per capita rate of acquisition of the disease (Choisy et al., 2007). After studying the work done on spatial temporal disease modeling (Kallen, Arcuri & Murray, 1985; Lewis, Renclawowicz & Driessche, 2000; Li & Zou, 2009; Lou & Zhao, 2010; Lou & Zhao, 2011; Wang & Zhao, 2011; Martcheva & Prosper, 2012) the common terms used for spatial spread diffusion coefficients and location dependent parameters.

In the generic model, human and mosquito populations are divided into susceptible and infectious as these are the common compartments. Next, the movement of human and mosquito population are included as the intention is to find out if the diffusion in heterogeneous environment affects the spread of the infection. To derive the diffusion models, it is assumed that individuals' spatial dispersal can be described as random walks. This means that at large spatial scale, the group of dispersing humans and mosquitoes behave comparatively to a group of particles diffusing in Brownian motion (Cantrell & Cosner, 2003).

First of all, the random walk is assumed to take place on a straight line. An organism moves along a straight line in discrete time by jumping one step to the right or one step to the left. Normally the chances of going left or right is equal hence the probability of the organism going left or right is $\frac{1}{2}$. Next, temporal (time) step is indicated as Δt and spatial step as Δx . Let $p(x, t)$ denote the number of organism at location x at time t . After a time step Δt , the organisms which were at x has now moved to the left, $x - \Delta x$ or the right, $x + \Delta x$. In addition, half of those which were at $x - \Delta x$ and half of those which were at $x + \Delta x$ have moved to x . Hence, the number of organism at location x , at time $t + \Delta t$ is described by the equation

$$p(x, t + \Delta t) = \frac{1}{2} p(x - \Delta x, t) + \frac{1}{2} p(x + \Delta x, t). \quad (3.1)$$

Using Taylor's expansion of the function $p(x, t)$ the following is derived:

$$p(x, t + \Delta t) = p(x, t) + \frac{\partial p}{\partial t}(x, t)\Delta t + \frac{1}{2} \frac{\partial^2 p}{\partial t^2}(x, t)(\Delta t)^2 + \dots, \quad (3.2)$$

$$\frac{1}{2} p(x - \Delta x, t) = \frac{1}{2} p(x, t) + \frac{1}{2} \frac{\partial p}{\partial x}(x, t)(-\Delta x) + \frac{1}{4} \frac{\partial^2 p}{\partial x^2}(x, t)(-\Delta x)^2 + \dots, \quad (3.3)$$

$$\frac{1}{2} p(x + \Delta x, t) = \frac{1}{2} p(x, t) + \frac{1}{2} \frac{\partial p}{\partial x}(x, t)(\Delta x) + \frac{1}{4} \frac{\partial^2 p}{\partial x^2}(x, t)(\Delta x)^2 + \dots, \quad (3.4)$$

and by plugging (3.2), (3.3) and (3.4) into (3.1),

$$\frac{\partial p}{\partial t}(x, t)\Delta t + \dots = \frac{1}{2} \frac{\partial^2 p}{\partial x^2}(x, t)(\Delta x)^2 + \dots \quad (3.5)$$

It is assumed that Δx and Δt are very small, hence the higher order terms in Taylor's expansion are smaller than the terms shown in equation (3.5). Furthermore, the equation (3.5) is divided by Δt , obtaining

$$\frac{\partial p}{\partial t}(x, t) = \frac{(\Delta x)^2}{2\Delta t} \frac{\partial^2 p}{\partial x^2}(x, t) + \dots \quad (3.6)$$

$$\text{Assuming that } \Delta x \rightarrow 0, \Delta t \rightarrow 0, \text{ then } \frac{(\Delta x)^2}{2\Delta t} \rightarrow D. \quad (3.7)$$

Replacing the limits in equation (3.7) in equation (3.6) gives $\frac{\partial p}{\partial t}(x, t) = D \frac{\partial^2 p}{\partial x^2}(x, t)$, the diffusion equation where D is the diffusion rate.

The human population is divided into susceptible (S_H) and infectious (I_H) where time, t and location, x . The spatial density of susceptible and infectious human populations are $S_H(t, x)$ and $I_H(t, x)$. It is assumed that the density of total human population, $N_H = S_H + I_H$, follows the logistic population growth law thus

$$\frac{\partial N_H(t, x)}{\partial t} = D_H \frac{\partial^2 N_H(t, x)}{\partial x^2} + B_H N_H(t, x) \left[1 - \frac{N_H(t, x)}{K(x)} \right] \quad (3.8)$$

In logistic growth, a population's per capita growth rate gets smaller and smaller as the population size approaches a maximum value which is imposed by limited resources in

the environment and that is known as the carrying capacity. $D_H \frac{\partial^2 N_H(t, x)}{\partial t^2}$ depicts the diffusion of total human population across the environment. D_H is the diffusion coefficient which is the rate of movement of human population, $K(x)$ the carrying capacity and B_H is the natural growth rate. As the equation is subject to Neumann boundary, biologically it is assumed that $N_H(t, x) = H(x), \forall t > 0$, thus the total human density stabilizes at $H(x)$ (Lou & Zhao, 2011). The mosquito population is also divided into two compartments, namely susceptible (S_M) and infectious (I_M). The density of total mosquito population is $N_M = S_M + I_M$.

There are a few notable differences between the initial generic model and Lou and Zhao's (2011) model. The first difference is that, in this model, there is a susceptible human (S_H) compartment. Infectious human (I_H) recovers from the disease and become susceptible once more. In addition, it is assumed that infectious human and mosquito first contracted the illness before the latent period at the same location, where else Lou and Zhao (2011) considered nonlocal cases. This means that they considered cases acquired from a different location. As mosquito is the main vector of mosquito-borne diseases, the channel of transfer of infection is similar for all of these diseases. Biting rate of mosquito, β is assumed to be constant in this initial generic model however, it is location dependent, ie. $\beta(x)$ in Lou and Zhao's (2011). The differential equations for the initial generic model

are formulated according to the Balance Law where $\left\{ \begin{matrix} net & rate \\ of & change \end{matrix} \right\} = \left\{ \begin{matrix} rate \\ in \end{matrix} \right\} - \left\{ \begin{matrix} rate \\ out \end{matrix} \right\}$. (3.9)

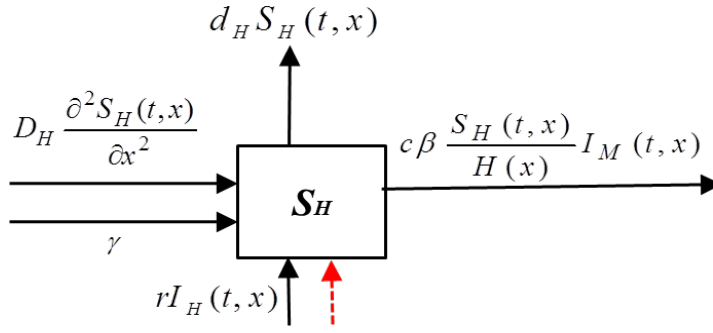


Figure 3.1: Schematic diagram of susceptible human (S_H) compartment

As mentioned earlier, individuals' spatial movement are considered as random walk like Brownian motion. In Figure 3.1, the diffusion of susceptible human population through environment is described by the term $D_H \frac{\partial^2 S_H}{\partial x^2}$. This depicts the aspect of movement coming from symmetric random displacements. D_H represents the speed of spatial diffusion, that is mean square distance covered per unit time. $\frac{\partial^2 S_H}{\partial x^2}$ is the change in the rate of change in the density of susceptible human population in the x direction. New recruitment of susceptible human is through birth and immigration at rate γ per unit time. Next, those who are infectious recover from the disease and return to susceptible class at the constant rate r per unit time. The duration of infectious period is $1/r$ time.

A susceptible human can get infected if bitten by an infectious mosquito. The average number of mosquito bites which causes transmission of disease from infectious mosquito to susceptible human is the product of c , the transmission probability per bite from infectious mosquito (I_M) to susceptible human (S_H) and β , the biting rate of mosquitoes meaning the number of bites per unit time per mosquito density. The aim here

is that we would like to obtain the parameter in a constant per density (human) form. Next, $c\beta$ is multiplied with $\left(\frac{I_M}{N_M}\right)$ which is the probability that mosquitoes are infectious.

Therefore it becomes $c\beta\left(\frac{I_M(t,x)}{N_M(t,x)}\right)$ meaning the average number of mosquito bites

which causes transmission of disease from infectious mosquito to susceptible human per

mosquito density. From there, $c\beta\left(\frac{I_M(t,x)}{N_M(t,x)}\right)$ is multiplied with $\frac{N_M(t,x)}{H(x)}$ which is, the

ratio of mosquito to human, resulting in the average number of mosquito bites which

causes transmission of disease from infectious mosquito to human per human density. The

force of infection is the rate at which new infections emerge per susceptible density. For

this model, the force of infection is $c\beta\left(\frac{I_M(t,x)}{H(x)}\right)$. Therefore we have

$c\beta\left(\frac{I_M(t,x)}{H(x)}\right)S_H(t,x)$ which gives us the density of susceptible human getting bitten by

infectious mosquitoes and acquiring the disease. Thus, the density of new cases is

$c\beta\frac{S_H(t,x)}{H(x)}I_M(t,x)$. Susceptible individuals die a natural death at rate d_H . This death is of

natural mortality and not dependent on the disease. The lifespan of a human is $1/d_H$ time.

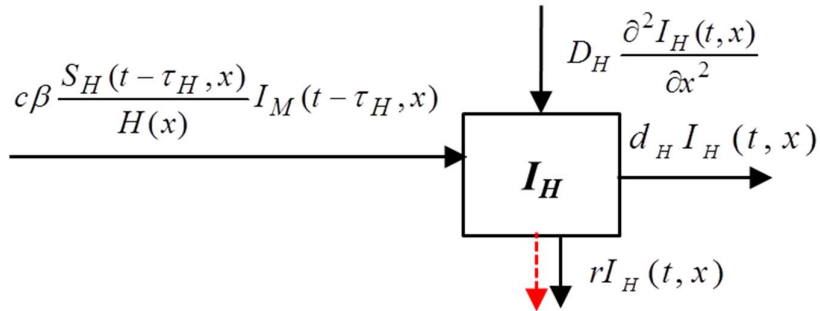


Figure 3.2: Schematic diagram of infectious human (I_H) compartment

When a susceptible human got bitten by an infectious mosquito, the individual will acquire the disease making them infected. Initially, pathogen is too scarce in the human body for him or her to transmit the disease to susceptible mosquitoes. After a latent period τ_H , the individual will be able to transmit the disease meaning they are infectious. It is considered that infectious cases are initiated when an infectious mosquito takes a blood meal from a susceptible human before the human latent period, $t - \tau_H$. The multiplication of the average number of bites which allows transmission, $c\beta$ and the probability of available infectious mosquitoes before the latent period, $\left(\frac{I_M(t - \tau_H, x)}{N_M(t - \tau_H, x)} \right)$ results in $c\beta \left(\frac{I_M(t - \tau_H, x)}{N_M(t - \tau_H, x)} \right)$. This is the average number of mosquito bites that causes the spread of the disease to susceptible humans per mosquito density. Next, $c\beta \left(\frac{I_M(t - \tau_H, x)}{N_M(t - \tau_H, x)} \right)$ is multiplied by $\frac{N_M(t - \tau_H, x)}{H(x)}$, the ratio of mosquito to human population before latent period, obtaining the average number of mosquito bites which causes transmission of disease from mosquito to human per human density. Therefore $c\beta \left(\frac{I_M(t - \tau_H, x)}{H(x)} \right) S_H(t - \tau_H, x)$ means the density of susceptible human who acquired malaria. Density of new infectious human cases is $c\beta \frac{S_H(t - \tau_H, x)}{H(x)} I_M(t - \tau_H, x)$ as shown in Figure 3.2. Infectious humans move randomly at the rate of $D_H \frac{\partial^2 I_H}{\partial x^2}$. For simplicity, those who are infectious are not assumed to be with reduced mobility or quarantined. This means that those who are sick are presumed to be able to move just as much as those who are healthy. Those who have

recovered become susceptible again at rate r per unit time. Similar to the susceptible pool, infectious individuals succumb to natural mortality at rate d_H per unit time.

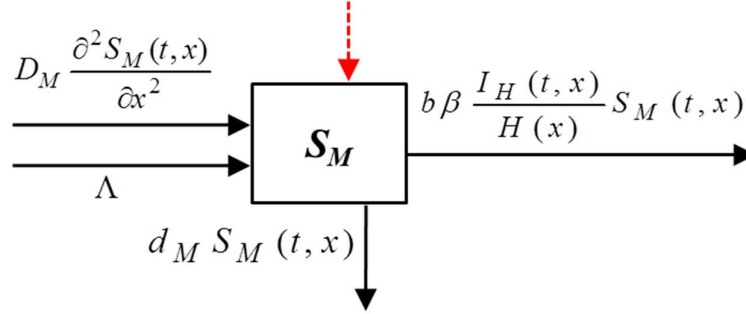


Figure 3.3: Schematic diagram of susceptible mosquito (S_M) compartment

New admission of susceptible mosquito is by birth at rate Λ . Susceptible mosquitoes are assumed to diffuse through environment randomly at $D_M \frac{\partial^2 S_M}{\partial x^2}$ as depicted in Figure 3.3.

D_M is the diffusion coefficient for mosquito population. Susceptible mosquitoes that consumed pathogen in blood meal will acquire the infection at rate $b\beta \frac{I_H(t,x)}{H(x)}$.

Multiplying b , the transmission probability per bite from infectious human (I_H) to susceptible mosquito (S_M) with β , is the number of bites per unit time which transmit the disease from I_H to S_M per mosquito density. Subsequently, the product of $b\beta$ and $\frac{I_H(t,x)}{H(x)}$, probability of human is infectious, gives the average number of bites which

causes transmission of disease from infectious human to susceptible mosquito per mosquito density. New density of infectious cases for mosquito population is

$b\beta \frac{I_H(t,x)}{H(x)} S_M(t,x)$. The lifespan of mosquitoes is $1/d_M$ time hence mosquitoes

naturally die at rate d_M per unit time.

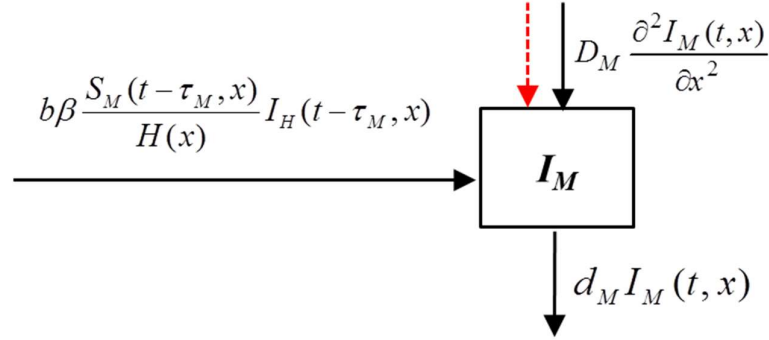


Figure 3.4: Schematic diagram of infectious mosquito (I_M) compartment

In Figure 3.4, the movement of infectious mosquitoes are assumed to be constant and at the same rate as susceptible mosquitoes. For the infectious mosquito compartment, susceptible mosquito acquire the disease by taking blood meal on infectious human and became infected when it ingests the pathogen. However, it cannot transmit the infection yet as the concentration of the pathogen is too low. The mosquito only becomes infectious after a latent period, τ_M . Similar to that of infectious human, it is assumed that a mosquito is exposed to the infection before the mosquito latent period, $t - \tau_M$.

$b\beta \left(\frac{I_H(t - \tau_M, x)}{H(x)} \right) S_M(t - \tau_M, x)$ is the density of new infectious mosquitoes. Infectious

mosquitoes die at the same rate as those which are susceptible at rate d_M .

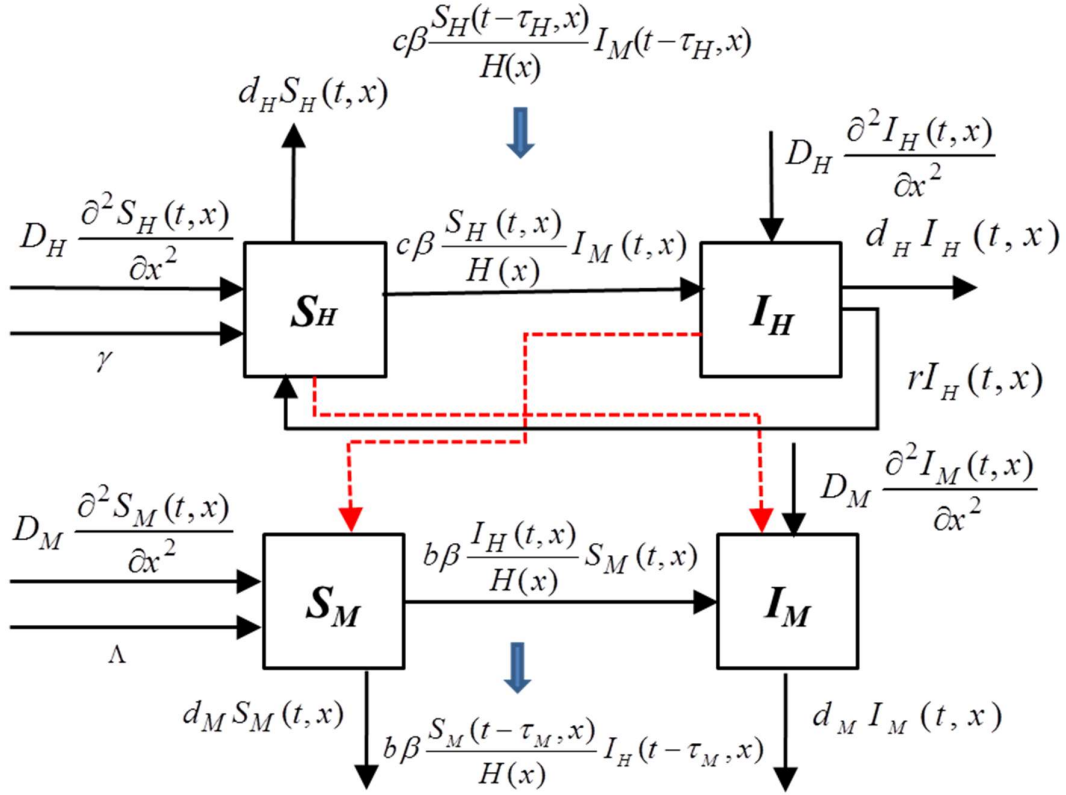


Figure 3.5: The integrated initial generic reaction-diffusion model for mosquito-borne diseases.

Combining all the compartments (Figures 3.1-3.4) discussed, the compartmental model in Figure 3.5 is attained. The system of partial differential equations is as follows:

$$\frac{\partial S_H(t, x)}{\partial t} = D_H \frac{\partial^2 S_H(t, x)}{\partial x^2} + \gamma - \frac{c\beta}{H(x)} S_H(t, x) I_M(t, x) + r I_H - d_H S_H(t, x) \quad (3.10)$$

$$\frac{\partial I_H(t, x)}{\partial t} = D_H \frac{\partial^2 I_H(t, x)}{\partial x^2} + \frac{c\beta}{H(x)} S_H(t - \tau_H, x) I_M(t - \tau_H, x) - (d_H + r) I_H(t, x) \quad (3.11)$$

$$\frac{\partial S_M(t, x)}{\partial t} = D_M \frac{\partial^2 S_M(t, x)}{\partial x^2} + \Lambda - \frac{b\beta}{H(x)} S_M(t, x) I_H(t, x) - d_M S_M(t, x) \quad (3.12)$$

$$\frac{\partial I_M(t, x)}{\partial t} = D_M \frac{\partial^2 I_M(t, x)}{\partial x^2} - d_M I_M(t, x) + \frac{b\beta}{H(x)} S_M(t - \tau_M, x) I_H(t - \tau_M, x). \quad (3.13)$$

The Neumann boundary condition on domain Ω which is the spatial habitat with boundary $\partial\Omega$ where $\mathbf{n}$ denotes the exterior normal to $\partial\Omega$:

$$\frac{\partial S_H}{\partial \mathbf{n}} = \frac{\partial I_H}{\partial \mathbf{n}} = \frac{\partial S_M}{\partial \mathbf{n}} = \frac{\partial I_M}{\partial \mathbf{n}} = 0, t > 0, x \in \partial\Omega. \quad (3.14)$$

The boundary condition is called a no flux or reflecting boundary condition because individuals do not leave, they are reflected back into Ω .

The parameters (non-negative) for the system of partial differential equations above are as shown in Table 3.1.

Table 3.1: Parameters for the Initial Model

Parameter	Definition	Unit (Example)
diffusion rate for humans, D_H	Describes the random spread of humans across space/environment. Diffusivity of the population, and is a measurement of how efficiently individuals disperse toward lower densities (Trewenack, 2008). For 1D, the movement will be either left or right, randomly. Diffusion: net movement of a substance from region of high concentration to region of low concentration.	$\text{km}^2 \cdot \text{day}^{-1}$
diffusion rate for mosquitoes, D_M	Similar to above.	$\text{km}^2 \cdot \text{day}^{-1}$
human recruitment rate, γ	Admission of susceptible human via birth and immigration-constant rate.	day^{-1}
transmission probability per bite from $I_M \rightarrow S_H$, c	The likelihood that the disease transmit from infectious mosquito to susceptible human when a mosquito takes blood meal.	NIL

Table 3.1 continued

human death rate, d_H	The ratio of total deaths to total population in a specified community or area per time. (usually is given per 1000 population: crude death rate)	day^{-1}
mosquito recruitment rate, Λ	Admission of susceptible mosquitoes via birth.	day^{-1}
transmission probability per bite from $I_H \rightarrow S_M$, b	The likelihood that the disease transmit from infectious human to susceptible mosquito when a mosquito takes blood meal.	NIL
mosquito death rate, d_M	The ratio of total death to total population in a specified community or area per time.	day^{-1}
latent period in humans, τ_H	The time from susceptible human gets infected to becoming infectious.	days
latent period in mosquitoes, τ_M	The time from susceptible mosquito gets infected to becoming infectious.	days
biting rate of mosquitoes on humans, β	The number of bites by a mosquito per unit time	day^{-1}

3.2 Methodology for Numerical Analysis and Validation

In determining the ability of the initial generic model to produce results for different mosquito-borne diseases, simulation results from this model will be compared with the results from models for malaria and dengue, taken from literature. In cases where any parameter value is unavailable, it would be determined upon obtaining the best fit curve in comparison with the numerical results from literature. If the initial generic model is found to be unable to produce results which are in agreement with literature, the model will be refined. The refined model's simulations would then be compared once more with literature. Only when all results are found to be in good agreement with literature, the

generic model would have been established. Subsequently, to validate the generic model, the reliability of the generic model to reproduce actual prevalence of a few mosquito-borne diseases by comparing the generic model's simulation results with actual cases in different locations is carried out. Further explanation is as follows.

Firstly, the governing equations of the initial generic model for transmission of mosquito-borne diseases are nonlinear therefore they need to be solved numerically. The differential equations are discretized and solved using explicit finite difference and Crank Nicolson method as described in Section 3.3. Using the initial data and parameter values from literature, results for infectious human and mosquito population from the initial generic model and literature are compared. In this study, comparison is done with Lou and Zhao's malaria model (2011). Since the objective of this study is to develop a generic model, it is essential to examine if the current model can reproduce results of a different mosquito-borne disease model from literature. Hence, for this particular reason, the next step is to compare the results from the initial generic model with a spatio-temporal model for dengue (Wang & Zhao, 2011). If the results are not in good agreement, the initial generic model would be refined and then comparison will start again from the first literature. However, if results are in good agreement, comparison of simulations with results from temporal mosquito-borne diseases models (ordinary differential equations models) will be explored next.

The diffusion rates for both human and mosquito population are set to zero. This step will cause the second derivative to be eliminated. In order to preserve simplicity of the model, all parameter values are assumed to be constant and spatial heterogeneity is not considered. Hence, this would automatically transform the set of partial

differentialequations to ordinary differential equations changing the spatio-temporal model to a temporal model. Comparison of the results from the temporal generic model with literature is investigated next. Since that in this study a generic model is to be developed, the intention is to find out if the temporal model is able to reproduce simulation results for more than one mosquito-borne diseases. Two mosquito-borne diseases are investigated here namely dengue and malaria (Esteva & Vargas, 1998, Chitnis, 2005) as discussed in Section 4.2. If the generic model is unable to reproduce temporal model's result, the generic model is further refined. Nevertheless, when the generic model manages to generate simulations which are complementary to the few chosen literature, the next step is validation.

The validation steps of the generic model are shown in Figure 3.6. In the beginning, the actual cases in identified locations are collected. The prevalence of a mosquito-borne disease can be calculated by adding new cases, taking into account the number of days a person is in the infectious state. Prevalence means the number of people who has this disease at a given time. This method where actual cases are preprocessed is described by Teoh (2016). Comparison will be done for the temporal generic model first, therefore diffusion rate is set to zero. Initial data for human population of a certain location is obtained from Statistics Department. The initial data for mosquito population is difficult to acquire therefore the best estimate which fits the actual prevalence would be chosen. Parameter values are collected according to the different locations studied and stated in Chapter 5.

The system is solved and comparison between simulations and actual prevalence for each location carried out. Subsequently, the spatial factor is incorporated. To obtain the

initial value for infectious human population, first of all, the actual prevalence is divided by the area of a location. This enables the density of infectious cases of each location to be calculated. Next, since this model considers one dimensional environment, the distance between two locations can be calculated by taking into account the coordinates at geographic coordinate system. This is represented by latitude and longitude, thus the distance (usually in kilometres) between the locations can be computed. The locations, for example are denoted as $(x_0 = 0, x_1, x_2, x_3, \dots, x_n = u), u \in \mathbb{R}^+, n \in \mathbb{Z}^+$ meaning the starting point is $x = 0$ and the next point is $x = x_1$, therefore the distance between these two locations is x_1 km. Next, using the geographic coordinate system, if it is calculated that the distance between x_1 and x_2 is a km, then $x_2 = x_1 + a$ km. This is repeated until all the locations are obtained. Curve fitting is carried out by determining the best mathematical function that fits population density versus location data points $(x_0 = 0, x_1, x_2, x_3, \dots, x_n = u)$. This function is the initial data for infectious human population. If the curve is a poor fit, interpolation of the data points can be used as the initial data. This is then utilised as the initial data for infectious human.

The same steps are repeated for susceptible humans. However, for mosquito population, there is no actual data available thus the value will be estimated from comparison of the best fit result with actual cases. Parameter values are taken from statistical data and literature. Parameter values for human are taken from population data. Diffusion rate is estimated, as the actual speed of random movement of human and mosquito per square area per time, is difficult to determine. Therefore, the values are decided by finding the best fit result to the actual prevalence. These steps are repeated for another chosen mosquito-borne disease. In cases where the actual prevalence of a specific mosquito-borne diseases fluctuates, the best fit curve for the actual cases will be obtained.

The reason is because the reaction-diffusion generic model depicts the mean trend of a disease, therefore it is unable to depict fluctuation. However, it provides the average behavior of the spread of disease and ignore stochastic events. Taking this reason into account, it is apt to compare the generic model's simulation with the general behavior of the actual spread of the disease.

For validation purpose of this study, simulated cases from the temporal and spatio-temporal generic model are compared with actual prevalence for three mosquito-borne diseases, that is, malaria, dengue and Zika virus. Firstly, notified malaria cases in four districts in Sarawak, namely Kapit, Song, Belaga and Marudi from week 39 in 2012 to week 22 in 2013 are taken from reports in Sarawak Weekly Epid News by Sarawak State Health Department (Sarawak Health Department, 2012). Secondly, dengue prevalence in Kuching, Sibu, Bintulu and Miri from week 39 in 2012 to week 9 in 2015 are extracted from the same report. Lastly, actual Zika virus cases are provided from a research discussion with Artificial Intelligence in Medical Epidemiology (AIME) (research engagement, September 7, 2016). The temporal generic model's simulation is compared with Zika virus prevalence in Rio de Janeiro, Brazil from week 52 in 2015 to week 24 in 2016. For spatio-temporal generic model, comparison is against prevalence from four different neighborhoods namely Guaratiba, Santa Cruz, Campo Grande and Bangu from week 52 in 2015 to week 24 in 2016.

3.3 Model Implementation

The reaction-diffusion model which consists of equations (3.10)-(3.13) is solved numerically to study the spread of mosquito-borne diseases. One of the most popular

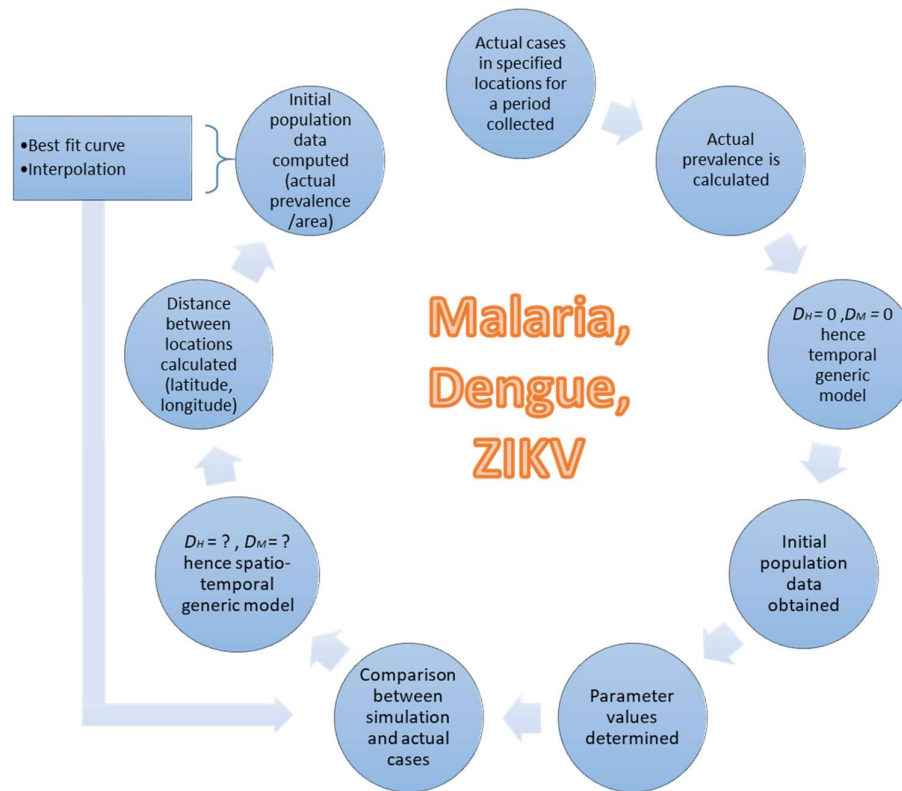


Figure 3.6: Methodology for Validation of the Generic Model

numerical techniques for solving partial differential equations are finite difference methods.

In this section, two numerical methods are examined to decide the best method for the generic model. The two methods used are explicit and Crank Nicolson scheme. In the explicit scheme, population at time $j + 1$ depends on the population at time j . At time t_n , forward difference is used, and space derivative at position x_i , a second-order central

difference. Therefore after discretization, equation (3.10) is $\frac{S_{H_i}^{j+1} - S_{H_i}^j}{\Delta t} = D_H \left(\frac{S_{H_{i+1}}^j - 2S_{H_i}^j + S_{H_{i-1}}^j}{(\Delta x)^2} \right) + \gamma - \frac{c\beta}{H} S_{H_i}^j I_{M_i}^j + r I_{H_i}^j - d_H S_{H_i}^j$. This can be rearranged with the

quantities on time $j+1$ on the left hand side and quantities on time j on the right hand side:

$$S_{H_i}^{j+1} = \Delta t \left(D_H \left(\frac{S_{H_{i+1}}^j - 2S_{H_i}^j + S_{H_{i-1}}^j}{(\Delta x)^2} \right) + \gamma - \frac{c\beta}{H} S_{H_i}^j I_{M_i}^j + r I_{H_i}^j - d_H S_{H_i}^j \right) + S_{H_i}^j. \quad (3.15)$$

$S_{H_i}^{j+1}$ can be computed since $S_{H_{i+1}}^j, S_{H_i}^j, S_{H_{i-1}}^j, I_{H_i}^j$ and $I_{M_i}^j$ are known. Using the same method, equations (3.11)-(3.13) become:

$$I_{H_i}^{j+1} = \Delta t \left(D_H \left(\frac{I_{H_{i+1}}^j - 2I_{H_i}^j + I_{H_{i-1}}^j}{(\Delta x)^2} \right) + \frac{c\beta}{H} S_{H_i}^j I_{M_i}^j - r I_{H_i}^j - d_H I_{H_i}^j \right) + I_{H_i}^j \quad (3.16)$$

$$S_{M_i}^{j+1} = \Delta t \left(D_M \left(\frac{S_{M_{i+1}}^j - 2S_{M_i}^j + S_{M_{i-1}}^j}{(\Delta x)^2} \right) + \lambda - \frac{b\beta}{H} S_{M_i}^j I_{H_i}^j - d_M S_{M_i}^j \right) + S_{M_i}^j \quad (3.17)$$

and

$$I_{M_i}^{j+1} = \Delta t \left(D_M \left(\frac{I_{M_{i+1}}^j - 2I_{M_i}^j + I_{M_{i-1}}^j}{(\Delta x)^2} \right) - \frac{b\beta}{H} S_{M_i}^j I_{H_i}^j - d_M I_{M_i}^j \right) + I_{M_i}^j. \quad (3.18)$$

Numerical results from this model will be compared with Lou and Zhao's (2011) model to determine whether this initial generic model is able to reproduce their results. Initial values

are taken from (Lou & Zhao, 2011) except for susceptible human (S_H) as there is no such compartment in their model:

$$I_H(x, \phi) = 20 - \cos 2x, S_M(x, \phi) = 140 - 5 \cos 2x, I_M(x, \phi) = 19 - 2 \cos 2x \text{ and } S_H(x, \phi) = 8 - \cos 2x, \forall \phi \in [-\tau_H, 0], x \in [0, \pi].$$

Consider Neumann boundary condition where

$$\frac{\partial S_H(0, t)}{\partial x} = 0, \frac{\partial I_H(0, t)}{\partial x} = 0, \frac{\partial S_M(0, t)}{\partial x} = 0, \frac{\partial I_M(0, t)}{\partial x} = 0, \text{ and } \frac{\partial S_H(\pi, t)}{\partial x} = 0, \frac{\partial I_H(\pi, t)}{\partial x} = 0$$

$$\frac{\partial S_M(\pi, t)}{\partial x} = 0, \frac{\partial I_M(\pi, t)}{\partial x} = 0.$$

To find the value at the corresponding boundaries, using Neumann boundary condition, central finite difference approximation is applied at $x=0$, that is $i=0$, therefore

$$\frac{\partial S_H(0, t)}{\partial x} = \frac{S_{H2}^j - S_{H0}^j}{2\Delta x} = 0, \frac{\partial I_H(0, t)}{\partial x} = \frac{I_{H2}^j - I_{H0}^j}{2\Delta x} = 0, \frac{\partial S_M(0, t)}{\partial x} = \frac{S_{M2}^j - S_{M0}^j}{2\Delta x} = 0,$$

and $\frac{\partial I_M(0, t)}{\partial x} = \frac{I_{M2}^j - I_{M0}^j}{2\Delta x} = 0$.

$$\frac{\partial S_H(0, t)}{\partial x} = \frac{S_{H2}^{j+1} - S_{H0}^{j+1}}{2\Delta x} = 0, \frac{\partial I_H(0, t)}{\partial x} = \frac{I_{H2}^{j+1} - I_{H0}^{j+1}}{2\Delta x} = 0,$$

$$\frac{\partial S_M(0, t)}{\partial x} = \frac{S_{M2}^{j+1} - S_{M0}^{j+1}}{2\Delta x} = 0 \text{ and } \frac{\partial I_M(0, t)}{\partial x} = \frac{I_{M2}^{j+1} - I_{M0}^{j+1}}{2\Delta x} = 0.$$

At $x=\pi$ that is $i=n$, the derivative is expanded about that point using the central

difference approximation again, thus $\frac{\partial S_H(\pi, t)}{\partial t} = \frac{S_{Hn+1}^j - S_{Hn-1}^j}{2\Delta t} = 0,$

$$\frac{\partial I_H(\pi, t)}{\partial t} = \frac{I_{H_{n+1}}^j - I_{H_{n-1}}^j}{2\Delta t} = 0, \frac{\partial S_M(\pi, t)}{\partial t} = \frac{S_{M_{n+1}}^j - S_{M_{n-1}}^j}{2\Delta t} = 0 \text{ and}$$

$$\frac{\partial I_M(0, t)}{\partial t} = \frac{I_{M_{n+1}}^j - I_{M_{n-1}}^j}{2\Delta t} = 0. \text{ In addition, } \frac{\partial S_H(\pi, t)}{\partial t} = \frac{S_{H_{n+1}}^{j+1} - S_{H_{n-1}}^{j+1}}{2\Delta t} = 0,$$

$$\frac{\partial I_H(\pi, t)}{\partial t} = \frac{I_{H_{n+1}}^{j+1} - I_{H_{n-1}}^{j+1}}{2\Delta t} = 0, \frac{\partial S_M(\pi, t)}{\partial t} = \frac{S_{M_{n+1}}^{j+1} - S_{M_{n-1}}^{j+1}}{2\Delta t} = 0$$

$$\text{and } \frac{\partial I_M(\pi, t)}{\partial t} = \frac{I_{M_{n+1}}^{j+1} - I_{M_{n-1}}^{j+1}}{2\Delta t} = 0.$$

This method is computationally fast however, for the result to be stable, $\frac{D_M \Delta t}{(\Delta x)^2} <$

0.5. Parameters used are shown in Table 3.2 and taken from Lou and Zhao (2011).

Table 3.2: Values of parameters used for comparison with Lou and Zhao (2011)

Parameter	Value
diffusion rate for humans, D_H	$1 \text{ km}^2 \cdot \text{day}^{-1}$
diffusion rate for mosquitoes, D_M	$1.25 \times 10^{-2} \text{ km}^2 \cdot \text{day}^{-1}$
human recruitment rate, γ	$1/(2.4 \times 10^3) \text{ day}^{-1}$ (Wang & Zhao, 2011)
transmission probability per bite from $I_M \rightarrow S_H$, c	5.0×10^{-1}
human death rate, d_H	$1/(2.56 \times 10^4) \text{ day}^{-1}$
recovery rate, r	$1.0 \times 10^{-2} \text{ day}^{-1}$
mosquito recruitment rate, Λ	20 day^{-1}
transmission probability per bite from $I_H \rightarrow S_M$, b	5.0×10^{-1}

Table 3.2 continued

mosquito death rate, d_M	$1.0 \times 10^{-1} \text{ day}^{-1}$
latent period in humans, τ_H	$1.0 \times 10^1 \text{ days}$
latent period in mosquitoes, τ_M	$1.0 \times 10^1 \text{ days}$
biting rate of mosquitoes on humans, β	$3.0 \times 10^{-1} \text{ day}^{-1}$

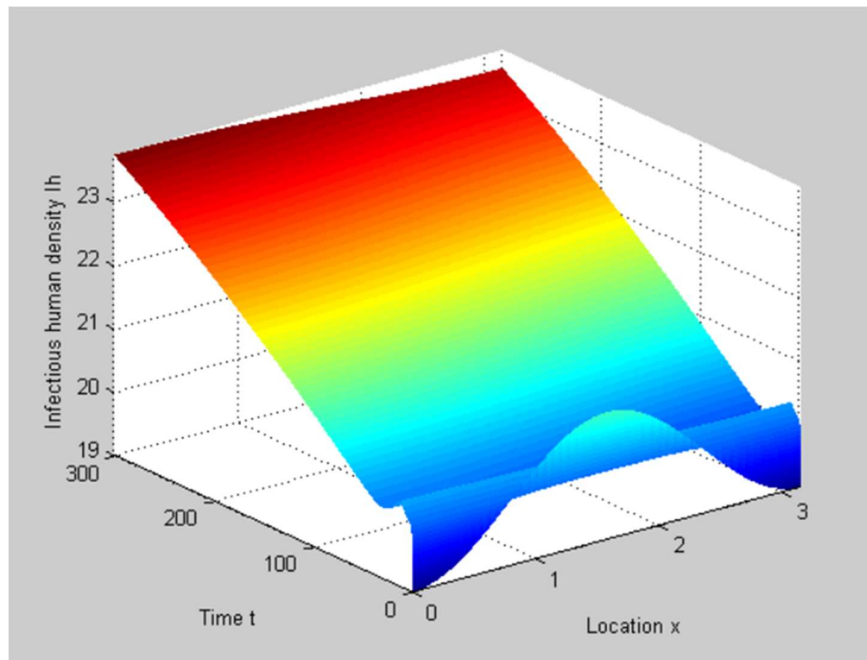


Figure 3.7: The density of infectious human (I_H) in time and space for the initial generic model using explicit finite difference scheme.

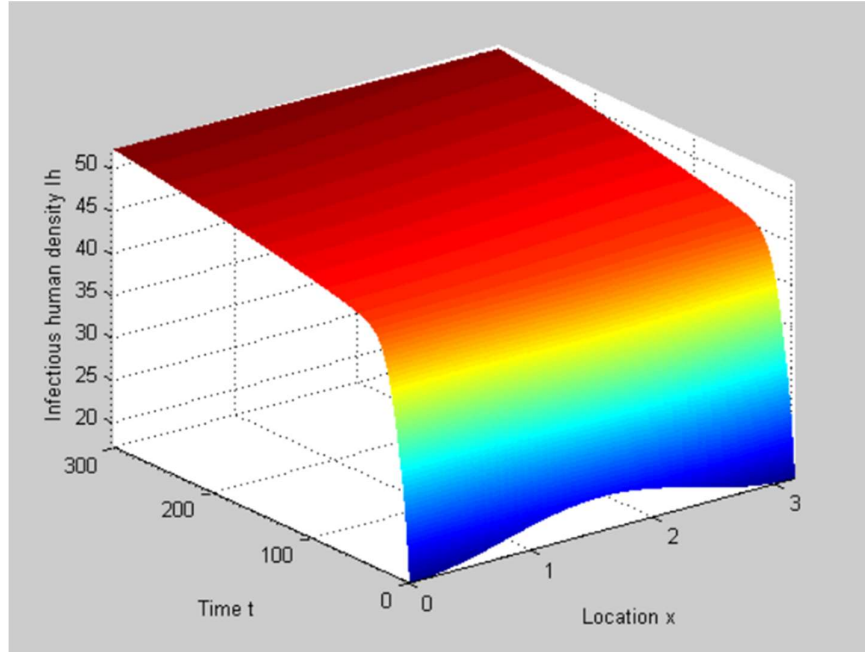


Figure 3.8: The density of infectious mosquito (I_M) in time and space for the initial generic model using explicit finite difference scheme.

It is shown in Figures 3.7 and 3.8 the simulations of the infectious human and mosquito density obtained using explicit finite difference method. The density of infectious human (I_H) increases to an average of 23.6 across locations by day 300. The behaviour of the spread differs from Lou and Zhao (2011) as it does not reach an equilibrium. For mosquito population, the result reaches an equilibrium from day 51 onwards. The behavior of the spread is similar to Lou and Zhao (2011) however, the magnitude is higher. This is most likely because infectious human who have recovered and returns to the susceptible state (S_H) is considered in this initial model.

Next, Crank Nicolson method is used as it is well known for being unconditionally stable for diffusion equations (Thomas, 1995). Firstly, for equation (3.10), the focus is at the point $(x_i, t^{j+\frac{1}{2}})$ using the centered difference approximation hence

$$\frac{\partial S_H(x_i, t^{j+\frac{1}{2}})}{\partial t} \approx \frac{S_H(x_i, t^{j+1}) - S_H(x_i, t^j)}{\Delta t}, \text{ which can be denoted as } \frac{S_{H_i}^{j+1} - S_{H_i}^j}{\Delta t}.$$

The term $\frac{\partial^2 S_H(x_i, t^{j+\frac{1}{2}})}{\partial x^2}$ is approximated using the average of the second centered differences for $\frac{\partial^2 S_H(x_i, t^{j+1})}{\partial x^2}$ and $\frac{\partial^2 S_H(x_i, t^j)}{\partial x^2}$.

Hence,

$$\frac{\partial^2 S_H(x_i, t^{j+\frac{1}{2}})}{\partial x^2} \approx \frac{1}{2} \left[\frac{S_H(x_{i+1}, t^{j+1}) - 2S_H(x_i, t^{j+1}) + S_H(x_{i-1}, t^{j+1})}{(\Delta x)^2} + \frac{S_H(x_{i+1}, t^j) - 2S_H(x_i, t^j) + S_H(x_{i-1}, t^j)}{(\Delta x)^2} \right]$$

which translates to

$$\frac{\partial^2 S_H(x_i, t^{j+\frac{1}{2}})}{\partial x^2} \approx \frac{1}{2(\Delta x)^2} (S_{H_i}^{j+1} - 2S_{H_i}^{j+1} + S_{H_{i-1}}^{j+1} + S_{H_{i+1}}^j - 2S_{H_i}^j + S_{H_{i-1}}^j).$$

Next, to discretize the equation for infectious human (3.11), $\frac{\partial I_H(x_i, t^{j+\frac{1}{2}})}{\partial t} \approx \frac{I_{H_i}^{j+1} - I_{H_i}^j}{\Delta t}$

$$\text{and } \frac{\partial^2 I_H(x_i, t^{j+\frac{1}{2}})}{\partial x^2} \approx \frac{1}{2(\Delta x)^2} (I_{H_i}^{j+1} - 2I_{H_i}^{j+1} + I_{H_{i-1}}^{j+1} + I_{H_{i+1}}^j - 2I_{H_i}^j + I_{H_{i-1}}^j).$$

In addition, to be substituted into equation (3.12) for susceptible and (3.13) infectious

mosquito respectively, $\frac{\partial S_M(x_i, t^{j+\frac{1}{2}})}{\partial t} \approx \frac{S_{M_i}^{j+1} - S_{M_i}^j}{\Delta t}$, $\frac{\partial I_M(x_i, t^{j+\frac{1}{2}})}{\partial t} \approx \frac{I_{M_i}^{j+1} - I_{M_i}^j}{\Delta t}$ and

$$\frac{\partial^2 I_M(x_i, t^{j+\frac{1}{2}})}{\partial x^2} \approx \frac{1}{2(\Delta x)^2} (I_{M_i}^{j+1} - 2I_{M_i}^{j+1} + I_{M_{i-1}}^{j+1} + I_{M_{i+1}}^j - 2I_{M_i}^j + I_{M_{i-1}}^j).$$

Applying these onto (3.10)–(3.13) will transform them to:

$$\begin{aligned} \frac{S_{H_i}^{j+1} - S_{H_i}^j}{\Delta t} = & D_H \frac{1}{2(\Delta x)^2} (S_{H_i}^{j+1} - 2S_{H_i}^{j+1} + S_{H_{i-1}}^{j+1} + S_{H_{i+1}}^j - 2S_{H_i}^j + S_{H_{i-1}}^j) + \gamma - \\ & \frac{c\beta}{H} \left(\frac{S_{H_i}^j + S_{H_i}^{j+1}}{2} \right) \left(\frac{I_{M_i}^j + I_{M_i}^{j+1}}{2} \right) - d_H \left(\frac{S_{H_i}^j + S_{H_i}^{j+1}}{2} \right) + r \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right) \end{aligned} \quad (3.19)$$

$$\begin{aligned} \frac{I_{H_i}^{j+1} - I_{H_i}^j}{\Delta t} = & D_H \frac{1}{2(\Delta x)^2} (I_{H_i}^{j+1} - 2I_{H_i}^{j+1} + I_{H_{i-1}}^{j+1} + I_{H_{i+1}}^j - 2I_{H_i}^j + I_{H_{i-1}}^j) + \\ & \frac{c\beta}{H} \left(\frac{S_{H_i}^j + S_{H_i}^{j+1}}{2} \right) \left(\frac{I_{M_i}^j + I_{M_i}^{j+1}}{2} \right) - d_H \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right) - r \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right) \end{aligned} \quad (3.20)$$

$$\begin{aligned} \frac{S_{M_i}^{j+1} - S_{M_i}^j}{\Delta t} = & D_M \frac{1}{2(\Delta x)^2} (S_{M_i}^{j+1} - 2S_{M_i}^{j+1} + S_{M_{i-1}}^{j+1} + S_{M_{i+1}}^j - 2S_{M_i}^j + S_{M_{i-1}}^j) + \Lambda - \\ & \frac{b\beta}{H} \left(\frac{S_{M_i}^j + S_{M_i}^{j+1}}{2} \right) \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right) - d_M \left(\frac{S_{M_i}^j + S_{M_i}^{j+1}}{2} \right) \end{aligned} \quad (3.21)$$

and

$$\begin{aligned}
\frac{I_{M_i}^{j+1} - I_{M_i}^j}{\Delta t} &= D_M \frac{1}{2(\Delta x)^2} (I_{M_i}^{j+1} - 2I_{M_i}^{j+1} + I_{M_{i-1}}^{j+1} + I_{M_{i+1}}^j - 2I_{M_i}^j + I_{M_{i-1}}^j) + \\
&\quad \frac{b\beta}{H} \left(\frac{S_{M_i}^j + S_{M_i}^{j+1}}{2} \right) \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right) - d_M \left(\frac{I_{M_i}^j + I_{M_i}^{j+1}}{2} \right).
\end{aligned} \tag{3.22}$$

Rearranging (3.19)– (3.22) yields:

$$\begin{aligned}
&S_{H_{i+1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) + S_{H_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{c\beta}{4H} (I_{M_i}^j + I_{M_i}^{j+1}) + \frac{d_H}{2} \right) + S_{H_{i-1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) = \\
&S_{H_{i+1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) + \gamma + S_{H_i}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{c\beta}{4H} (I_{M_i}^j + I_{M_i}^{j+1}) - \frac{d_H}{2} \right) + S_{H_{i-1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) \\
&+ r \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right),
\end{aligned} \tag{3.23}$$

$$\begin{aligned}
&I_{H_{i+1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) + I_{H_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right) + I_{H_{i-1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) = I_{H_{i+1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) + \\
&I_{H_i}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right) + I_{H_{i-1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) + \frac{c\beta}{H} \left(\frac{S_{H_i}^j + S_{H_i}^{j+1}}{2} \right) \left(\frac{I_{M_i}^j + I_{M_i}^{j+1}}{2} \right)
\end{aligned} \tag{3.24}$$

$$\begin{aligned}
&S_{M_{i+1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) + S_{M_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{b\beta}{4H} (I_{H_i}^j + I_{H_i}^{j+1}) + \frac{d_M}{2} \right) + S_{M_{i-1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) = \\
&S_{M_{i+1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right) + \Lambda + S_{M_i}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{b\beta}{4H} (I_{H_i}^j + I_{H_i}^{j+1}) - \frac{d_M}{2} \right) + S_{M_{i-1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right)
\end{aligned} \tag{3.25}$$

$$\begin{aligned}
& I_{M_{i+1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) + I_{M_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right) + I_{M_{i-1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) = I_{M_{i+1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right) + \\
& I_{M_i}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right) + I_{M_{i-1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right) + \frac{b\beta}{H} \left(\frac{S_{M_i}^j + S_{M_i}^{j+1}}{2} \right) \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right).
\end{aligned} \tag{3.26}$$

Applying Neumann boundary condition to the corresponding boundaries as mentioned in the explicit scheme, $S_{H_2}^j = S_{H_0}^j$ and $S_{H_2}^{j+1} = S_{H_0}^{j+1}$ and replacing these into equation (3.23) yields:

$$\begin{aligned}
& S_{H_2}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + S_{H_1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{c\beta}{4H} (I_{M_1}^j + I_{M_1}^{j+1}) + \frac{d_H}{2} \right) = S_{H_2}^j \left(\frac{D_H}{(\Delta x)^2} \right) + \gamma \\
& + S_{H_1}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{c\beta}{4H} (I_{M_1}^j + I_{M_1}^{j+1}) - \frac{d_H}{2} \right) + r \left(\frac{I_{H_1}^j + I_{H_1}^{j+1}}{2} \right).
\end{aligned} \tag{3.27}$$

Likewise, $I_{H_2}^j = I_{H_0}^j$ and $I_{H_2}^{j+1} = I_{H_0}^{j+1}$ are substituted into equation (3.24) hence:

$$\begin{aligned}
& I_{H_2}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + I_{H_1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right) = I_{H_2}^j \left(\frac{D_H}{(\Delta x)^2} \right) + I_{H_1}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right) \\
& + \frac{c\beta}{H} \left(\frac{S_{H_1}^j + S_{H_1}^{j+1}}{2} \right) \left(\frac{I_{M_1}^j + I_{M_1}^{j+1}}{2} \right).
\end{aligned} \tag{3.28}$$

The same technique is utilized on equations (3.25) and (3.26), where $S_{M_2}^j = S_{M_0}^j$,

$S_{M_2}^{j+1} = S_{M_0}^{j+1}$, $I_{M_2}^j = I_{M_0}^j$ and $I_{M_2}^{j+1} = I_{M_0}^{j+1}$, resulting in:

$$\begin{aligned}
& S_{M2}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + S_{M1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{b\beta}{4H} (I_{H1}^j + I_{H1}^{j+1}) + \frac{d_M}{2} \right) = S_{M2}^j \left(\frac{D_M}{(\Delta x)^2} \right) \\
& + \Lambda + S_{M1}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{b\beta}{4H} (I_{H1}^j + I_{H1}^{j+1}) - \frac{d_M}{2} \right)
\end{aligned} \tag{3.29}$$

$$\begin{aligned}
& I_{M2}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + I_{M1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right) = I_{M2}^j \left(\frac{D_M}{(\Delta x)^2} \right) + I_{M1}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right) \\
& + \frac{b\beta}{H} \left(\frac{S_{M1}^j + S_{M1}^{j+1}}{2} \right) \left(\frac{I_{H1}^j + I_{H1}^{j+1}}{2} \right).
\end{aligned} \tag{3.30}$$

As explained in the explicit scheme using central difference approximation,

$S_{Hn+1}^j = S_{Hn-1}^j$ and $S_{Hn+1}^{j+1} = S_{Hn-1}^{j+1}$ and plugging these into equation (3.23) begets:

$$\begin{aligned}
& S_{Hn-1}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + S_{Hn}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{c\beta}{4H} (I_{Mn}^j + I_{Mn}^{j+1}) + \frac{d_H}{2} \right) = S_{Hn-1}^j \left(\frac{D_H}{(\Delta x)^2} \right) + \gamma \\
& + S_{Hn}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{c\beta}{4H} (I_{Mn}^j + I_{Mn}^{j+1}) - \frac{d_H}{2} \right) + r \left(\frac{I_{Hn}^j + I_{Hn}^{j+1}}{2} \right).
\end{aligned} \tag{3.31}$$

In addition, $I_{Hn+1}^j = I_{Hn-1}^j$ and $I_{Hn+1}^{j+1} = I_{Hn-1}^{j+1}$ are replaced into equation (3.24):

$$\begin{aligned}
& I_{Hn-1}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + I_{Hn}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right) \\
& = I_{Hn-1}^j \left(\frac{D_H}{(\Delta x)^2} \right) + I_{Hn}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right) + \frac{c\beta}{H} \left(\frac{S_{Hn}^j + S_{Hn}^{j+1}}{2} \right) \left(\frac{I_{Mn}^j + I_{Mn}^{j+1}}{2} \right).
\end{aligned} \tag{3.32}$$

Similar method is applied on equations (3.25) and (3.26) where $S_{Mn+1}^j = S_{Mn-1}^j$,

$S_{Mn+1}^{j+1} = S_{Mn-1}^{j+1}$, $I_{Mn+1}^j = I_{Mn-1}^j$ and $I_{Mn+1}^{j+1} = I_{Mn-1}^{j+1}$, obtaining:

$$\begin{aligned}
& S_{M_{n-1}}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + S_{M_n}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{b\beta}{4H} (I_{H_n}^j + I_{H_n}^{j+1}) + \frac{d_M}{2} \right) = S_{M_{n-1}}^j \left(\frac{D_M}{(\Delta x)^2} \right) \\
& + \Lambda + S_{M_n}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{b\beta}{4H} (I_{H_n}^j + I_{H_n}^{j+1}) - \frac{d_M}{2} \right)
\end{aligned} \tag{3.33}$$

$$\begin{aligned}
& I_{M_{n-1}}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + I_{M_n}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right) = I_{M_{n-1}}^j \left(\frac{D_M}{(\Delta x)^2} \right) + I_{M_n}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right) \\
& + \frac{b\beta}{H} \left(\frac{S_{M_n}^j + S_{M_n}^{j+1}}{2} \right) \left(\frac{I_{H_n}^j + I_{H_n}^{j+1}}{2} \right).
\end{aligned} \tag{3.34}$$

Equations (3.23)-(3.34) form an algebraic system; hence the system is arranged in matrix form as done by Li and Zou (2009) to ease solving it. From this system,

$$A \begin{bmatrix} S_{H1}^{j+1} \\ S_{H2}^{j+1} \\ \vdots \\ S_{H_{n-1}}^{j+1} \\ S_{Hn}^{j+1} \end{bmatrix} = B \begin{bmatrix} S_{H1}^j \\ S_{H2}^j \\ \vdots \\ S_{H_{n-1}}^j \\ S_{Hn}^j \end{bmatrix} + \begin{bmatrix} \gamma \\ \gamma \\ \vdots \\ \gamma \\ \gamma \end{bmatrix} \tag{3.35}$$

$$C \begin{bmatrix} I_{H1}^{j+1} \\ I_{H2}^{j+1} \\ \vdots \\ I_{H_{n-1}}^{j+1} \\ I_{Hn}^{j+1} \end{bmatrix} = D \begin{bmatrix} I_{H1}^j \\ I_{H2}^j \\ \vdots \\ I_{H_{n-1}}^j \\ I_{Hn}^j \end{bmatrix} + \begin{bmatrix} \frac{c\beta}{H} \left(\frac{S_{H1}^j + S_{H1}^{j+1}}{2} \right) \left(\frac{I_{M1}^j + I_{M1}^{j+1}}{2} \right) \\ \frac{c\beta}{H} \left(\frac{S_{H2}^j + S_{H2}^{j+1}}{2} \right) \left(\frac{I_{M2}^j + I_{M2}^{j+1}}{2} \right) \\ \vdots \\ \frac{c\beta}{H} \left(\frac{S_{H_{n-1}}^j + S_{H_{n-1}}^{j+1}}{2} \right) \left(\frac{I_{M_{n-1}}^j + I_{M_{n-1}}^{j+1}}{2} \right) \\ \frac{c\beta}{H} \left(\frac{S_{Hn}^j + S_{Hn}^{j+1}}{2} \right) \left(\frac{I_{Mn}^j + I_{Mn}^{j+1}}{2} \right) \end{bmatrix} \tag{3.36}$$

$$E \begin{bmatrix} S_{M1}^{j+1} \\ S_{M2}^{j+1} \\ \vdots \\ S_{M_{n-1}}^{j+1} \\ S_{Mn}^{j+1} \end{bmatrix} = F \begin{bmatrix} S_{M1}^j \\ S_{M2}^j \\ \vdots \\ S_{M_{n-1}}^j \\ S_{Mn}^j \end{bmatrix} + \begin{bmatrix} \Lambda \\ \Lambda \\ \vdots \\ \Lambda \\ \Lambda \end{bmatrix} \quad (3.37)$$

$$G \begin{bmatrix} I_{M1}^{j+1} \\ I_{M2}^{j+1} \\ \vdots \\ I_{M_{n-1}}^{j+1} \\ I_{Mn}^{j+1} \end{bmatrix} = H \begin{bmatrix} I_{M1}^j \\ I_{M2}^j \\ \vdots \\ I_{M_{n-1}}^j \\ I_{Mn}^j \end{bmatrix} + \begin{bmatrix} \frac{b\beta}{H} \left(\frac{S_{M1}^j + S_{M1}^{j+1}}{2} \right) \left(\frac{I_{H1}^j + I_{H1}^{j+1}}{2} \right) \\ \frac{b\beta}{H} \left(\frac{S_{M2}^j + S_{M2}^{j+1}}{2} \right) \left(\frac{I_{H2}^j + I_{H2}^{j+1}}{2} \right) \\ \vdots \\ \frac{b\beta}{H} \left(\frac{S_{M_{n-1}}^j + S_{M_{n-1}}^{j+1}}{2} \right) \left(\frac{I_{H_{n-1}}^j + I_{H_{n-1}}^{j+1}}{2} \right) \\ \frac{b\beta}{H} \left(\frac{S_{Mn}^j + S_{Mn}^{j+1}}{2} \right) \left(\frac{I_{Hn}^j + I_{Hn}^{j+1}}{2} \right) \end{bmatrix} \quad (3.38)$$

$$\text{where } A = \begin{bmatrix} A1 & M1 & \cdots & 0 & 0 \\ M2 & A2 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & A(n-1) & M2 \\ 0 & 0 & \cdots & M1 & An \end{bmatrix}, \quad (3.39)$$

$$B = \begin{bmatrix} AA1 & N1 & \cdots & 0 & 0 \\ N2 & AA2 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & AA(n-1) & N2 \\ 0 & 0 & \cdots & N1 & AAn \end{bmatrix}, \quad (3.40)$$

$$C = \begin{bmatrix} M3 & M1 & \cdots & 0 & 0 \\ M2 & M3 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & M3 & M2 \\ 0 & 0 & \cdots & M1 & M3 \end{bmatrix}, \quad (3.41)$$

$$D = \begin{bmatrix} N3 & N1 & \cdots & 0 & 0 \\ N2 & N3 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & N3 & N2 \\ 0 & 0 & \cdots & N1 & N3 \end{bmatrix}, \quad (3.42)$$

$$E = \begin{bmatrix} M51 & M1 & \cdots & 0 & 0 \\ M2 & M52 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & M5(n-1) & M2 \\ 0 & 0 & \cdots & M1 & M5n \end{bmatrix}, \quad (3.43)$$

$$F = \begin{bmatrix} N51 & N1 & \cdots & 0 & 0 \\ N2 & N52 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & N5(n-1) & N2 \\ 0 & 0 & \cdots & N1 & N5n \end{bmatrix}, \quad (3.44)$$

$$G = \begin{bmatrix} M6 & M1 & \cdots & 0 & 0 \\ M2 & M6 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & M6 & M2 \\ 0 & 0 & \cdots & M1 & M6 \end{bmatrix}, \quad (3.45)$$

$$\text{and } H = \begin{bmatrix} N6 & N1 & \cdots & 0 & 0 \\ N2 & N6 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & N6 & N2 \\ 0 & 0 & \cdots & N1 & N6 \end{bmatrix}. \quad (3.46)$$

Furthermore, to add to the above,

$$Ai = \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{c\beta}{4H} (I_{M_i}^j + I_{M_i}^{j+1}) + \frac{d_H}{2} \right), \quad (3.47)$$

$$M1 = \left(\frac{-D_H}{(\Delta x)^2} \right), \quad (3.48)$$

$$M2 = \left(\frac{-D_H}{2(\Delta x)^2} \right), \quad (3.49)$$

$$M3 = \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right), \quad (3.50)$$

$$M5i = \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{b\beta}{4H} (I_{H_i}^j + I_{H_i}^{j+1}) + \frac{d_M}{2} \right). \quad (3.51)$$

$$M6 = \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right), \quad (3.52)$$

$$N6 = \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right), \quad (3.53)$$

$$N1 = \left(\frac{D_H}{(\Delta x)^2} \right), \quad (3.54)$$

$$N2 = \left(\frac{D_H}{2(\Delta x)^2} \right), \quad (3.55)$$

$$N3 = \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right), \quad (3.56)$$

$$AAi = \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{c\beta}{4H} (I_{M_i}^j + I_{M_i}^{j+1}) - \frac{d_H}{2} \right) \quad (3.57)$$

$$\text{and } N5i = \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{b\beta}{4H} (I_{Hi}^j + I_{Hi}^{j+1}) - \frac{d_M}{2} \right). \quad (3.58)$$

Equations (3.35)-(3.38) are solved simultaneously. Parameter values are shown in Table 3.2, except $(1/2400) \text{ day}^{-1}$ (Wang & Zhao, 2011). In addition, $\Delta x = \pi/50$ and $\Delta t = 0.1$ are used. The simulation result for this set of parameters and initial data can be seen in Figures 3.9 and 3.10. The density of both infectious human and mosquito increases and reaches a limiting value over time. Results across locations display similar behavior. These results reach an endemic equilibrium meaning the disease prevails in both the human and mosquito population in 300 days. The spread of infectious humans (I_H) in Figure 3.9 exhibits similar behavior and density to Lou and Zhao's (2011) Figure 1. Moreover, the result of the spread of infectious mosquitoes (I_M) in Figure 3.10 displays similar behavior as Lou and Zhao's (2011) Figure 1. However, the density of infectious mosquito (I_M) of the initial model is higher. Consequently, as no immunity is assumed, infectious humans are at risk of getting infected once more and they are capable of infecting susceptible mosquitoes, increasing density of infectious mosquito. However, Lou and Zhao (2011) did not consider this occurrence.

The results obtained from Crank Nicolson finite difference scheme shows that the solution to the generic model displays a much smoother increase in the infectious human density over time. Comparison of the results for both human and mosquito populations with Lou and Zhao (2011) revealed that the behavior of the spread by this generic model system is similar. In addition, comparing these results to explicit finite difference method demonstrated that the best method for the solution of the generic model is Crank Nicolson as this method does not produce stiff increment over the time and locations studied.

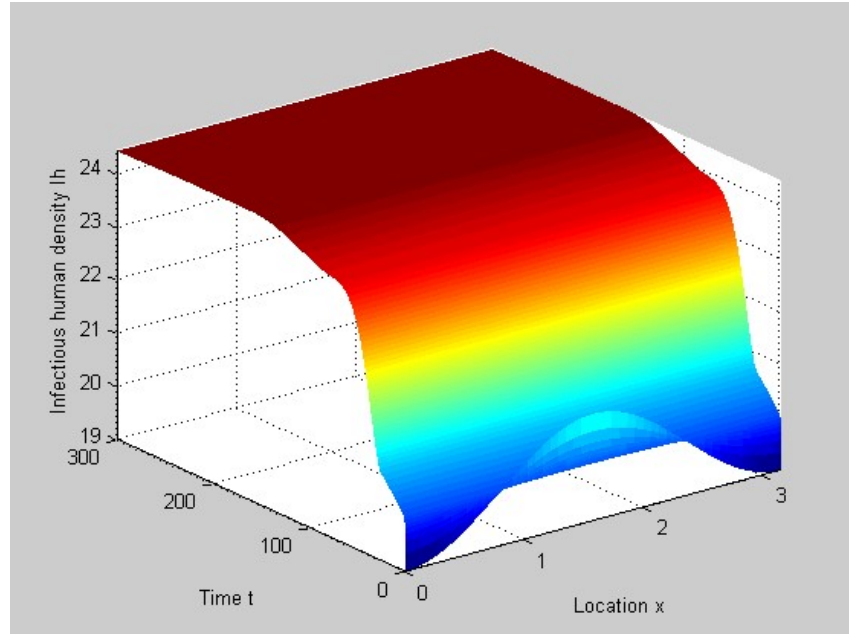


Figure 3.9: The density of infectious human (I_H) in time and space for the initial generic model using Crank Nicolson scheme.

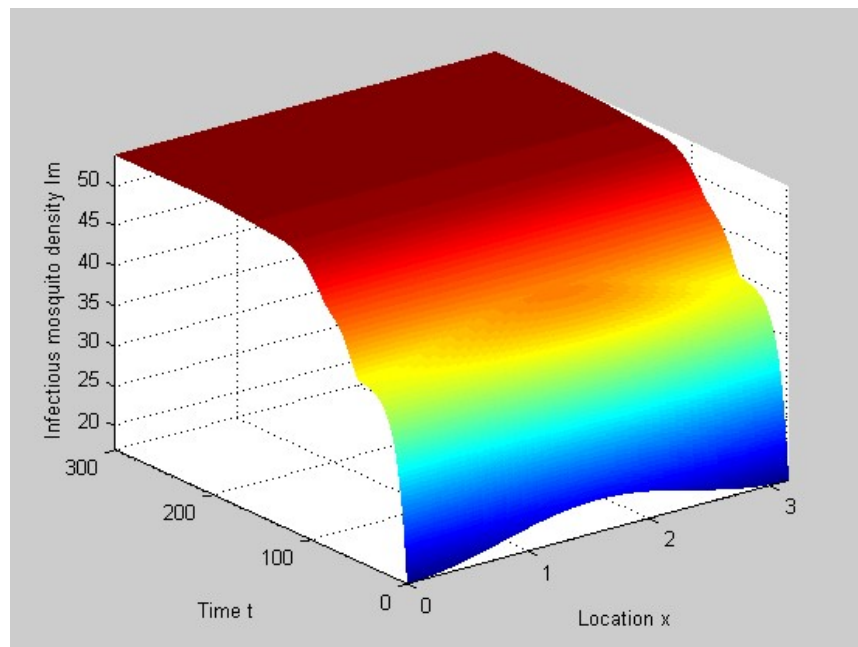


Figure 3.10: The density of infectious mosquito (I_M) in time and space for the initial generic model using Crank Nicolson scheme.

Another drawback of the explicit scheme is that there is strong restriction to the time step size and if the condition is not met, the solution will become unstable and oscillate. It is found that the time step needs to be reduced to obtain a stable solution. Therefore, from now onwards, Crank Nicolson method is used to solve the generic model.

3.4 Numerical Analysis of the Initial Model

The effect of spatial heterogeneity and human diffusion rate on the disease risk is explored next. Location dependent parameters such as $\beta(x) = 0.1(1.1 + \cos(2x))$ and $\Lambda(x) = 20(1.1 + \cos(2x))$ are adopted from Lou and Zhao (2011) to analyze the effect of spatial heterogeneity on the domain where the two ends are assumed as rural areas and the mid-point as urban. To calculate the implicit R_0 , the theory of basic reproduction numbers for reaction-diffusion epidemic models by Wang and Zhao (2012) as explained thoroughly in Section 4.1.5 is applied. The implicit basic reproduction number is found to be 3.663. Considering $\beta = 0.3$ and $\Lambda = 20$, the explicit basic reproduction number from the spatially averaged system, $R_0 = 2.185$. This discovery confirms the notion that spatially averaged system may undervalue the disease burden (Lou & Zhao, 2011).

Next, human diffusion D_H is varied from 0.5 to 1.5, to examine the effect on disease risk R_0 . As shown in Figure 3.11, the basic reproduction number R_0 decreases with the increment of human diffusion coefficient, meaning the number of secondary cases reduces with the rise of human mobility. This means that the upsurge in the random mobility of human population will cause the infection risk to decline. Hence, the higher the rate of humans' diffusion, the higher the possibility that eventually the disease will die out.

This observation was explored by Lou and Zhao (2011) and Wang and Zhao (2011) and their findings were complementary. The possible explanation to this is that mosquito-borne diseases are spread by mosquitoes. After taking a blood meal on an infectious human, the same mosquito has to then take a blood meal on a susceptible human therefore if both infectious and susceptible humans move at a higher rate, the chances of these bites to materialize will be less.

Following the study on the effect of spatial heterogeneity on R_0 by Lou and Zhao (2011), equation $H(x) = 100(1.1 - \delta \cos(2x))$ is set where $\delta \in [0,1]$. In this way, δ changes from 0 to 1, signifying the migration of human from rural to urban area. As δ increases, the basic reproduction number increases from 3.5 to around 7.5 which is slightly more than double as shown in Figure 3.12. Hence, this suggests that urbanization causes the disease risk to increase. If migration out of rural area can be controlled, the spread of the disease can be reduced significantly.

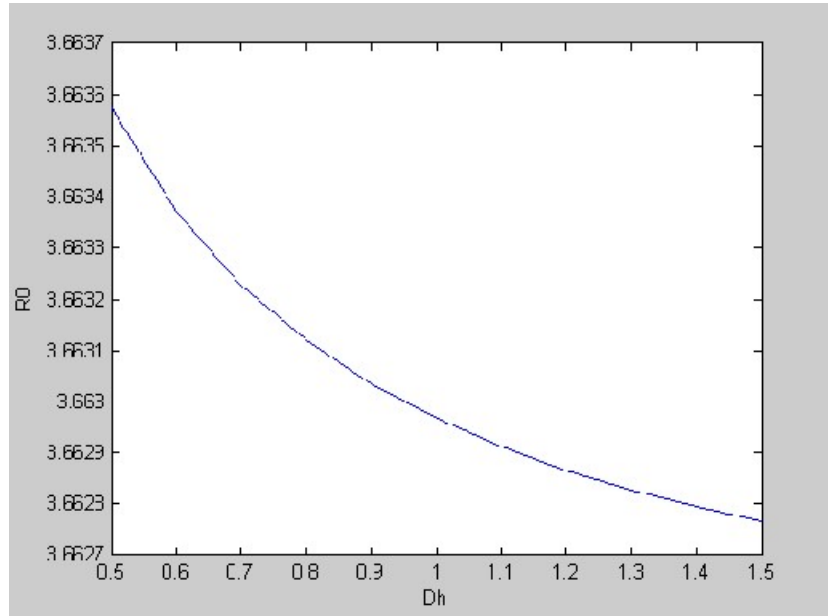


Figure 3.11: R_0 is an decreasing function of D_H

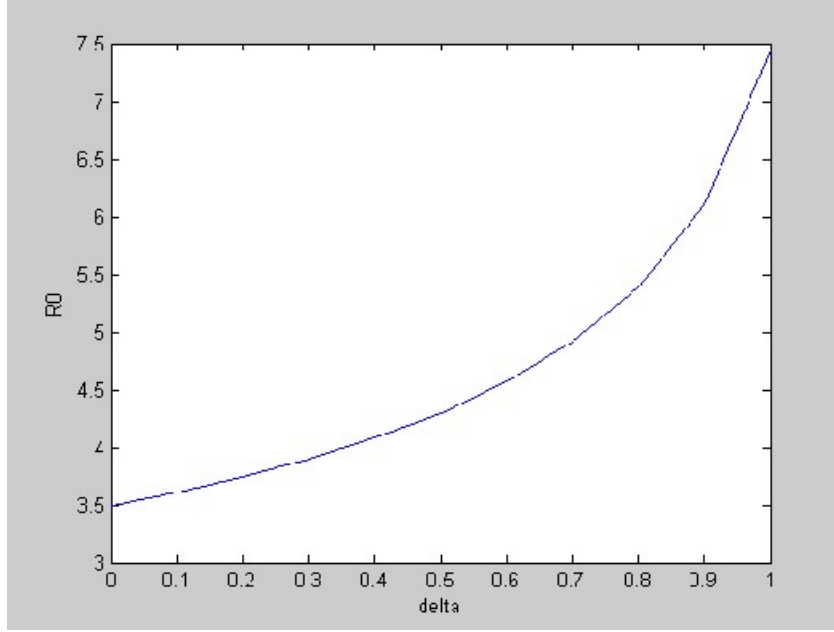


Figure 3.12: R_0 is an increasing function of δ

The initial generic model is capable of producing simulation results which corresponds to Lou and Zhao's (2011) malaria model. Subsequently, the next step is to examine whether it is capable of reproducing Wang and Zhao's (2011) dengue model's numerical results. Initial conditions and parameter values from Wang and Zhao (2011) are adopted to compare results. The initial data is:

$$S_H(\phi, x) = 0.03, I_H(\phi, x) = 0.22, S_M(\psi, x) = 1 \text{ and } I_M(\psi, x) = -2x + 2 \quad \forall \phi \in [-\tau_H, 0], \\ \psi \in [-\tau_M, 0], x \in [0, 1]$$

and parameter values are shown in Table 3.3 unless stated otherwise.

As shown in Figure 3.13, the behavior of the density of infectious human (I_H) is different from Wang and Zhao's Figure 1 (2011). The initial model's infectious human density decreases from $t = 0$ to $t = 10$ days and then increases from then onwards to time t

= 60 days. Results are the same across locations as parameters and initial data used are constant except for infectious mosquito density. The limiting value at time day $t = 60$ is the same as Wang and Zhao's (2011) but theirs increases from $t = 0$ to approximately $t = 10$ days before decreasing. The density of infectious mosquitoes (I_M) as depicted in Figure 3.14 displays a similar behavior and density to Wang and Zhao's (2011). On locations situated up to 0.7km from the origin, infectious mosquito density showed an initial decrement until day $t = 20$. After that, the density increases all the way till day 60. However, locations situated further than 0.7km the origin displayed an increment from day 0 to day 60. The comparison of differences in parameters and compartments used among the three models (initial, Lou and Zhao (2011) and Wang and Zhao (2011)) are shown in Table 3.4. Since the initial generic model is unable to display satisfactory result for infectious human density thus a refinement of the initial model will be carried out.

Table 3.3: Values of parameters used for comparison with Wang and Zhao (2011)

Parameter	Value
diffusion rate for humans, D_H	$1.0 \times 10^{-2} \text{ km}^2 \cdot \text{day}^{-1}$
diffusion rate for mosquitoes, D_M	$2.0 \times 10^{-2} \text{ km}^2 \cdot \text{day}^{-1}$
human recruitment rate, γ	$(1/(2.4 \times 10^3)) \text{ day}^{-1}$
transmission probability per bite from $I_M \rightarrow S_H$, c	7.5×10^{-1}
human death rate, d_H	$1/(2.4 \times 10^4) \text{ day}^{-1}$
recovery rate, r	$2.0 \times 10^{-2} \text{ day}^{-1}$
mosquito recruitment rate, Λ	$6.2 \times 10^{-1} \text{ day}^{-1}$ (best fit)

Table 3.3 continued

transmission probability per bite from $I_H \rightarrow S_M, b$	3.75×10^{-1}
mosquito death rate, d_M	$1/14 \text{ day}^{-1}$
latent period in humans, τ_H	5 days
latent period in mosquitoes, τ_M	1.0×10^1 days
biting rate of mosquitoes on humans, β	$3.0 \times 10^{-1} \text{ day}^{-1}$
Total human population, H	1.0×10^2

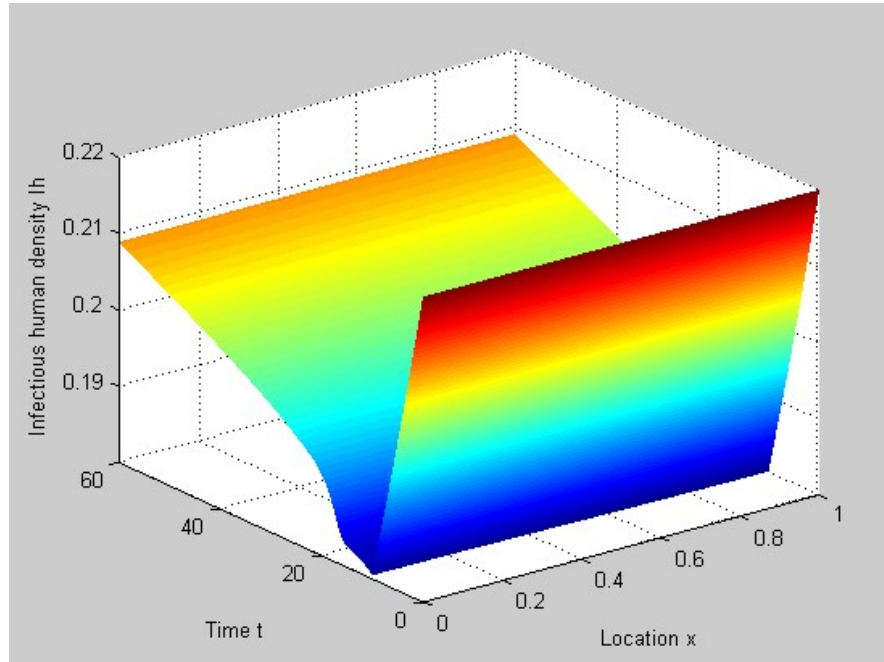


Figure 3.13: The density of infectious human (I_H) in time and space for the initial generic model using parameter values from Wang and Zhao (2011).

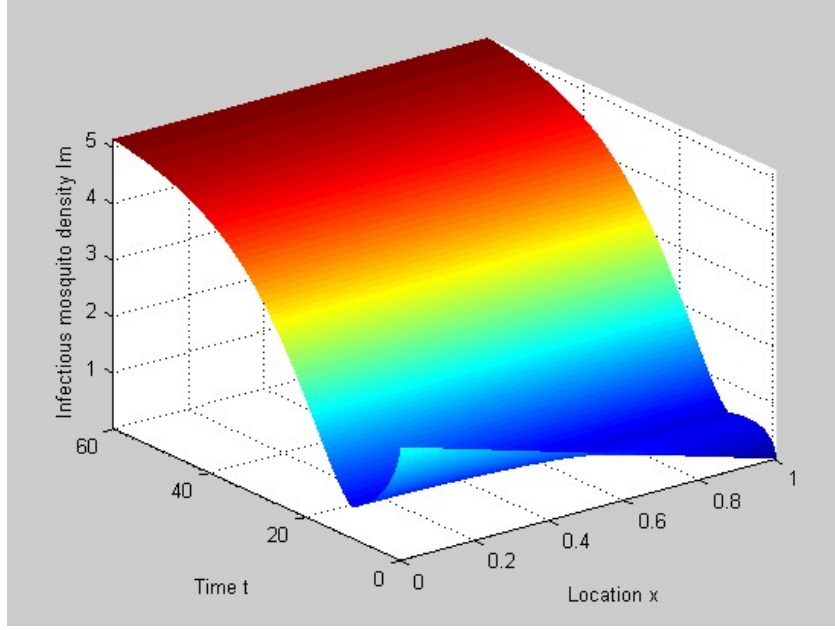


Figure 3.14: The density of infectious mosquito (I_M) in time and space for the initial generic model using parameter values from Wang and Zhao (2011).

3.5 Formulation of the Generic Model

Refinement of the initial model is to be implemented. Immunity and superinfection are excluded as the model is designed to be applicable to most mosquito-borne diseases and the main focus is the commonality in the transmission of these diseases. The compartments for both population remain in the refinement of the initial model. The spatial density of susceptible and infectious human populations are $S_H(t, x)$ and $I_H(t, x)$. In addition, $S_M(t, x)$ and $I_M(t, x)$ are the spatial density of susceptible and infectious mosquito respectively. It was previously assumed that $N_H(t, x) = H(x), \forall t > 0$, thus the total human density stabilizes at $H(x)$ which was assumed to be constant for all x in the simulations. However, in the generic model, the total human population is the sum of susceptible and infectious humans, $N_H = S_H + I_H$. Furthermore, total mosquito density is $N_M = S_M + I_M$.

The total human and mosquito density at any point x and time t are thus $N_H(t, x)$ and $N_M(t, x)$ respectively.

Adopting Wang and Zhao's (2011) work, the biting rate of mosquitoes on humans were considered to be density dependent on N_H , hence β is replaced with $\frac{gN_H}{1 + g\lambda N_H}$.

These are special cases of Holling type II functional response (Castillo-Chavez, Velasco-Hernandez & Fridman, 1994) where it follows the assumption that the consumer is limited by its capacity to process food. The new parameters introduced here are: g , the searching rate of a mosquito, meaning the rate at which a mosquito encounters a human per unit of human density and λ , is the time taken for a mosquito to complete a blood meal for each bite taken. For the type II response, the rate of consumption of blood meal rises as the human density increases, however, it will reach a plateau at which the biting rate stays constant even if the human density grows. This is because the higher the human density, the lower the proportion of human being bitten by a mosquito. So if there are a lot of humans available, the time spent on searching for human is reduced while the available time spent on taking a blood meal increases hence the proportion reaches a maximum when all available time is spent taking blood meal, limiting the number of humans the mosquito can bite, causing a plateau.

Since comparison of results from the generic model and Wang and Zhao's (2011) is to be carried out, some notable differences between them are discussed here. Firstly, Wang and Zhao (2011) considered SEIR (Susceptible-Exposed-Infectious-Recovered) for human population where the recovered state is included, thus immunity is acknowledged to last for a defined duration before waning and the individual returned to being susceptible again.

The exposed class is the state where the individuals are infected but the pathogen count is too low for active transmission to a susceptible mosquito. For mosquito population, the SEI (Susceptible-Exposed-Infectious) model takes into account the incubation period and the recovered class is not added because mosquitoes do not recover from the disease. On the other hand, the generic model consists of only susceptible and infectious compartments for both human and mosquito population. To maintain simplicity, the current generic model assumes that the infectious individuals transmit the disease to susceptible individuals in the same location. This is different from Wang and Zhao (2011) where they considered nonlocal transmission. The diffusion rates for infectious and susceptible classes for both human and mosquito population are considered the same in the generic model. However, Wang and Zhao (2011) considered the speed of random movement of susceptible and infectious as different as they presume those who are ill move less. Lastly, disease-induced deaths are not taken into account in the generic model but on the contrary included by Wang and Zhao (2011).

As shown in Figure 3.15, the partial differential equation for susceptible human (S_H) in equation (3.7) is thus changed to:

$$\frac{\partial S_H(t, x)}{\partial t} = D_H \frac{\partial^2 S_H(t, x)}{\partial x^2} + \gamma - c \frac{g N_H(t, x)}{1 + g \lambda N_H(t, x)} \frac{I_M(t, x)}{N_H(t, x)} S_H(t, x) + r I_H - d_H S_H(t, x). \quad (3.59)$$

Next, equation (3.8) for infectious human (I_H) is now replaced with:

$$\frac{\partial I_H(t, x)}{\partial t} = D_H \frac{\partial^2 I_H(t, x)}{\partial x^2} + c \frac{g N_H(t - \tau_H, x)}{1 + g \lambda N_H(t - \tau_H, x)} \frac{I_M(t - \tau_M, x)}{N_H(t - \tau_H, x)} S_H(t - \tau_H, x) - (d_H + r) I_H(t, x), \quad (3.60)$$

while equation (3.9) for susceptible mosquito (S_M) now becomes

$$\frac{\partial S_M(t, x)}{\partial t} = D_M \frac{\partial^2 S_M(t, x)}{\partial x^2} + \Lambda - b \frac{g N_H(t, x)}{1 + g \lambda N_H(t, x)} \frac{I_H(t, x)}{N_H(t, x)} S_M(t, x) - d_M S_M(t, x), \quad (3.61)$$

and lastly, equation (3.10) that governs the rate of change of the infectious mosquito

(I_M) over time is now

$$\frac{\partial I_M(t, x)}{\partial t} = D_M \frac{\partial^2 I_M(t, x)}{\partial x^2} - d_M I_M(t, x) + b \frac{g N_H(t - \tau_M)}{1 + g \lambda N_H(t - \tau_M)} \frac{I_H(t - \tau_H, x)}{N_H(t - \tau_M)} S_M(t - \tau_M, x). \quad (3.62)$$

Neumann boundary condition is imposed on the system of equations (3.59-3.62) hence the domain Ω which is the spatial habitat with the boundary $\partial\Omega$ where $\mathbf{n}$ denotes the exterior normal to $\partial\Omega$:

$$\frac{\partial S_H}{\partial \mathbf{n}} = \frac{\partial I_H}{\partial \mathbf{n}} = \frac{\partial S_M}{\partial \mathbf{n}} = \frac{\partial I_M}{\partial \mathbf{n}} = 0, t > 0, x \in \partial\Omega. \quad (3.63)$$

3.6 Discussion

A generic SI (susceptible-infectious) mosquito-borne diseases model based on reaction-diffusion equations is presented in this chapter. Spatial component has been added to consider the spread of the disease in the environment which is continuous. Considering the dynamics of the transmission of mosquito-borne diseases, a single model which is applicable for multiple mosquito-borne diseases had been formulated. The development of this initial model is illustrated in this chapter. The system of partial differential equations is solved using explicit finite difference and Crank Nicolson method. Numerical simulations from the initial generic spatio-temporal model and Lou and Zhao (2011) model are compared. It is found that the infectious human (I_H) density is complementary to literature. Moreover, the effect of random movement of human on the spread of the disease has been

investigated numerically and it is shown that the hike in diffusion rate causes the infection risk to dwindle. Thus, the faster human diffuses through space, the lower the spread of the mosquito-borne disease. Also, it is recognized that urbanization contributes to increment in disease risk. These findings coincide with Lou and Zhao's (2011) numerical results. Nonetheless, the initial generic model is incapable of reproducing Wang and Zhao's (2011) simulation for infectious human (I_H) thus refinement is performed and the generic model is presented.

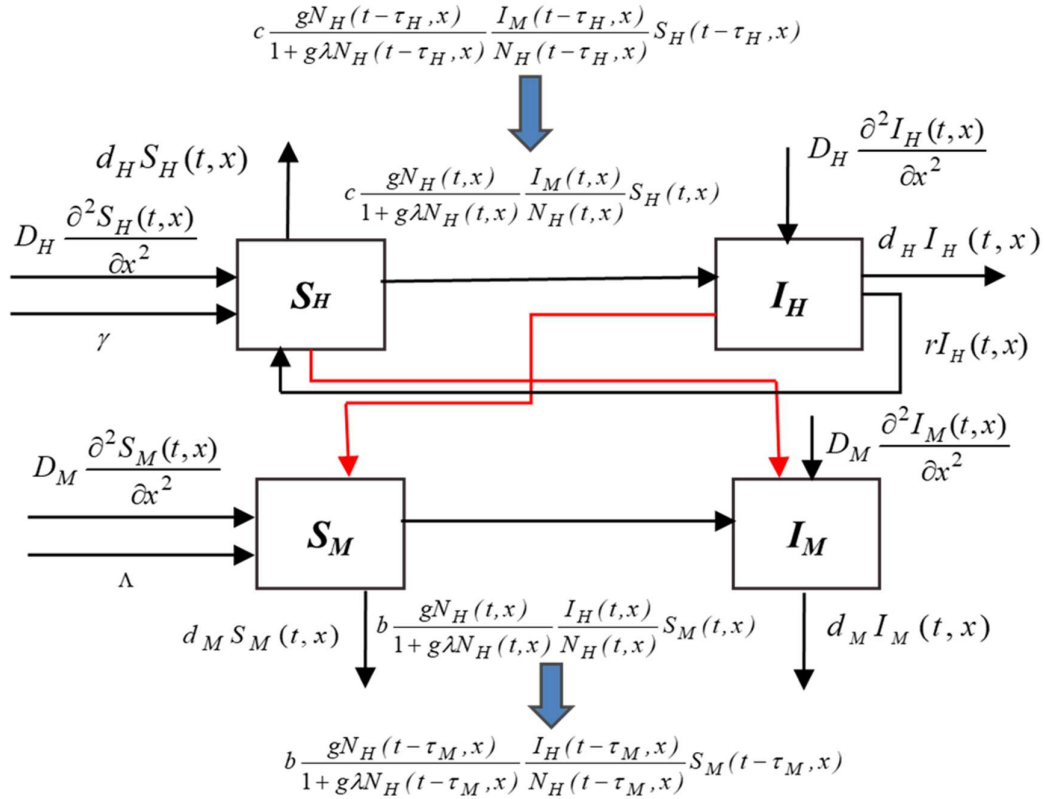


Figure 3.15: The compartmental model for the reaction-diffusion system of equations (3.59)-(3.62).

Table 3.4: Comparison among initial generic model, Lou & Zhao (2011) and Wang & Zhao (2011).

	Initial model	Lou & Zhao (2011)	Wang & Zhao (2011)
1. Compartments	S_H, I_H, S_M, I_M	I_H, S_M, I_M	$S_H, E_H, I_H, R_H, S_M, E_M, I_M$ (R : Recovered)
2. Recruitment rate for S_H	γ (constant)	None (as no S_H compartment)	constant
3. Transmission rate for I_M	$\frac{b\beta S_M(t-\tau_m, x)I_H(t-\tau_m, x)}{H}$ does not include infection age	Consider the movement of latent individuals thus inclusive infection age	Consider the movement of latent individuals thus inclusive infection age
4. Transmission rate for I_H	$\frac{c\beta S_H(t-\tau, x)I_M(t-\tau, x)}{H}$	Similar to initial model except $S_H = H(x) - I_H$	Consider the movement of latent individuals thus inclusive infection age
5. Recruitment rate for S_M	μ (constant)	$\mu(x)$	logistic growth, fecundity considered
6. Biting rate	β (constant)	$\beta(x)$ includes location	$\frac{bN_H}{1 + mN_H}$ where m is bh and h is time for mosquito to complete a blood meal.
7. Disease-induced deaths	none	none	For both $\frac{I_m}{I_h}$ (constant)
8. Recovery rate	r (from $I_H \rightarrow S_H$)	rate out from I_M	Constant (from $I_H \rightarrow R_H$)
9. Diffusion rate for humans	Same for susceptible and infectious	Same for susceptible and infectious	Infectious humans mobility rate is lower

Parameters and symbols used are in Table 3.1 unless explained in Table 3.4.

CHAPTER 4

THEORETICAL AND NUMERICAL ANALYSIS OF THE GENERIC MODEL

4.0 Introduction

In Chapter 3, the governing equations and parameters of the initial model for transmission of multiple mosquito-borne diseases were discussed. Numerical results from the initial model were agreeable with Lou and Zhao (2011) but unfortunately found to be dissimilar from Wang and Zhao (2011). This comparison is significant because the difference led to the refinement hence the formulation of the generic model. The refinement carried out is that the biting rate of mosquitoes which was constant in the initial model, is now altered to be density dependent on human population. The generic model is analyzed theoretically and numerically in this chapter. In addition, the traveling wave solution which connects the disease-free equilibrium and endemic equilibrium for the generic model is studied. The effect of human mobility and spatial heterogeneity on the transmission of the disease is numerically explored.

4.1 Theoretical Analysis of the Generic Model

The basic properties of the generic model (3.59)-(3.62) are considered in this section. The basic reproduction number, R_0 is the threshold value where when $R_0 > 1$, a disease will invade a population, otherwise, the disease will die out. Moreover, the stability of the disease-free and endemic equilibrium for this generic model is studied.

4.1.1 Krein-Rutman Theorem

Krein-Rutman theorem plays a vital role in the analysis of nonlinear partial differential equations. It serves as a foundation for the proof of existence of principal eigenvalues which can be instrumental in the study of the stability of solutions.

Let X be a Banach space. By a cone $K \subset X$ means a closed convex set such that $\lambda K \subset K$ for all $\lambda \geq 0$ and $K \cap (-K) = \{0\}$. Let X^* denote the dual space of X and the set $K^* := \{l \in X^* : l(x) \geq 0 \forall x \in K\}$ is called the dual cone of K . It is easily seen that K^* is closed and convex, and $\lambda K^* \subset K^*$ for any $\lambda \geq 0$. If a cone has nonempty interior K^0 , then it is called a solid cone.

According to the theorem:

Let X be a Banach space, $K \subset X$ a total cone and $T : X \rightarrow X$ a compact linear operator that is positive with positive spectral radius $r(T)$. $r(T)$ is an eigenvalue with an eigenvector $u \in K \setminus \{0\} : Tu = r(T)u$. Furthermore, $r(T^*) = r(T)$ is an eigenvalue of T^* with an eigenvector $u^* \in K^*$.

Furthermore, this theorem can be used to derive the following theorem.

Let X be a Banach space $K \subset X$ a solid cone, $T : X \rightarrow X$ a compact linear operator which is strongly positive, ie. $Tu \geq 0$ if $u > 0$. Therefore

(i) $r(T) > 0$ and $r(T)$ is a simple eigenvalue with an eigenvector $v \in K^0$, there is no other eigenvalue with a positive eigenvector.

(ii) $|\lambda| < r(T)$ for all eigenvalues $\lambda \neq r(T)$.

Since that r is a simple eigenvalue of T if there exists $v \neq 0$ such that $Tv = rv$ and $(rI - T)^n w = 0$ for some $n \geq 1$ indicates $w \in \text{span}\{v\}$.

4.1.2 The Principal Eigenvalue

The standard (matrix) eigenvalue problem is to determine real or complex numbers, $\lambda_1, \lambda_2, \dots, \lambda_n$ (eigenvalues) and corresponding nonzero vectors, $x_1, x_2, \dots, x_n$ (eigenvectors) that satisfy the equation $Ax = \lambda x$ where A is a given real or complex $n \times n$ matrix. The principal eigenvalue is the largest eigenvalue. It is a basic notion associated with an elliptic operator.

For example, the study of semi-linear elliptic problems in bounded domains often involves the principal eigenvalue of an associated linear operator. The existence of principal eigenvalue was discussed by Wang and Zhao (2012) by establishing sufficient conditions where the spectral bound of the associated operator is a geometrically simple eigenvalue with a positive eigenvector. Assuming there exists a number $d_0 > 0$ and integer $1 < i_1 < k$ so

that $d_i(x) \geq d_0 \forall x \in \Omega$, $1 \leq i \leq i_1$ and $d_{i+1}(x) = 0 \forall x \in \Omega$, $1 < i < i_2 := k - i_1$. Let $Y_1 = C(\overline{\Omega}, \mathbb{R}^{i_1})$ and $Y_2 = C(\overline{\Omega}, \mathbb{R}^{i_2})$. Splitting the cooperative matrix $M(x)$ into

$M(x) = \begin{pmatrix} M_{11}(x) & M_{12}(x) \\ M_{21}(x) & M_{22}(x) \end{pmatrix}$, where M_{11} is a $i_1 \times i_1$ matrix and M_{22} is a $i_2 \times i_2$ matrix. Setting

$$u_{i1} = (u_1, \dots, u_{i1})^T, u_{i2} = (u_{i1+1}, \dots, u_k)^T, \nabla \cdot (d_{i1}(x) \nabla u_{i1}) = \text{diag}(\nabla \cdot (d_1(x) \nabla u_1), \dots, \nabla \cdot (d_{i1}(x) \nabla u_{i1})).$$

Let $Q(t)$ be the solution semigroup on X associated with the linear parabolic system:

$$\frac{\partial u_{i1}}{\partial t} = \nabla \cdot (d_{i1}(x) \nabla u_{i1}) + M_{11}(x) u_{i1} + M_{12}(x) u_{i2}, \quad t > 0, x \in \Omega,$$

$$\begin{aligned}\frac{\partial \mathbf{u}_{i2}}{\partial t} &= M_{21}(x)\mathbf{u}_{i1} + M_{22}(x)\mathbf{u}_{i2}, \quad t > 0, x \in \Omega, \\ \frac{\partial \mathbf{u}_{i1}}{\partial \nu} &= 0, \quad t > 0, x \in \partial\Omega.\end{aligned}$$

It follows that $Q(t)$ is a positive C_0 -semigroup on X and its generator B can be written as

$$B = \begin{pmatrix} L_1 + M_{11} & M_{12} \\ M_{21} & M_{22} \end{pmatrix}, \quad \text{where } L_1(\mathbf{u}_{i1})(x) := \nabla \cdot (\mathbf{d}_{i1}(x) \nabla \mathbf{u}_{i1}).$$

Note that B is a closed and resolvent positive operator. Let $T_2(t)\phi_2(x) = e^{M_{22}(x)t}\phi_2(x)$ therefore $T_2(t)$ is a positive C_0 -semigroup on Y_2 and its generator M_{22} is resolvent-positive. It follows that

$$(\lambda I - M_{22})^{-1}\phi_2 = \int_0^\infty e^{-\lambda t} T_2(t)\phi_2 dt \quad \forall \lambda > s(M_{22}), \phi_2 \in Y_2.$$

Thus, a one-parameter family of linear operators is defined: $\mathcal{L}_\lambda = L_1 + M_{11} + M_{12}(\lambda I - M_{22})^{-1}M_{21} \quad \forall \lambda > s(M_{22})$.

Setting $\mathbf{u}_K = (u_1, \dots, u_k)^T$, $\nabla \cdot (d_K(x) \nabla \mathbf{u}_K) = \text{diag}(\nabla \cdot (d_1(x) \nabla u_1), \dots, \nabla \cdot (d_k(x) \nabla u_k))$ and considering all these hold, another theorem was presented by Wang and Zhao (2012):

$M(x)$ is cooperative for all $\forall x \in \overline{\Omega}$, for any $\lambda > s(M_{22})$, there exists some $x_\lambda \in \Omega$ such that $M_{11}(x_\lambda) + M_{12}(\lambda I - M_{22})^{-1}M_{21}(x_\lambda)$ is irreducible. If there exists $\lambda_0 > s(M_{22})$ and $\phi_0 > 0$ in Y_1 such that $\mathcal{L}_{\lambda_0}\phi_0 \geq \lambda_0\phi_0$, then the following statements are valid:

(i) $s(B)$ is a geometrically simple eigenvalue of the following elliptic eigenvalue problem:

$$\begin{aligned}\nabla \cdot (d_K(x) \nabla u_K) + M(x)u_K &= \lambda u_K, \quad x \in \Omega, \\ \frac{\partial u_i}{\partial \nu} &= 0 \quad \forall 1 \leq i \leq k \quad \text{with } d_i > 0, \quad x \in \partial\Omega\end{aligned}$$

with a positive eigenvector.

(ii) $s(B)$ is the unique $\lambda \in (s(M_{22}), \infty)$ with $s(\mathcal{L}_\lambda) = \lambda$.

(iii) $s(B)$ has the same sign as $s(\mathcal{L}_0)$ provided that $s(M_{22}) < 0$.

4.1.3 The Basic Reproduction Number

The basic reproduction number, R_0 is the expected number of secondary cases of an infection which one typical case could produce during its infectious period, in a completely susceptible population. Heesterbeek (2002) discussed that R_0 is arguably the most important quantity in the study of epidemics. R_0 has the threshold value that a disease will prevail in a population if $R_0 > 1$, otherwise it will die out if $R_0 < 1$. This threshold is important as it allows researchers and policy makers to determine the amount of control measures needed to eradicate infectious cases. For mosquito-borne diseases, one way to ensure that $R_0 < 1$ is by reducing the transmission of the disease by mosquitoes. Insecticide-treated bed nets and spraying repellents in the house can hinder humans from being bitten by mosquitoes thus reducing transmission.

The theory of basic reproduction number for compartmental epidemic models of parabolic type was developed by Wang and Zhao (2012) for the model

$$\begin{aligned} \frac{\partial u_i}{\partial t} &= \nabla \cdot (d_i(x) \nabla u_i) + F_i(x, u) - V_i(x, u), \quad 1 \leq i \leq n, t > 0, x \in \Omega \\ \frac{\partial u_i}{\partial \nu} &= 0 \quad \forall 1 \leq i \leq n \text{ with } d_i > 0, t > 0, x \in \partial\Omega. \end{aligned}$$

Let $F_i(x)$ be the rate of appearance of new infections in compartment i , V_i^+ be the rate of transfer of individuals into compartment i by all other means, and V_i^- be the rate of transfer of individuals out of compartment i . Following the system of ordinary differential equations for disease transmission model (Van den Driessche & Watmough, 2002):

$$\frac{dx}{dt} = f_i(x) = F_i(x) - V_i(x), \quad i = 1, 2, \dots, n, \text{ the following assumptions are made:}$$

(i) For each $1 \leq i \leq n$, functions $F_i(x, u), V_i^+(x, u), V_i^-(x, u)$ and $d_i(x)$ are non-negative and

continuous on $\bar{\Omega} \times \mathbb{R}_+^n$ and continuously differential with respect to u .

(ii) If $u_i = 0$, then $V_i^- = 0$. Thus if $u \in U_s$, then $V_i^- = 0$ for $i = 1, \dots, m$.

(iii) $F_i = 0$ for $i > m$.

(iv) If $u \in U_s$, then $F_i = V_i^+ = 0$ for $i = 1, \dots, m$.

(v) $M_0(x)$ is defined as $M^0(x) := \left(\frac{\partial f_i(x, u^0(x))}{\partial u_j} \right)_{m+1 \leq i, j \leq n}$ where u^0 is a disease-free state.

$M_0(x)$ is cooperative $\forall x \in \bar{\Omega}$ and $\lambda^0(M^0) := s(\nabla \cdot (d_s \nabla) + M^0) < 0$.

(vi) $-V$ is cooperative $\forall x \in \bar{\Omega}$ and $\lambda^0(-V) := s(\nabla \cdot d_I \nabla) - V < 0$.

According to the theorem by Wang and Zhao (2012), letting (i)-(vi) hold, assume there exists

$d_0 > 0$, such that $d_i(x) \geq d_0$ for all $1 \leq i \leq m$.

If for the elliptic eigenvalue problem $-\nabla \cdot (d_I(x) \nabla \phi) + V(x)\phi = \mu F(x)\phi$, $x \in \Omega$,

$\frac{\partial \phi}{\partial \nu} = 0$, $x \in \partial\Omega$, there exists a unique positive eigenvalue μ_0 with a positive eigenfunction

$$\text{then } R_0 = r(-FB^{-1}) = r(-B^{-1}F) = \frac{1}{\mu_0}.$$

Furthermore, it is defined that $F(x)$ and $V(x)$ are two $m \times m$ matrices that are

$$F(x) = \left(\frac{\partial F_i(x, u^0(x))}{\partial u_j} \right)_{1 \leq i, j \leq m}, \quad V(x) = \left(\frac{\partial V_i(x, u^0(x))}{\partial u_j} \right)_{1 \leq i, j \leq m}, \text{ another theorem by Wang and}$$

Zhao (2012) mentioned that if (i)-(vi) hold, assuming $s(-V_{22}) < 0$. Let $B_1 := \nabla \cdot (d_{I1} \nabla) - V_1$,

where $V_1 := V_{11} - V_{12}V_{22}^{-1}V_{21}$, then the following statements are valid:

(i) If $F_{12} = 0$ and $F_{22} = 0$, then $R_0 = r(-B^{-1}F) = r(-B^{-1}F_1)$, where $F_1 = F_{11} - V_{12}V_{22}^{-1}F_{21}$.

(ii) If $F_{21} = 0$ and $F_{22} = 0$, then $R_0 = r(-B^{-1}F) = r(-B^{-1}F_2)$, where $F_2 := F_{11} - F_{12}V_{22}^{-1}V_{21}$.

4.1.4 Threshold Dynamics

In the beginning, the basic properties of the generic model (3.55)-(3.58) are considered. Let

$\kappa := C(\bar{\Omega}, \mathbb{R}^4)$ be the Banach space with supremum norm $\|\cdot\|_\kappa$. The concept of norm

established the concept of length of a vector in $\mathbb{R}^n$. Let V be a vector space. A function $\alpha : V$

$\rightarrow \mathbb{R}$ is called a norm on V if it has the following properties:

(i) $\alpha(x) \geq 0$, $\alpha(x) = 0$ only for $x = 0$ (positivity)

(ii) $\alpha(rx) = |r| \alpha(x)$ for all $r \in \mathbb{R}$ (homogeneity)

(iii) $\alpha(x + y) \leq \alpha(x) + \alpha(y)$ (triangle inequality).

A vector space on which a norm is defined is called a normed vector space. A Banach space is a complete normed vector space. Thus, a Banach space is a vector space that allows the computation of vector length and distance between vectors. It is complete as a Cauchy sequence of vectors always converges to a particular limit that is within the space. A Cauchy sequence is a sequence whose elements become arbitrarily close to each other as the sequence progresses. For $\tau \geq 0$, let $\tau = \max\{\tau_M, \tau_H\}$ hence, τ is the maximum between τ_M , the mosquito latent period and τ_H , the human latent period.

A metric space X is strongly ordered if for every open subset U in X the following holds:

- (a) There exist $a, b \in U$ with $a \ll x \ll b \ \forall x \in U$, and
- (b) There exists $x \in U$ with $a \ll x \ll b \ \forall a, b \in U$ with $a \ll b$.

Then define $C = C([- \tau, 0], \kappa)$ with norm $\|\phi\| = \max_{\theta \in [- \tau, 0]} \|\phi(\theta)\|_\kappa$. Next, C is a Banach space. Allowing $C_\tau = C([- \tau, 0], \kappa^+)$ and representing $\kappa^+ := C(\bar{\Omega}, \mathbb{R}_+^4)$, both (κ, κ^{-1}) and (C, C^+) are strongly ordered spaces.

Given a function $u : [- \tau, \sigma) \rightarrow \kappa$ for $\sigma > 0$, prescribe $u_t \in C$ by $u_t(\theta) = u(t + \theta), \theta \in [- \tau, 0]$. Set κ_1 and C_τ be the subsets in κ and C defined by

$$\kappa_1 := \left\{ \phi = (\phi_1, \phi_2, \phi_3, \phi_4)^T \in \kappa^+ : 0 \leq \phi_1(x), \phi_2(x) \leq H(x), \forall x \in \bar{\Omega} \right\}. \quad \text{Let } \kappa := C(\bar{\Omega}, \mathbb{R})$$

thus $\kappa^+ := C(\bar{\Omega}, \mathbb{R}_+)$. Consequently, let us suppose that $Y_i(t) : \kappa_1 \rightarrow \kappa_1, t \geq 0, i = 1, 2, 3, 4$ be the semigroups associated with $D_H \Delta - d_H, D_H \Delta - (d_H + r), D_M \Delta - d_M$ and $D_M \Delta - d_M$, respectively, subject to Neumann boundary condition. Let $A_i : D(A_i) \rightarrow \kappa$ be the generator of Y_i . $Y(t) = (Y_1(t), Y_2(t), Y_3(t), Y_4(t)) : \kappa \rightarrow \kappa$ is a semigroup by the operator

$A := (A_1, A_2, A_3, A_4)$ defined on $D(A) := D(A_1) \times D(A_2) \times D(A_3) \times D(A_4)$. It follows in Wang and Zhao (2011) that for each $t > 0$, $Y(t)$ is compact and positive.

Define $F = (F_1, F_2, F_3, F_4): C_\tau \rightarrow \kappa$ by

$$F_1(\phi)(x) = \gamma - \frac{cg\phi_1(0, x)\phi_4(0, x)}{1 + g\lambda\phi_H(0, x)} + r\phi_2(0, x), \quad (4.1)$$

$$F_2(\phi)(x) = \frac{cg\phi_1(-\tau_H, x)\phi_4(-\tau_H, x)}{1 + g\lambda\phi_H(-\tau_H, x)} - r\phi_2(0, x), \quad (4.2)$$

$$F_3(\phi)(x) = \frac{bg\phi_3(0, x)\phi_2(0, x)}{1 + g\lambda\phi_H(0, x)}, \quad (4.3)$$

$$F_4(\phi)(x) = \frac{bg\phi_3(-\tau_M, x)\phi_2(-\tau_M, x)}{1 + g\lambda\phi_H(-\tau_M, x)}, \quad (4.4)$$

for all $x \in \bar{\Omega}$ and $\phi = (\phi_1, \phi_2, \phi_3, \phi_4) \in C_\tau$ where $\phi_H = \phi_1 + \phi_2$ and $\phi_M = \phi_3 + \phi_4$.

So (3.55)-(3.58) can be written as the following:

$$\begin{aligned} \frac{du}{dt} &= Au + F(u_t), \quad t > 0 \\ u_0 &= \phi \in C_\tau. \end{aligned} \quad (4.5)$$

Since $F(\phi)$ is locally Lipschitz continuous on C_τ , it is adopted from Martin and Smith (1990) that for any $\phi \in C_\tau$, there exists a unique non-continuable mild solution $u(t, \phi)$ such that $u_t(\phi) \in C_\tau$ for all t in its maximal interval of existence. In addition, $u(t, \phi)$ is a classical solution of (3.55)-(3.58) with Neumann boundary for $t > \tau$. A solution for a partial differential equation of order k is at least continuously differentiable k times, meaning all derivatives in this equation exist and are continuous. Hence, it is called classical solution. Any classical solution is a mild solution. A mild solution is a classical solution if and only if it is continuously differentiable.

4.1.5 Basic Reproduction Number of the Generic Model

The theory of basic reproduction number for compartmental models of reaction diffusion models by Wang and Zhao (2012) discussed in Section 4.1.3 is applied here. This enables the effect of spatial heterogeneity on the spread of diseases to be evaluated. The focus is on one dimensional spatial environment as the purpose is to simplify matters. In this study, the one dimensional environment is limited to $\Omega = (0, \pi)$. Neumann boundary is introduced to the generic model therefore $\frac{\partial I_H(0,t)}{\partial x} = \frac{\partial I_H(1,t)}{\partial x} = \frac{\partial I_M(0,t)}{\partial x} = \frac{\partial I_M(1,t)}{\partial x} = 0$. The aim is to study the consequence of spatial heterogeneity on the transmission of disease.

From the model, the disease-free equilibrium is $(S_H^0, 0, S_M^0, 0)$ where $S_H^0 = \frac{\gamma}{d_H}$ and

$S_M^0 = \frac{\Lambda}{d_M}$. Adopting the method by Wang and Zhao (2012), the elliptic eigenvalue problem

associated with linear parabolic system are these ordinary differential equations:

$$\begin{aligned} \lambda I_H &= \frac{d}{dx} \left(D_H \frac{dI_H}{dx} \right) + c \frac{g}{1 + g\lambda \left(\frac{\gamma}{d_H} \right)} I_M(t - \tau_H, x) - (r + d_H) I_H, \quad x \in (0,1) \\ \lambda I_M &= \frac{d}{dx} \left(D_M \frac{dI_M}{dx} \right) + b \frac{g}{1 + g\lambda \left(\frac{\gamma}{d_H} \right)} \frac{\Lambda}{d_M} I_H(t - \tau_M, x) - d_M I_M, \quad x \in (0,1). \end{aligned} \tag{4.6}$$

Lemma 4.1.1 Problem (4.6) has a principal eigenvalue λ^* with a positive eigenfunction.

Proof.

Substituting $I_H = \varphi_1$ and $I_M = \varphi_2$ in (4.10), the eigenvalue problem is written as below in order to apply the theorem presented in Section 4.1.2:

$$\lambda\varphi_1 = \frac{d}{dx}\left(D_H \frac{d\varphi_1}{dx}\right) + c \frac{g}{1 + g\lambda\left(\frac{\gamma}{d_H}\right)} \varphi_2(t - \tau_H, x) - (r + d_H)\varphi_1, \quad x \in (0,1) \quad (4.7)$$

$$\lambda\varphi_2 = \frac{d}{dx}\left(D_M \frac{d\varphi_2}{dx}\right) + b \frac{g}{1 + g\lambda\left(\frac{\gamma}{d_H}\right)} \frac{\Lambda}{d_M} \varphi_1(t - \tau_M, x) - d_M \varphi_2, \quad x \in (0,1) \quad (4.8)$$

$$\frac{\partial\varphi_1(0,t)}{\partial x} = \frac{\partial\varphi_1(1,t)}{\partial x} = \frac{\partial\varphi_2(0,t)}{\partial x} = \frac{\partial\varphi_2(1,t)}{\partial x} = 0.$$

$D_M \frac{d^2\varphi_2}{dx^2}$ is ignored because the impact of the movement of mosquitoes is not studied here.

This is because the movement of mosquitoes is at a smaller spatial scale compared to humans' as human mobility plays a much more significant role. Thus (4.8) becomes

$$\lambda\varphi_2 = b \frac{g}{1 + g\lambda\left(\frac{\gamma}{d_H}\right)} \frac{\Lambda}{d_M} \varphi_1(t - \tau_M, x) - d_M \varphi_2, \quad x \in (0,1). \text{ Adopting the definition by Wang}$$

and Zhao (2012), the generator which is closed and resolvent positive, B is found to be

$$B = \begin{pmatrix} \frac{d}{dx}\left(D_H \frac{d\varphi_1}{dx}\right) - (r + d_H) & c \frac{g}{1 + g\lambda\left(\frac{\gamma}{d_H}\right)} \frac{\gamma}{d_H} \\ b \frac{g}{1 + g\lambda\left(\frac{\gamma}{d_H}\right)} \frac{\Lambda}{d_M} & -d_M \end{pmatrix}. \text{ Following this, the linear operator } L_\lambda$$

becomes

$$L_\lambda = \frac{d}{dx}\left(D_H \frac{d\varphi}{dx}\right) + c \frac{g}{1 + g\lambda\left(\frac{\gamma}{d_H}\right)} \frac{\gamma}{d_H} (\lambda I - (-d_M))^{-1} b \frac{g}{1 + g\lambda\left(\frac{\gamma}{d_H}\right)} \frac{\Lambda}{d_M} \varphi - (r + d_H)\varphi,$$

$$\forall \lambda > -d_M \quad x \in (0,1).$$

Let $\frac{g}{1+g\lambda\left(\frac{\gamma}{d_H}\right)} \geq 0$ and $\frac{g}{1+g\lambda\left(\frac{\gamma}{d_H}\right)} \neq 0$, there exists an interval $[e, f] \subset (0, \pi)$ such that

$$\frac{g}{1+g\lambda\left(\frac{\gamma}{d_H}\right)} > 0 \text{ for } \forall x \in [e, f]. \text{ Let } A := c.b.\gamma.. \min_{x \in [e, f]} \frac{g}{1+g\lambda\left(\frac{\gamma}{d_H}\right)} \frac{g}{1+g\lambda\left(\frac{\gamma}{d_H}\right)} \Lambda, \text{ and}$$

λ_1 is the principal eigenvalue of the eigenvalue problem

$$\frac{d}{dx} \left(D_H \frac{d\varphi}{dx} \right) - (r + d_H) \varphi = \lambda \varphi, \quad x \in (e, f), \quad \varphi(e) = \varphi(f) = 0, \text{ with } \varphi^*(x) \text{ is a positive}$$

eigenfunction.

$$\text{Since } \lambda_0 := \frac{(\lambda_1 - d_M) d_H d_M + \sqrt{(d_H d_M^2 + \lambda_1 d_H d_M)^2 + 4 d_H d_M A}}{2 d_H d_M} \text{ and } A > 0 \text{ hence}$$

$$\lambda_0 > -d_M,$$

$$\begin{aligned} L_{\lambda_0} \varphi^*(x) &\geq \frac{d}{dx} \left(D_H \frac{d\varphi^*(x)}{dx} \right) + (\lambda_0 I - (-d_M))^{-1} \frac{A}{d_H d_M} \varphi - (r + d_H) \varphi^*(x), \\ &= \left(\lambda_1 + \frac{A}{(\lambda_0 + d_M) d_H d_M} \right) \varphi^*(x) \\ &= \lambda_0 \varphi^*(x), \quad \forall x \in (c, d). \end{aligned}$$

Thus $L_{\lambda_0} \varphi^*(x) \geq \lambda_0 \varphi^*(x)$, $\forall x \in (c, d)$ for all $x \in (0, \pi) \setminus \{c, d\}$. Thereupon, $e^{\lambda_0 t} \varphi_0(x)$ is

a subsolution of the integral form to the system $u_t = L_{\lambda_0} u$. By Section 4.1.2, using the second

theorem by Wang and Zhao (2012), equations in (4.7-4.8) has an eigenvalue with a

nonnegative eigenfunction and the eigenfunction is positive.

Lemma 4.1.2 Let ν_1 be the unique positive eigenvalue of the eigenvalue problem

$$-\frac{d}{dx}\left(D_H \frac{d\varphi}{dx}\right) + (r + d_H)\varphi = \nu \frac{bg \frac{\Lambda}{d_M} cg \frac{\gamma}{d_H}}{(1 + \lambda g \frac{\gamma}{d_H})d_M (1 + \lambda g \frac{\gamma}{d_H})} \varphi, \quad x \in (0,1) \quad (4.9)$$

$$\frac{\partial \varphi(0,t)}{\partial x} = \frac{\partial \varphi(1,t)}{\partial x} = 0, \text{ with a positive eigenfunction thus } R_0 = \frac{1}{\nu_1}.$$

Proof.

Firstly, to use the second theorem presented in Section 4.1.3 in this thesis (Wang & Zhao,

2012), it is defined that $F(x) := \begin{pmatrix} 0 & c \frac{g}{1 + g\lambda \left(\frac{\gamma}{d_H}\right)} \frac{\gamma}{d_H} \\ b \frac{g}{1 + g\lambda \left(\frac{\gamma}{d_H}\right)} \frac{\Lambda}{d_M} & 0 \end{pmatrix}$ and

$$B = \begin{pmatrix} L_1 + M_{11} & M_{12} \\ M_{21} & M_{22} \end{pmatrix} = \begin{pmatrix} \frac{d}{dx} D_H \frac{d\varphi_1}{dx} - (r + d_H) & c \frac{g}{1 + g\lambda \left(\frac{\gamma}{d_H}\right)} \frac{\gamma}{d_H} \\ b \frac{g}{1 + g\lambda \left(\frac{\gamma}{d_H}\right)} \frac{\Lambda}{d_M} & -d_M \end{pmatrix} \text{ for the model (3.55-}$$

3.58). According to the first theorem discussed in Section 4.1.3, thus $r(-B^{-1}F) = 1/\nu_1$.

The computation of R_0 is carried out numerically for the generic system using the

principal eigenvalue problem (4.9), adopting the method by Wang and Zhao (2012). Say

$h = 1/(n+1)$, and $x_i = ih$ for $1 \leq i \leq n$ with $x_0 = 0$ to $x_{n+1} = \pi$. Subsequently,

$$\frac{d}{dx} \left(D_H \frac{d\varphi}{dx} \right) = \frac{-D_H}{h^2} [\varphi(x_{i+1}) - 2\varphi(x_i) + \varphi(x_{i-1})], \quad \forall x \in [1, n] \quad \text{and} \quad \text{applying} \quad \text{Neumann}$$

boundary condition, $i = 0$, $\frac{d}{dx} \varphi = 0$, thus $\frac{1}{h} [\varphi(x_1) - \varphi(x_0)] = 0$, so $\varphi(x_0) = \varphi(x_1)$ is acquired.

Similarly, when $i = n$, $\frac{d}{dx} \varphi = 0$, thus $\frac{1}{h} [\varphi(x_{n+1}) - \varphi(x_n)] = 0$, $\varphi(x_{n+1}) = \varphi(x_n)$.

Approximating (4.9) enables us to obtain

$$Eu + Ru = \nu Su \tag{4.10}$$

where $u = (u_1, u_2, \dots, u_n)^T$,

$$E = \frac{1}{h^2} \begin{pmatrix} D_H & -D_H & 0 & \cdots & 0 \\ -D_H & 2D_H & -D_H & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & 2D_H & -D_H \\ 0 & 0 & \cdots & -D_H & D_H \end{pmatrix},$$

$$R = \begin{pmatrix} r + d_H & 0 & 0 & \cdots & 0 \\ 0 & r + d_H & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & r + d_H & 0 \\ 0 & 0 & \cdots & 0 & r + d_H \end{pmatrix},$$

and

$$S = \begin{pmatrix} \frac{bcg^2\Lambda\gamma}{\left(1+g\lambda\frac{\gamma}{d_H}\right)^2 d_M^2 d_H} & 0 & \dots & 0 & 0 \\ 0 & \frac{bcg^2\Lambda\gamma}{\left(1+g\lambda\frac{\gamma}{d_H}\right)^2 d_M^2 d_H} & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \dots & \frac{bcg^2\Lambda\gamma}{\left(1+g\lambda\frac{\gamma}{d_H}\right)^2 d_M^2 d_H} & 0 \\ 0 & 0 & \dots & \dots & \frac{bcg^2\Lambda\gamma}{\left(1+g\lambda\frac{\gamma}{d_H}\right)^2 d_M^2 d_H} \end{pmatrix}.$$

If $K=E+R$, then (4.10) becomes $Ku = \nu Su$. Consequently, let $u_0 = (1,1,\dots,1)^T$, and define an

iteration sequence $v_k = K^{-1}Su_{k-1}$, $k \geq 1$, $u_k = \frac{v_k}{\|v_k\|_\infty}$, $k \geq 1$ where v_k is attained by solving

$Kv_k = Su_{k-1}$. If eigenvalues of $K^{-1}S$ are given by $\varphi_1 > |\varphi_2| \geq |\varphi_3| \geq \dots \geq |\varphi_n|$ and ω_1 is an

eigenvector corresponding to φ_1 , this implies that $\lim_{k \rightarrow \infty} \|v_k\|_\infty = v_1$, $\lim_{k \rightarrow \infty} v_k = \frac{\omega_1}{\|\omega_1\|_\infty}$, giving us

the approximations of v_1 and its eigenfunction, respectively. Thus, it is found that $R_0 = \frac{1}{v_1}$.

Linearizing the system of equations (3.55-3.58) at the disease-free equilibrium

$E_0 = (S_H^0, 0, S_M^0, 0) = \left(\frac{\gamma}{d_H}, 0, \frac{\Lambda}{d_M}, 0\right)$ as applied by Wang and Zhao (2011), equations (3.56)

and (3.58) becomes

$$\frac{\partial I_H(t, x)}{\partial t} = D_H \frac{\partial^2 I_H(t, x)}{\partial x^2} + c \frac{gN_H}{1 + g\lambda N_H} \frac{\gamma}{d_H} I_M(t - \tau_H, x) - (d_H + r) I_H(t, x) \quad (4.11)$$

$$\frac{\partial I_M(t, x)}{\partial t} = D_M \frac{\partial^2 I_M(t, x)}{\partial x^2} - d_M I_M(t, x) + b \frac{gN_H}{1 + g\lambda N_H} \frac{\Lambda}{d_M} I_H(t - \tau_H, x). \quad (4.12)$$

Adopting the Krein-Rutmann theorem as discussed in Section 4.1.1, $r(L_\varepsilon) > 0$ is the unique eigenvalue of the L_ε having a strong eigenvector (Wang & Zhao, 2011). As L_ε is a strongly positive linear operator and following the uniqueness of the eigenvalue, thus $r(L_\varepsilon) = r(M_\varepsilon)$.

$$M_\varepsilon = \begin{pmatrix} \frac{\varepsilon}{d_M} & \frac{cg \frac{\gamma}{d_H}}{(1 + \lambda g \frac{\gamma}{d_H})(r + d_H)} \\ \frac{bg \frac{\Lambda}{d_M}}{(1 + \lambda g \frac{\gamma}{d_H})d_M} & \frac{\varepsilon}{(r + d_H)} \end{pmatrix} \quad \text{where its spectral radius } r(M_\varepsilon) \text{ is an}$$

eigenvalue with a positive eigenvector in $\mathbb{R}^2$. Each element in M_ε is positive thus the

$$\text{explicit } R_0 \text{ for the system (4.11)-(4.12) is } R_0 = \sqrt{\frac{bgS_M^0}{(1 + \lambda gS_H^0)d_M} \times \frac{cgS_H^0}{(1 + \lambda gS_H^0)(r + d_H)}}.$$

$$\text{Taking } \varepsilon \rightarrow 0^+, \text{ where } M_0 = \begin{pmatrix} 0 & \frac{cg \frac{\gamma}{d_H}}{(1 + \lambda g \frac{\gamma}{d_H})(r + d_H)} \\ \frac{bg \frac{\Lambda}{d_M}}{(1 + \lambda g \frac{\gamma}{d_H})d_M} & 0 \end{pmatrix},$$

$$\text{hence } R_0 = r(L) = r(M_0) = \sqrt{\frac{bg \frac{\Lambda}{d_M}}{(1 + \lambda g \frac{\gamma}{d_H})d_M} \times \frac{cg \frac{\gamma}{d_H}}{(1 + \lambda g \frac{\gamma}{d_H})(r + d_H)}}.$$

The basic reproduction number is the threshold value where when $R_0 > 1$, the disease prevails in the population and when $R_0 < 1$, the disease dies out.

4.1.6 Equilibrium points of the Generic Model

A dynamical system consists of a set of differential equations. The equilibrium point of a dynamical system is the solution for the set which does not change in time. To inspect the situation in the future, a system can be analyzed at its equilibrium point. Disease-free equilibrium points are steady states where there is no infection in the population. Diseased compartments for this model are infectious human population I_H and infectious mosquito population I_M . The equilibrium point for the generic model can be determined by setting equations (3.55)-(3.58) as zero and calculating the values for each variable. The disease-free equilibrium, $E_0 = (S_H^0, 0, S_M^0, 0) = \left(\frac{\gamma}{d_H}, 0, \frac{\Lambda}{d_M}, 0 \right)$. This model is studied without diffusion and each compartment is scaled by the total population to ease analysis.

Hence, $I_h = \frac{I_H}{N_H}$, $I_m = \frac{I_M}{N_M}$ and working with fractional quantities,

$S_h + I_h = 1 \rightarrow S_h = 1 - I_h$ and $S_m + I_m = 1 \rightarrow S_m = 1 - I_m$. As the fractions are differentiated with respect to time,

$$\frac{dI_h}{dt} = \frac{d}{dt} \left(\frac{I_H}{N_H} \right) = \frac{N_H \frac{d}{dt} I_H - I_H \frac{d}{dt} N_H}{(N_H)^2} = \frac{1}{N_H} \left(\frac{d}{dt} I_H - I_H \frac{d}{dt} N_H \right) =$$

$$\frac{cg}{1 + g\lambda N_H} I_m N_M \frac{(1 - I_h)}{N_H} - r I_h - \gamma \frac{I_h}{N_H} \quad (4.13)$$

$$\text{and } \frac{dI_m}{dt} = \frac{1}{N_M} \left(\frac{d}{dt} I_M - I_m \frac{d}{dt} N_M \right) = \frac{bg}{1 + g\lambda N_H} I_h N_H \frac{(1 - I_m)}{N_M} - \Lambda \frac{I_m}{N_M}. \quad (4.14)$$

Both the human and mosquito population have to be positive hence the domain for the solutions is: $\Omega = \{(I_h, I_m, N_H, N_M) \in \mathbb{R}_4^+ \mid I_h \leq 1, I_m \leq 1, N_H, N_M > 0\}$.

According to Chitnis *et al.* (2006), assuming that the initial conditions lie in Ω , the system of equations above has a unique solution which remains in $\Omega, \forall t \geq 0$. Setting equations (4.13) and (4.14) to zero and solving them gives the equilibrium point, $E = (I_h^*, I_m^*)$ where

$$I_h^* = \frac{cg I_m^* N_M^*}{cg I_m^* N_M^* + r N_H^* + rg \lambda N_H^{*2} + \gamma(1 + g \lambda N_H^*)} \quad \text{and}$$

$$I_m^* = \frac{bg I_h^* N_H^*}{\Lambda(1 + g \lambda N_H^*) + bg I_h^* N_H^*}.$$

For all equilibrium points on $\Omega \cap \partial \mathbb{R}_4^+$, $I_h = I_m = 0$. If any of the diseased compartment is zero, the other is also zero. To demonstrate this, (4.13) and (4.14) are equate to zero, and it is shown below that if any of the diseased class is zero, then $I_h = I_m = 0$.

$$\text{Since } I_h^* = \frac{cg I_m^* N_M^*}{cg I_m^* N_M^* + r N_H^* + rg \lambda N_H^{*2} + \gamma(1 + g \lambda N_H^*)}, \quad I_m = 0 \text{ if and only if } I_h = 0$$

$$\text{and } I_m^* = \frac{bg I_h^* N_H^*}{\Lambda(1 + g \lambda N_H^*) + bg I_h^* N_H^*}, \quad I_h = 0, \text{ if and only if } I_m = 0.$$

The disease-free equilibrium, E_0 is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. To show this, first of all, the disease-free equilibrium point, E_0 , is where $I_h = I_m = 0$. The stability of the equilibrium can be decided by the eigenvalues of a Jacobian matrix.

If all the Jacobian's eigenvalues are negative values then the equilibrium is asymptotically stable. The Jacobian matrix is checked at the E_0 thus it is found to be

$$\begin{pmatrix} \frac{dI_h}{dt} / \frac{\partial I_h}{\partial I_h} & \frac{dI_h}{dt} / \frac{\partial I_h}{\partial I_m} \\ \frac{dI_m}{dt} / \frac{\partial I_m}{\partial I_h} & \frac{dI_m}{dt} / \frac{\partial I_m}{\partial I_m} \end{pmatrix} = \begin{pmatrix} -(r + d_H) & \frac{cg\Lambda d_H}{(1 + g\lambda \frac{\gamma}{d_H})\gamma d_M} \\ \frac{bg\gamma d_M}{(1 + g\lambda \frac{\gamma}{d_H})\Lambda d_H} & -d_M \end{pmatrix}.$$

The eigenvalues of A are

$$\frac{-(r + d_H + d_M) \pm \sqrt{(r + d_H + d_M)^2 - 4(r + d_H)(d_M) \left(1 - \frac{\Lambda \gamma d_H (r + d_H)}{d_M (\Lambda r \gamma + \gamma \Lambda d_H)} R_0^2\right)}}{2}.$$

When $R_0 < 1$, all eigenvalues are negative thus E_0 is locally asymptotically stable. However when $R_0 > 1$, the equilibrium is unstable as there exists an eigenvalue with positive real part.

Lemma 4.1.3 If $R_0 > 1$, such that the condition

$bcg^2 \frac{\Lambda}{d_M} \frac{\gamma}{d_H} - \left(1 + g\lambda \frac{\gamma}{d_H}\right)^2 d_M (r + d_H) > 0$ holds then there exist at least an endemic equilibrium point.

Proof. From $E = (I_h^*, I_m^*)$, the endemic equilibrium E_e is obtained:

$$I_h^* = \frac{cgI_m^* N_M^* \left(1 + g\lambda \frac{\gamma}{d_H}\right)^2 d_M (r + d_H) (R_0^2 - 1)}{\left(cgI_m^* N_M^* + rN_H^* + rg\lambda N_H^2 + \gamma(1 + g\lambda N_H)\right) \left(bcg^2 \frac{\Lambda}{d_M} \frac{\gamma}{d_H} - \left(1 + g\lambda \frac{\gamma}{d_H}\right)^2 d_M (r + d_H)\right)}$$

and $I_m^* = \frac{bgI_h^* N_H^* \left(1 + g\lambda \frac{\gamma}{d_H}\right)^2 d_M (r + d_H) (R_0^2 - 1)}{\left(bgI_h^* N_H^* + (1 + g\lambda N_H)\Lambda\right) \left(bcg^2 \frac{\Lambda}{d_M} \frac{\gamma}{d_H} - \left(1 + g\lambda \frac{\gamma}{d_H}\right)^2 d_M (r + d_H)\right)}.$

It can be clearly seen from here that if $R_0 > 1$, then the endemic equilibrium lies in Ω as these points can be clearly defined. If $R_0 = 1$, disease-free equilibrium is acquired instead. These points are invalid should $R_0 < 1$ as they are negative value.

4.2 Numerical Analysis of the Generic Model

To resolve the system of partial differential equations and to examine the simulations, the numerical method discussed in Section 3.2 is utilized. The equations (3.55-3.58) are discretized and solved using the Crank Nicolson method. Since the initial model's numerical result for infectious humans did not agree with Wang and Zhao (2011), the intention is to discover whether simulations from this generic model are agreeable. In order to run the simulation, initial data applied is:

$$S_H(\phi, x) = 0.03, I_H(\phi, x) = 0.22, S_M(\psi, x) = 1 \text{ and } I_M(\psi, x) = -2x + 2 \quad \forall \phi \in [-\tau_H, 0], \\ \psi \in [-\tau_M, 0], x \in [0, 1].$$

Using the centered difference approximation and average of second centered differences, equations (3.55)-(3.58) are discretized accordingly:

$$\begin{aligned}
\frac{S_{Hi}^{j+1} - S_{Hi}^j}{\Delta t} = & D_H \frac{1}{2(\Delta x)^2} (S_{Hi}^{j+1} - 2S_{Hi}^{j+1} + S_{Hi-1}^{j+1} + S_{Hi+1}^j - 2S_{Hi}^j + S_{Hi-1}^j) \\
& - c \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{Hi}^j + S_{Hi}^{j+1}}{2} \right) \left(\frac{I_{Mi}^j + I_{Mi}^{j+1}}{2} \right) \\
& - d_H \left(\frac{S_{Hi}^j + S_{Hi}^{j+1}}{2} \right) + r \left(\frac{I_{Hi}^j + I_{Hi}^{j+1}}{2} \right), \tag{4.15}
\end{aligned}$$

$$\begin{aligned}
\frac{I_{Hi}^{j+1} - I_{Hi}^j}{\Delta t} = & D_H \frac{1}{2(\Delta x)^2} (I_{Hi}^{j+1} - 2I_{Hi}^{j+1} + I_{Hi-1}^{j+1} + I_{Hi+1}^j - 2I_{Hi}^j + I_{Hi-1}^j) \\
& + c \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{Hi}^j + S_{Hi}^{j+1}}{2} \right) \left(\frac{I_{Mi}^j + I_{Mi}^{j+1}}{2} \right) \\
& - d_H \left(\frac{I_{Hi}^j + I_{Hi}^{j+1}}{2} \right) - r \left(\frac{I_{Hi}^j + I_{Hi}^{j+1}}{2} \right), \tag{4.16}
\end{aligned}$$

$$\begin{aligned}
\frac{S_{Mi}^{j+1} - S_{Mi}^j}{\Delta t} = & D_M \frac{1}{2(\Delta x)^2} (S_{Mi}^{j+1} - 2S_{Mi}^{j+1} + S_{Mi-1}^{j+1} + S_{Mi+1}^j - 2S_{Mi}^j + S_{Mi-1}^j) + \Lambda - \\
& b \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{Mi}^j + S_{Mi}^{j+1}}{2} \right) \left(\frac{I_{Hi}^j + I_{Hi}^{j+1}}{2} \right) - d_M \left(\frac{S_{Mi}^j + S_{Mi}^{j+1}}{2} \right), \tag{4.17}
\end{aligned}$$

and

$$\begin{aligned} \frac{I_{M_i}^{j+1} - I_{M_i}^j}{\Delta t} = & D_M \frac{1}{2(\Delta x)^2} (I_{M_i}^{j+1} - 2I_{M_i}^{j+1} + I_{M_{i-1}}^{j+1} + I_{M_{i+1}}^j - 2I_{M_i}^j + I_{M_{i-1}}^j) + \\ & b \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} \left(\frac{S_{M_i}^j + S_{M_i}^{j+1}}{2} \right) \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right) - d_M \left(\frac{I_{M_i}^j + I_{M_i}^{j+1}}{2} \right). \end{aligned} \quad (4.18)$$

Writing the discretized equations (4.15)-(4.18) explicitly in the $(j+1)$ time:

$$\begin{aligned} S_{H_{i+1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) + S_{H_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} (I_{M_i}^j + I_{M_i}^{j+1}) + \frac{d_H}{2} \right) \\ + S_{H_{i-1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) = S_{H_{i+1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) + \gamma \\ + S_{H_i}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} (I_{M_i}^j + I_{M_i}^{j+1}) - \frac{d_H}{2} \right) \\ + S_{H_{i-1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) + r \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right), \end{aligned} \quad (4.19)$$

$$\begin{aligned} I_{H_{i+1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) + I_{H_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right) + I_{H_{i-1}}^{j+1} \left(\frac{-D_H}{2(\Delta x)^2} \right) = I_{H_{i+1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) + \\ I_{H_i}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right) + I_{H_{i-1}}^j \left(\frac{D_H}{2(\Delta x)^2} \right) \\ + c \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} \left(\frac{S_{H_i}^j + S_{H_i}^{j+1}}{2} \right) \left(\frac{I_{M_i}^j + I_{M_i}^{j+1}}{2} \right) \end{aligned} \quad (4.20)$$

$$\begin{aligned}
& S_{M_{i+1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) + S_{M_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \left(\frac{b}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} (I_{H_i}^j + I_{H_i}^{j+1}) + \frac{d_M}{2} \right) + \\
& S_{M_{i-1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) = S_{M_{i+1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right) + \Lambda \\
& + S_{M_i}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \left(\frac{b}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} (I_{H_i}^j + I_{H_i}^{j+1}) - \frac{d_M}{2} \right) + S_{M_{i-1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right)
\end{aligned} \tag{4.21}$$

$$\begin{aligned}
& I_{M_{i+1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) + I_{M_i}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right) + I_{M_{i-1}}^{j+1} \left(\frac{-D_M}{2(\Delta x)^2} \right) = I_{M_{i+1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right) + \\
& \text{and } I_{M_i}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right) + I_{M_{i-1}}^j \left(\frac{D_M}{2(\Delta x)^2} \right) \\
& + c \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} \left(\frac{S_{M_i}^j + S_{M_i}^{j+1}}{2} \right) \left(\frac{I_{H_i}^j + I_{H_i}^{j+1}}{2} \right).
\end{aligned} \tag{4.22}$$

Correspondingly, the governing equations above is subjected to the Neumann boundary condition:

$$\begin{aligned}
& \frac{\partial S_H(0,t)}{\partial x} = 0, \frac{\partial I_H(0,t)}{\partial x} = 0, \frac{\partial S_M(0,t)}{\partial x} = 0, \frac{\partial I_M(0,t)}{\partial x} = 0, \text{ and} \\
& \frac{\partial S_H(1,t)}{\partial x} = 0, \frac{\partial I_H(1,t)}{\partial x} = 0, \frac{\partial S_M(1,t)}{\partial x} = 0, \frac{\partial I_M(1,t)}{\partial x} = 0.
\end{aligned}$$

From the above and as discussed in Section 3.2, applying the central finite approximation

$S_{H2}^j = S_{H0}^j$ and $S_{H2}^{j+1} = S_{H0}^{j+1}$ and replacing these into equation (4.19) yields:

$$\begin{aligned}
& S_{H2}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + S_{H1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} (I_{M1}^j + I_{M1}^{j+1}) + \frac{d_H}{2} \right) = \\
& S_{H2}^j \left(\frac{D_H}{(\Delta x)^2} \right) + \gamma + S_{H1}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} (I_{M1}^j + I_{M1}^{j+1}) - \frac{d_H}{2} \right) \\
& + r \left(\frac{I_{H1}^j + I_{H1}^{j+1}}{2} \right). \tag{4.23}
\end{aligned}$$

Likewise, $I_{H2}^j = I_{H0}^j$ and $I_{H2}^{j+1} = I_{H0}^{j+1}$ are substituted into (4.20) hence:

$$\begin{aligned}
& I_{H2}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + I_{H1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right) = I_{H2}^j \left(\frac{D_H}{(\Delta x)^2} \right) + I_{H1}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right) \\
& + c \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{H1}^j + S_{H1}^{j+1}}{2} \right) \left(\frac{I_{M1}^j + I_{M1}^{j+1}}{2} \right). \tag{4.24}
\end{aligned}$$

The same technique is utilized on (4.19) and (4.20), where $S_{M2}^j = S_{M0}^j$, $S_{M2}^{j+1} = S_{M0}^{j+1}$,

$I_{M2}^j = I_{M0}^j$ and $I_{M2}^{j+1} = I_{M0}^{j+1}$, obtaining:

$$\begin{aligned}
& S_{M2}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + S_{M1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \left(\frac{b}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} (I_{H1}^j + I_{H1}^{j+1}) + \frac{d_M}{2} \right) = \\
& S_{M2}^j \left(\frac{D_M}{(\Delta x)^2} \right) + \Lambda + S_{M1}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \left(\frac{b}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} (I_{H1}^j + I_{H1}^{j+1}) - \frac{d_M}{2} \right)
\end{aligned} \tag{4.25}$$

$$\begin{aligned}
& I_{M2}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + I_{M1}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right) = I_{M2}^j \left(\frac{D_M}{(\Delta x)^2} \right) + I_{M1}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right) \\
& + b \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{M1}^j + S_{M1}^{j+1}}{2} \right) \left(\frac{I_{H1}^j + I_{H1}^{j+1}}{2} \right).
\end{aligned} \tag{4.26}$$

At $x=1$, that is with $i=n$, using the central difference approximation, so $S_{H_{n+1}}^j = S_{H_{n-1}}^j$

and $S_{H_{n+1}}^{j+1} = S_{H_{n-1}}^{j+1}$ and replacing these into equation (4.19) begets:

$$\begin{aligned}
& S_{H_{n-1}}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + S_{H_n}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} (I_{Mn}^j + I_{Mn}^{j+1}) + \frac{d_H}{2} \right) = \\
& S_{H_{n-1}}^j \left(\frac{D_H}{(\Delta x)^2} \right) + \gamma + S_{H_n}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{c\beta}{4H} (I_{Mn}^j + I_{Mn}^{j+1}) - \frac{d_H}{2} \right) + r \left(\frac{I_{Hn}^j + I_{Hn}^{j+1}}{2} \right).
\end{aligned} \tag{4.27}$$

In addition, $I_{H_{n+1}}^j = I_{H_{n-1}}^j$ and $I_{H_{n+1}}^{j+1} = I_{H_{n-1}}^{j+1}$ are plugged into equation (4.20):

$$\begin{aligned}
& I_{H_{n-1}}^{j+1} \left(\frac{-D_H}{(\Delta x)^2} \right) + I_{H_n}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right) = I_{H_{n-1}}^j \left(\frac{D_H}{(\Delta x)^2} \right) + I_{H_n}^j \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right) \\
& + c \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} \left(\frac{S_{H_n}^j + S_{H_n}^{j+1}}{2} \right) \left(\frac{I_{M_n}^j + I_{M_n}^{j+1}}{2} \right). \tag{4.28}
\end{aligned}$$

Similar method is applied on equations (4.21) and (4.22) where $S_{M_{n+1}}^j = S_{M_{n-1}}^j$,

$S_{M_{n+1}}^{j+1} = S_{M_{n-1}}^{j+1}$, $I_{M_{n+1}}^j = I_{M_{n-1}}^j$ and $I_{M_{n+1}}^{j+1} = I_{M_{n-1}}^{j+1}$, hence:

$$\begin{aligned}
& S_{M_{n-1}}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + S_{M_n}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \left(\frac{b}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} (I_{H_n}^j + I_{H_n}^{j+1}) + \frac{d_M}{2} \right) = \\
& S_{M_{n-1}}^j \left(\frac{D_M}{(\Delta x)^2} \right) + \Lambda + S_{M_n}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} (I_{H_n}^j + I_{H_n}^{j+1}) - \frac{d_M}{2} \right) \tag{4.29}
\end{aligned}$$

$$\begin{aligned}
& I_{M_{n-1}}^{j+1} \left(\frac{-D_M}{(\Delta x)^2} \right) + I_{M_n}^{j+1} \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right) = I_{M_{n-1}}^j \left(\frac{D_M}{(\Delta x)^2} \right) + I_{M_n}^j \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right) \\
& + c \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} \left(\frac{S_{M_n}^j + S_{M_n}^{j+1}}{2} \right) \left(\frac{I_{H_n}^j + I_{H_n}^{j+1}}{2} \right). \tag{4.30}
\end{aligned}$$

The system of equations (4.19)-(4.30) form an algebraic system; hence the system is arranged in matrix form as done by Li and Zou (2009) to ease solving it. From this system,

$$A \begin{bmatrix} S_{H1}^{j+1} \\ S_{H2}^{j+1} \\ \vdots \\ S_{Hn-1}^{j+1} \\ S_{Hn}^{j+1} \end{bmatrix} = B \begin{bmatrix} S_{H1}^j \\ S_{H2}^j \\ \vdots \\ S_{Hn-1}^j \\ S_{Hn}^j \end{bmatrix} + \begin{bmatrix} \gamma \\ \gamma \\ \vdots \\ \gamma \\ \gamma \end{bmatrix}, \quad (4.31)$$

$$C \begin{bmatrix} I_{H1}^{j+1} \\ I_{H2}^{j+1} \\ \vdots \\ I_{Hn-1}^{j+1} \\ I_{Hn}^{j+1} \end{bmatrix} = D \begin{bmatrix} I_{H1}^j \\ I_{H2}^j \\ \vdots \\ I_{Hn-1}^j \\ I_{Hn}^j \end{bmatrix} + \begin{bmatrix} c \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{H1}^j + S_{H1}^{j+1}}{2} \right) \left(\frac{I_{M1}^j + I_{M1}^{j+1}}{2} \right) \\ c \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{H2}^j + S_{H2}^{j+1}}{2} \right) \left(\frac{I_{M2}^j + I_{M2}^{j+1}}{2} \right) \\ \vdots \\ c \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{Hn-1}^j + S_{Hn-1}^{j+1}}{2} \right) \left(\frac{I_{Mn-1}^j + I_{Mn-1}^{j+1}}{2} \right) \\ c \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{Hn}^j + S_{Hn}^{j+1}}{2} \right) \left(\frac{I_{Mn}^j + I_{Mn}^{j+1}}{2} \right) \end{bmatrix} \quad (4.32)$$

$$E \begin{bmatrix} S_{M1}^{j+1} \\ S_{M2}^{j+1} \\ \vdots \\ S_{Mn-1}^{j+1} \\ S_{Mn}^{j+1} \end{bmatrix} = F \begin{bmatrix} S_{M1}^j \\ S_{M2}^j \\ \vdots \\ S_{Mn-1}^j \\ S_{Mn}^j \end{bmatrix} + \begin{bmatrix} \Lambda \\ \Lambda \\ \vdots \\ \Lambda \\ \Lambda \end{bmatrix} \quad (4.33)$$

$$\begin{aligned}
G \begin{bmatrix} I_{M1}^{j+1} \\ I_{M2}^{j+1} \\ \vdots \\ I_{Mn-1}^{j+1} \\ I_{Mn}^{j+1} \end{bmatrix} &= H \begin{bmatrix} I_{M1}^j \\ I_{M2}^j \\ \vdots \\ I_{Mn-1}^j \\ I_{Mn}^j \end{bmatrix} + \begin{bmatrix} b \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{M1}^j + S_{M1}^{j+1}}{2} \right) \left(\frac{I_{H1}^j + I_{H1}^{j+1}}{2} \right) \\ b \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{M2}^j + S_{M2}^{j+1}}{2} \right) \left(\frac{I_{H2}^j + I_{H2}^{j+1}}{2} \right) \\ \vdots \\ b \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{Mn-1}^j + S_{Mn-1}^{j+1}}{2} \right) \left(\frac{I_{Hn-1}^j + I_{Hn-1}^{j+1}}{2} \right) \\ b \frac{g}{1+g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(\frac{S_{Mn}^j + S_{Mn}^{j+1}}{2} \right) \left(\frac{I_{Hn}^j + I_{Hn}^{j+1}}{2} \right) \end{bmatrix}
\end{aligned} \tag{4.34}$$

where

$$A = \begin{bmatrix} A1 & M1 & \cdots & 0 & 0 \\ M2 & A2 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & A(n-1) & M2 \\ 0 & 0 & \cdots & M1 & An \end{bmatrix}, \tag{4.35}$$

$$B = \begin{bmatrix} AA1 & N1 & \cdots & 0 & 0 \\ N2 & AA2 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & AA(n-1) & N2 \\ 0 & 0 & \cdots & N1 & AAn \end{bmatrix}, \tag{4.36}$$

$$C = \begin{bmatrix} M3 & M1 & \cdots & 0 & 0 \\ M2 & M3 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & M3 & M2 \\ 0 & 0 & \cdots & M1 & M3 \end{bmatrix}, \quad (4.37)$$

$$D = \begin{bmatrix} N3 & N1 & \cdots & 0 & 0 \\ N2 & N3 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & N3 & N2 \\ 0 & 0 & \cdots & N1 & N3 \end{bmatrix}, \quad (4.38)$$

$$E = \begin{bmatrix} V51 & M1 & \cdots & 0 & 0 \\ M2 & V52 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & V5(n-1) & M2 \\ 0 & 0 & \cdots & M1 & V5n \end{bmatrix}, \quad (4.39)$$

$$F = \begin{bmatrix} W51 & N1 & \cdots & 0 & 0 \\ N2 & W52 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & W5(n-1) & N2 \\ 0 & 0 & \cdots & N1 & W5n \end{bmatrix} \quad (4.40)$$

$$G = \begin{bmatrix} M6 & M1 & \cdots & 0 & 0 \\ M2 & M6 & \cdots & 0 & 0 \\ \vdots & \cdots & \cdots & \cdots & 0 \\ 0 & 0 & \cdots & M6 & M2 \\ 0 & 0 & \cdots & M1 & M6 \end{bmatrix}, \quad (4.41)$$

$$\text{and } H = \begin{bmatrix} N6 & N1 & \dots & 0 & 0 \\ N2 & N6 & \dots & 0 & 0 \\ \vdots & \dots & \dots & \dots & 0 \\ 0 & 0 & \dots & N6 & N2 \\ 0 & 0 & \dots & N1 & N6 \end{bmatrix}. \quad (4.42)$$

Furthermore, to add to the above,

$$Ai = \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} \left(I_{M_i}^j + I_{M_i}^{j+1} \right) + \frac{d_H}{2} \right), \quad (4.43)$$

$$M1 = \left(\frac{-D_H}{(\Delta x)^2} \right), \quad (4.44)$$

$$M2 = \left(\frac{-D_H}{2(\Delta x)^2} \right), \quad (4.45)$$

$$M3 = \left(\frac{1}{\Delta t} + \frac{D_H}{(\Delta x)^2} + \frac{r}{2} + \frac{d_H}{2} \right), \quad (4.46)$$

$$M6 = \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \frac{d_M}{2} \right), \quad (4.47)$$

$$AAi = \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \left(\frac{c}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{H_i}^j + N_{H_i}^{j+1}}{2} \right)} \left(I_{M_i}^j + I_{M_i}^{j+1} \right) - \frac{d_H}{2} \right), \quad (4.48)$$

$$N1 = \left(\frac{D_H}{(\Delta x)^2} \right), \quad (4.49)$$

$$N2 = \left(\frac{D_H}{2(\Delta x)^2} \right), \quad (4.50)$$

$$N3 = \left(\frac{1}{\Delta t} - \frac{D_H}{(\Delta x)^2} - \frac{r}{2} - \frac{d_H}{2} \right), \quad (4.51)$$

$$N6 = \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \frac{d_M}{2} \right), \quad (4.52)$$

$$V5i = \left(\frac{1}{\Delta t} + \frac{D_M}{(\Delta x)^2} + \left(\frac{b}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(I_{Hi}^j + I_{Hi}^{j+1} \right) + \frac{d_M}{2} \right), \quad (4.53)$$

and

$$W5i = \left(\frac{1}{\Delta t} - \frac{D_M}{(\Delta x)^2} - \left(\frac{b}{4} \right) \frac{g}{1 + g\lambda \left(\frac{N_{Hi}^j + N_{Hi}^{j+1}}{2} \right)} \left(I_{Hi}^j + I_{Hi}^{j+1} \right) - \frac{d_M}{2} \right). \quad (4.54)$$

The parameters used are taken from Wang and Zhao (2011) as shown in Table 3.3 except $g = 2$, $\lambda = 0.5 \text{ day}^{-1}$ and $A = 0.5 \text{ day}^{-1}$ as the objective is to explore whether the model is able to reproduce the results. The flowchart of the MATLAB algorithm to solve the system of equations for this generic model is shown in Figure 4.1. Simulations acquired show that the disease persists in both human and mosquito population as can be seen in Figures 4.2 and 4.3. Numerical results are compared and in Figure 4.2, the spread of infectious mosquito density for the proposed generic model resembles numerical simulations from Wang and Zhao's (2011). The value of the population density for mosquito coincides with the result by Wang and Zhao (2011) as well.

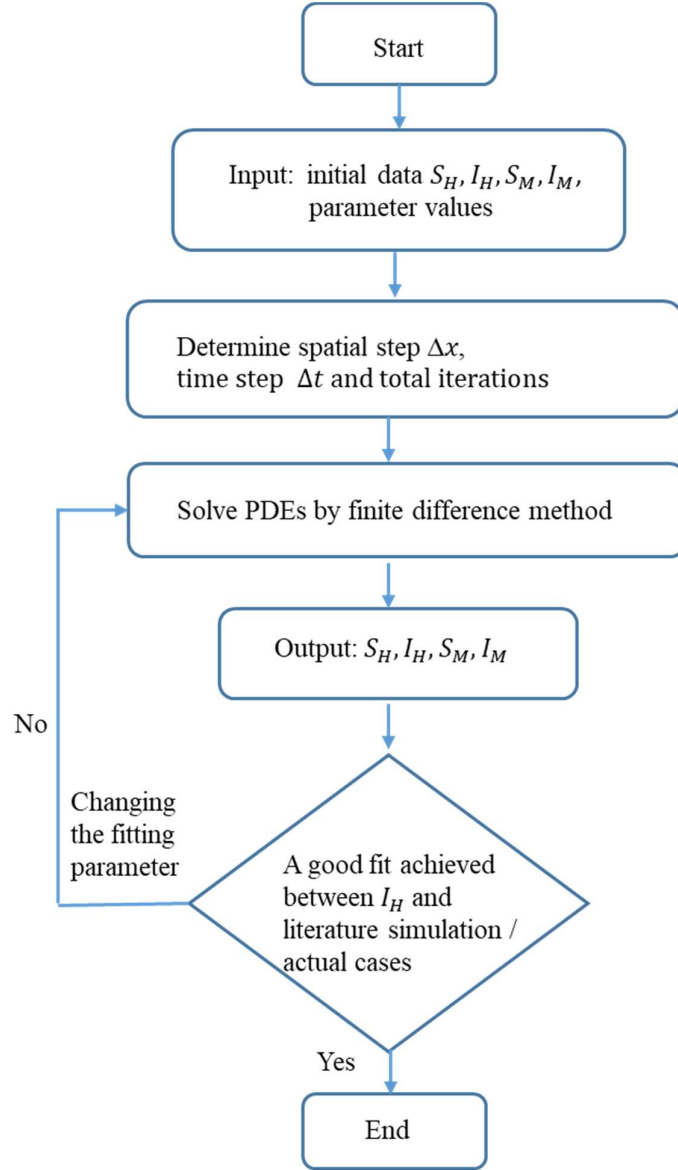


Figure 4.1: Flowchart of the MATLAB numerical procedure to solve the generic model.

Similarly, the spread of infectious human density seen in Figure 4.3 demonstrates corresponding behavior and magnitude as Wang and Zhao's (2011). At locations nearer to origin, infectious human density reaches a peak before decreases and reaches plateau. However, at locations further from the origin, density increases and reaches plateau. Next, this system of reaction-diffusion equations (3.55)-(3.58) is solved using parameter values

from Lou and Zhao (2011) and the initial data is as mentioned in Section 3.2 as the idea is to compare the result with Lou and Zhao's (2011). As the main differences between this system and the initial model are the terms for biting rate and total human population, minor adjustments can be made to the parameters to produce the initial model. $N_H = H = 100$ (Lou & Zhao, 2011), $g = \beta / H = 0.3 / 100 = 0.003$, and $\lambda = 0$ are set which immediately convert the biting rate $\frac{gN_H}{1 + g\lambda N_H}$, to β and this generic model to the system of the initial model.

When comparison is done, the same numerical results acquired are as shown in Figures 3.9 and 3.10. Hence, it can be concluded that the spatial-temporal generic model proposed is able to generate numerical results which are in good agreement with both simulations in Wang and Zhao (2011) and Lou and Zhao (2011).

Next, the motive is to find out if the generic model is able to reproduce temporal results. Numerical results from the generic model is to be compared with Vargas and Esteva's dengue model (1998) which is made up of a system of ordinary differential equations. Diffusion rate is not available in Esteva and Vargas (1998) as it is a temporal model. The notable difference between the generic model and Esteva and Vargas (1998) is that Esteva and Vargas (1998) divided the human population into three compartments SIR (Susceptible-Infectious-Recovered) and mosquito population into two compartments SI (Susceptible-Infectious) compartments. Infected humans recover and return to susceptible state in the generic model however Esteva and Vargas (1998) considered acquired immunity hence infectious humans who recover enter into the recovered compartment. The biting rate which depends on the human population in this generic model is considered as a constant by Esteva and Vargas (1998). Parameter values used are adopted from Esteva and Vargas (1998) and depicted in Table 4.1.

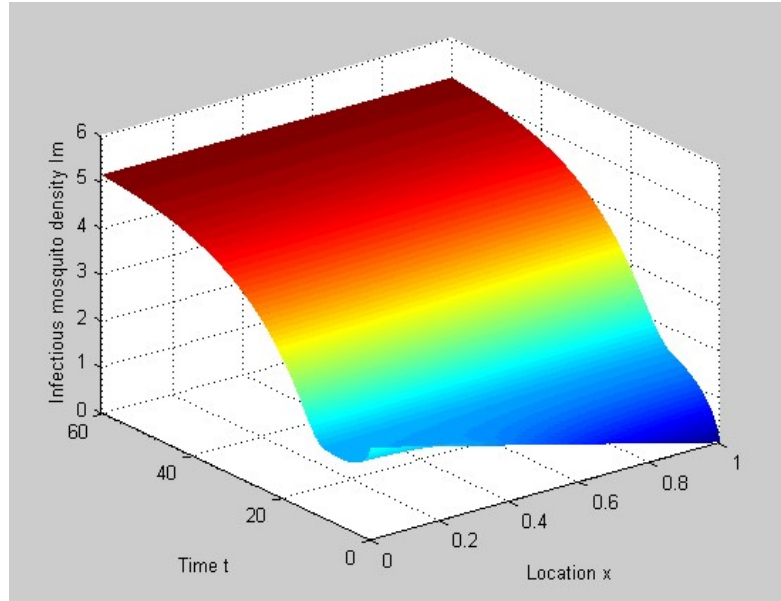


Figure 4.2: The density of infectious mosquitoes (I_M) in time and space for the generic model using parameter values from Wang and Zhao (2011).

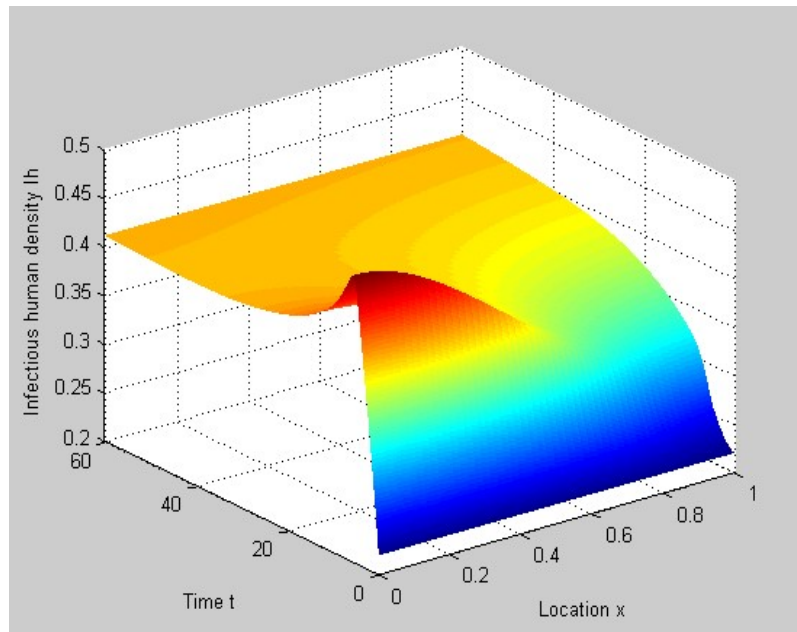


Figure 4.3: The density of infectious humans (I_H) in time and space for the generic model using parameter values from Wang and Zhao (2011).

Table 4.1: Values of parameters used for comparison with Esteva and Vargas (1998)

Parameter	Value
diffusion rate for humans, D_H	0
diffusion rate for mosquitoes, D_M	0
human recruitment rate, γ	$4.57 \times 10^{-1} \text{ day}^{-1}$
transmission probability per bite from $I_M \rightarrow S_H$, c	7.5×10^{-1}
human death rate, d_H	$4.57 \times 10^{-5} \text{ day}^{-1}$
recovery rate, r	$1.428 \times 10^{-1} \text{ day}^{-1}$
mosquito recruitment rate, Λ	$4.0 \times 10^2 \text{ day}^{-1}$ (best fit)
transmission probability per bite from $I_H \rightarrow S_M$, b	1
mosquito death rate, d_M	$2.5 \times 10^{-1} \text{ day}^{-1}$
biting rate of mosquitoes on humans, β	$5.0 \times 10^{-1} \text{ day}^{-1}$
searching rate of a mosquito, g	β/N_H
time taken for a mosquito to complete a blood meal, λ	0

Initial conditions utilized to obtain the simulation results for the generic model are

$$S_H = 9000, I_H = 1000, S_M = 1280 \text{ and } I_M = 320.$$

Setting $D_H = 0, D_M = 0, \tau_H = 0, \tau_M = 0, \lambda = 0$ and $g = \beta/N_H$ where β is the constant biting rate of mosquito.

This will instantly transform the spatio-temporal model to a temporal model. Thus, results obtained will be in terms of population versus time.

As shown in Figure 4.4, the infectious human and mosquito proportion for the generic model displays a similar behavior to the result by Esteva and Vargas (1998). In both models, the disease cases reduce and eventually die out. However, the disease takes a longer time to die out in the generic model. There are no infectious human cases by day 100 in Esteva and Vargas (1998) but only occurs after 190 days in the generic model. This is mainly because of the recovered compartment in Esteva and Vargas (1998). Those who recovered from the disease have acquired immunity and do not return to the susceptible state directly. On the contrary, in the generic model, those who recover from the infectious state return to susceptible making them vulnerable to the disease hence explains the longer period taken for the disease to perish from the population. A similar behavior in the decline of the disease is observed for infectious mosquito population. This shows that acquired immunity hasten the eradication of diseases in populations.

When the return of infectious humans who recovered to the susceptible human state is discarded in the generic model, the equation for susceptible human becomes

$$\frac{\partial S_H(t, x)}{\partial t} = D_H \frac{\partial^2 S_H(t, x)}{\partial x^2} + \gamma - c \frac{g N_H(t, x)}{1 + g \lambda N_H(t, x)} \frac{I_M(t, x)}{N_H(t, x)} S_H(t, x) - d_H S_H(t, x).$$

Numerical results by Esteva and Vargas (1998) are reproduced as shown in Figure 4.5. The pattern and magnitude of the proportion of both infectious human and mosquito population are identical.

The results from the generic model are also compared to simulations from Chitnis' temporal model (2005). The difference between these two models is that Chitnis (2005) considers SEIR (Susceptible-Exposed-Infectious-Recovered) compartments for the human

population and SEI (Susceptible-Exposed-Infectious) compartments for the mosquito population. This means that humans who are bitten by infectious mosquitoes will undergo a latent period before they become infectious. Besides that, acquired immunity in human is also being considered by Chitnis (2005) as the recovered compartment is taken into account. Apart from that, Chitnis (2005) also considered transmission of malaria from recovered humans to susceptible mosquito which is not taken into account in the generic model here. Since Chitnis (2005) considered the biting rate as constant and there are density dependent death rates for both populations, these aspects are considered in the parameters shown below. Parameter values for the simulation taken from Chitnis (2005) are displayed in Table 4.2. Initial conditions used were $S_H = 300$, $I_H = 30$, $S_M = 1000$ and $I_M = 50$. In Figure 4.6, the disease prevails in both populations which correspond to Chitnis' results (2005). The numerical result for infectious human closely resembles Chitnis' simulation (2005). However, the simulation of infectious mosquitoes differs slightly, as it increases sharply in the beginning, thereafter it displays a similar behavior to Chitnis' (2005). The magnitude of infectious mosquito population is lower than the result in Chitnis (2005). This is because Chitnis (2005) not only considered transmission of disease by infectious humans, but by recovered humans as well to susceptible mosquitoes and that explains the higher number of infectious mosquitoes.

Table 4.2: Values of parameters used for comparison with Chitnis (2005)

Parameter	Value
diffusion rate for humans, D_H	0
diffusion rate for mosquitoes, D_M	0
human recruitment rate, γ	$5.815 \times 10^{-2} \text{ day}^{-1}$
transmission probability per bite from $I_M \rightarrow S_H$, c	2.0×10^{-2}
human death rate, d_H	$4.212 \times 10^{-5} + (1 \times 10^{-7})N_H \text{ day}^{-1}$
recovery rate, r	$3.704 \times 10^{-3} \text{ day}^{-1}$
mosquito recruitment rate, Λ	$1.72 \times 10^1 \text{ day}^{-1}$ (best fit)
transmission probability per bite from $I_H \rightarrow S_M$, b	3.75×10^{-1}
mosquito death rate, d_M	$0.1429 + (2.279 \times 10^{-4})N_M \text{ day}^{-1}$
biting rate of mosquitoes on humans, β	$5.6 \times 10^{-1} \text{ day}^{-1}$
searching rate of a mosquito, g	β/N_H
time taken for a mosquito to complete a blood meal, λ	0

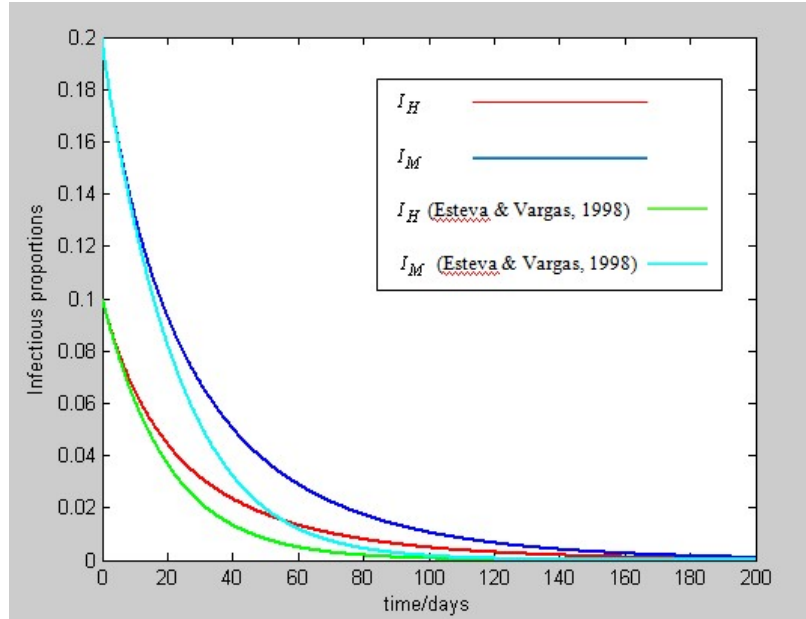


Figure 4.4: Comparison of numerical result of generic model with Esteva & Vargas (1998)

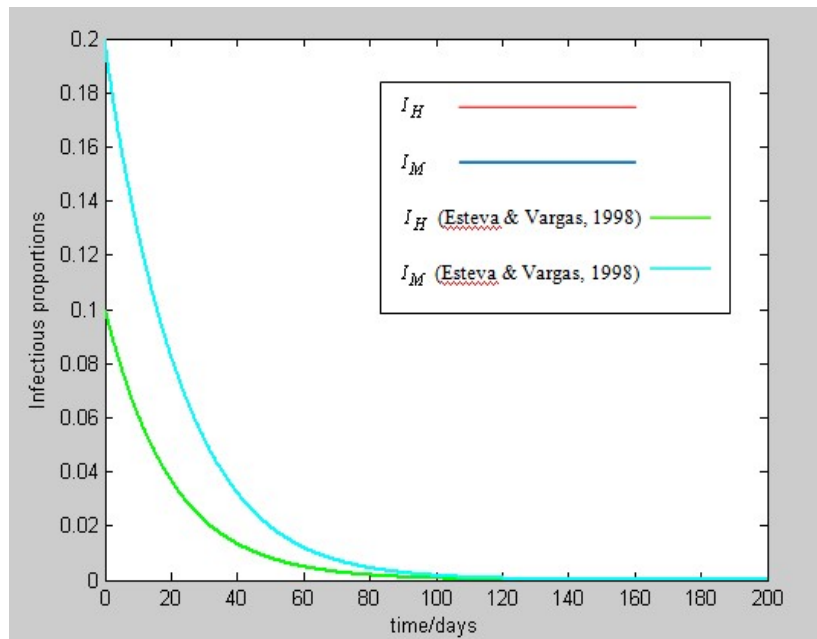


Figure 4.5: Comparison of numerical result of generic model when acquired immunity is added with Esteva & Vargas (1998)

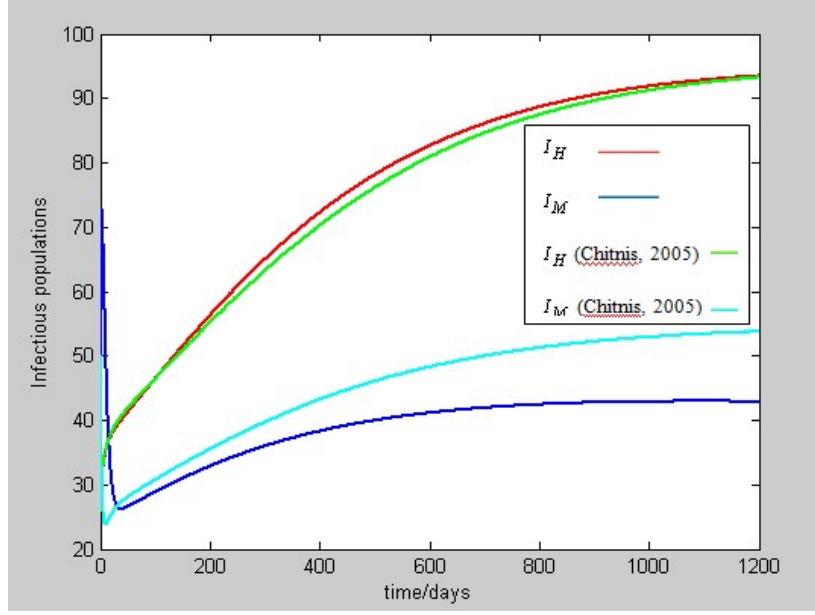


Figure 4.6: Comparison of numerical result of generic model with Chitnis (2005)

Taking into account the interaction between the susceptible human $S_H(t, x)$ and infectious mosquito $I_M(t, x)$, between susceptible mosquito $S_M(t, x)$ and infectious human $I_H(t, x)$; and the effect of diffusion, traveling wave solution is explored. To investigate the spatial spread of the disease, the existence of the traveling wave solution will be analyzed numerically and the minimum spread speed determined. Traveling wave solution represents an invasion process. A minimum spread speed tells us the lowest rate a disease disseminate geographically. In ecology, the spread speed is similar to invasion speed (Yao, Yu & Yuan, 2011). Invasion speed depicts the geographic range at which the population expands. According to the definition of traveling wave by Lewis, Renclawowicz & Driessche (2000), a traveling wave solution is the solution which connects the disease-free $(S_H^0, I_H^0, S_M^0, I_M^0)$ and endemic equilibrium $(S_H^*, I_H^*, S_M^*, I_M^*)$ of the system. It is in the form $S_H(t, x) = sh(x + \zeta t)$, $I_H(t, x) = ih(x + \zeta t)$, $S_M(t, x) = sm(x + \zeta t)$ and $I_M = im(x + \zeta t)$

where ς is the propagation speed. In this system (3.55-3.58), ς describes the speed at which the disease spreads geographically. The traveling wave front connects the two steady states

such that $\lim_{(x+\varsigma t) \rightarrow -\infty} (S_H, I_H, S_M, I_M) = (S_H^0, I_H^0, S_M^0, I_M^0)$ and

$\lim_{(x+\varsigma t) \rightarrow +\infty} (S_H, I_H, S_M, I_M) = (S_H^*, I_H^*, S_M^*, I_M^*)$. Replacing $z = x + \varsigma t$ gives

$$S_H(t, x) = sh(z), I_H(t, x) = ih(z), S_M(t, x) = sm(z), I_M(t, x) = im(z) \text{ and } N_H(t, x) = nh(z)$$

hence the equations (3.55-3.58) gives the following ordinary differential equations (ODEs):

$$\varsigma \frac{dsh}{dz} = D_H \frac{d^2 sh}{dz^2} + \gamma - c \frac{gnh(z)}{1 + g\lambda nh(z)} \frac{im(z)}{nh(z)} sh(z) - d_H sh(z) + rih(z), \quad (4.55)$$

$$\varsigma \frac{dih}{dz} = D_H \frac{d^2 ih}{dz^2} + c \frac{gnh(z - \varsigma \tau_H)}{1 + g\lambda nh(z - \varsigma \tau_H)} \frac{im(z - \varsigma \tau_H)}{nh(z - \varsigma \tau_H)} sh(z - \varsigma \tau_H) - rih(z) - d_H ih(z), \quad (4.56)$$

$$\varsigma \frac{dsm}{dz} = D_M \frac{d^2 sm}{dz^2} + \Lambda - b \frac{gnh(z)}{1 + g\lambda nh(z)} \frac{ih(z)}{nh(z)} sm(z) - d_m sm(z), \quad (4.57)$$

$$\varsigma \frac{dim}{dz} = D_M \frac{d^2 im}{dz^2} + b \frac{gnh(z - \varsigma \tau_M)}{1 + g\lambda nh(z - \varsigma \tau_M)} \frac{ih(z - \varsigma \tau_M)}{nh(z - \varsigma \tau_M)} sm(z - \varsigma \tau_M) - d_m im(z). \quad (4.58)$$

It can be seen that $x + \varsigma(t - \tau_H) = z - \varsigma \tau_H$ and likewise $x + \varsigma(t - \tau_M) = z - \varsigma \tau_M$.

Here the existence of traveling wave solution is shown numerically. To show the existence, the values of c which have positive solution for the ODEs (4.55-4.58) are analyzed for the boundary conditions where

$$sh(-\infty) = S_H^0, ih(-\infty) = I_H^0, sm(-\infty) = S_M^0, im(-\infty) = I_M^0, sh(+\infty) = S_H^*, ih(+\infty) = I_H^*, sm(+\infty) = S_M^* \text{ and } im(+\infty) = I_M^*.$$

Adopting the method discussed by Li and Zou (2009), the finite difference method with iterative technique that approximates equations (4.55-4.58) is used.

In the beginning, $\Re = (-\infty, \infty)$ is shortened to $[-A, A]$ where A is a huge value and dividing $[-A, A]$ equally to $-A = z_1 < z_2 < \dots < z_{2n} < z_{2n+1} = A$ where $z_i = z_1 + (i-1)h$ and

$h = 2A / 2n$. Using the conventional numeric differentiation, the equations (4.55-4.58) are discretized to:

$$\varsigma \frac{sh(z_i) - sh(z_{i-1})}{h} = D_H \frac{sh(z_{i+1}) - 2sh(z_i) + sh(z_{i-1}))}{h^2} + \gamma - c \frac{gnh(z_i)}{1 + g\lambda nh(z_i)} \frac{im(z_i)}{nh(z_i)} sh(z_i) - d_H sh(z_i) + rih(z_i), \quad (4.59)$$

$$\varsigma \frac{ih(z_i) - ih(z_{i-1}))}{h} = D_H \frac{ih(z_{i+1}) - 2ih(z_i) + ih(z_{i-1}))}{h^2} + c \frac{gnh(z_i - \varsigma\tau_H)}{1 + g\lambda nh(z_i - \varsigma\tau_H)} \frac{im(z_i - \varsigma\tau_H)}{nh(z_i - \varsigma\tau_H)} sh(z_i - \varsigma\tau_H) - d_H ih(z_i) - rih(z_i), \quad (4.60)$$

$$\varsigma \frac{sm(z_i) - sm(z_{i-1}))}{h} = D_M \frac{sm(z_{i+1}) - 2sm(z_i) + sm(z_{i-1}))}{h^2} + \Lambda - b \frac{gnh(z_i)}{1 + g\lambda nh(z_i)} \frac{ih(z_i)}{nh(z_i)} sm(z_i) - d_M sm(z_i), \quad (4.61)$$

and

$$\varsigma \frac{im(z_i) - im(z_{i-1}))}{h} = D_M \frac{im(z_{i+1}) - 2im(z_i) + im(z_{i-1}))}{h^2} + b \frac{gnh(z_i - \varsigma\tau_M)}{1 + g\lambda nh(z_i - \varsigma\tau_M)} \frac{ih(z_i - \varsigma\tau_M)}{nh(z_i - \varsigma\tau_M)} sm(z_i - \varsigma\tau_M) - d_M im(z_i). \quad (4.62)$$

These equations are then rearranged to the following algebraic equations

$$(D_H + \varsigma h)sh(z_{i-1}) - (2D_H + \varsigma h + d_H h^2)sh(z_i) + D_H sh(z_{i+1}) - ch^2 \frac{gnh(z_i)}{1 + g\lambda nh(z_i)} \frac{im(z_i)}{nh(z_i)} sh(z_i) + rh^2 ih(z_i) + \gamma h^2 = 0, \quad (4.63)$$

$$(D_H + \varsigma h)ih(z_{i-1}) - (2D_H + \varsigma h + rh^2 + d_H h^2)ih(z_i) + D_H ih(z_{i+1}) + ch^2 \frac{gnh(z_i - \varsigma\tau_H)}{1 + g\lambda nh(z_i - \varsigma\tau_H)} \frac{im(z_i - \varsigma\tau_H)}{nh(z_i - \varsigma\tau_H)} sh(z_i - \varsigma\tau_H) = 0, \quad (4.64)$$

$$(D_M + \varsigma h)sm(z_{i-1}) - (2D_M + \varsigma h + d_M h^2)sm(z_i) + D_M sm(z_{i+1}) - bh^2 \frac{gnh(z_i)}{1 + g\lambda nh(z_i)} \frac{ih(z_i)}{nh(z_i)} sm(z_i) + \Lambda h^2 = 0, \quad (4.65)$$

and

$$(D_M + \zeta h)im(z_{i-1}) - (2D_M + \zeta h + d_M h^2)im(z_i) + D_M im(z_{i+1}) + bh^2 \frac{gnh(z_i - \zeta \tau_M)}{1 + g\lambda nh(z_i - \zeta \tau_M)} \frac{ih(z_i - \zeta \tau_M)}{nh(z_i - \zeta \tau_M)} sm(z_i - \zeta \tau_M) = 0. \quad (4.66)$$

The parameters values are taken from Wang and Zhao (2011) as shown in Table 3.3 and $\lambda = 0.5$, $g = 2$.

Corresponding to these values, the boundary conditions are $sh(z_1) = 10$, $ih(z_1) = 0$, $sm(z_1) = 7$, $im(z_1) = 0$, $sh(z_{2n+1}) = 0.4625$, $ih(z_{2n+1}) = 9.5375$, $sm(z_{2n+1}) = 1.2134$ and $im(z_{2n+1}) = 5.7866$

that is the disease-free equilibrium and endemic equilibrium as the definition of travelling wave is that it connects these two equilibriums. The flowchart of the numerical routine to produce traveling wave solution is shown in Figure 4.7.

From the simulations in Figures 4.8 and 4.9, the existence of positive result for equations (4.55-4.58) shows that the traveling wave front exists and the minimum wave speed is 0.005km/day, for this set of parameter values. This means that the disease invades geographically at the shortest distance of 0.005km in a day in this situation. Any numerical result with $\zeta < 0.005$ will give a negative solution.

Next, the effect of human diffusion coefficient and spatial heterogeneity on the disease risk is investigated. Basic reproduction number R_0 is essential in the study of disease spread as it has a threshold value where the disease-free steady state is asymptotically stable

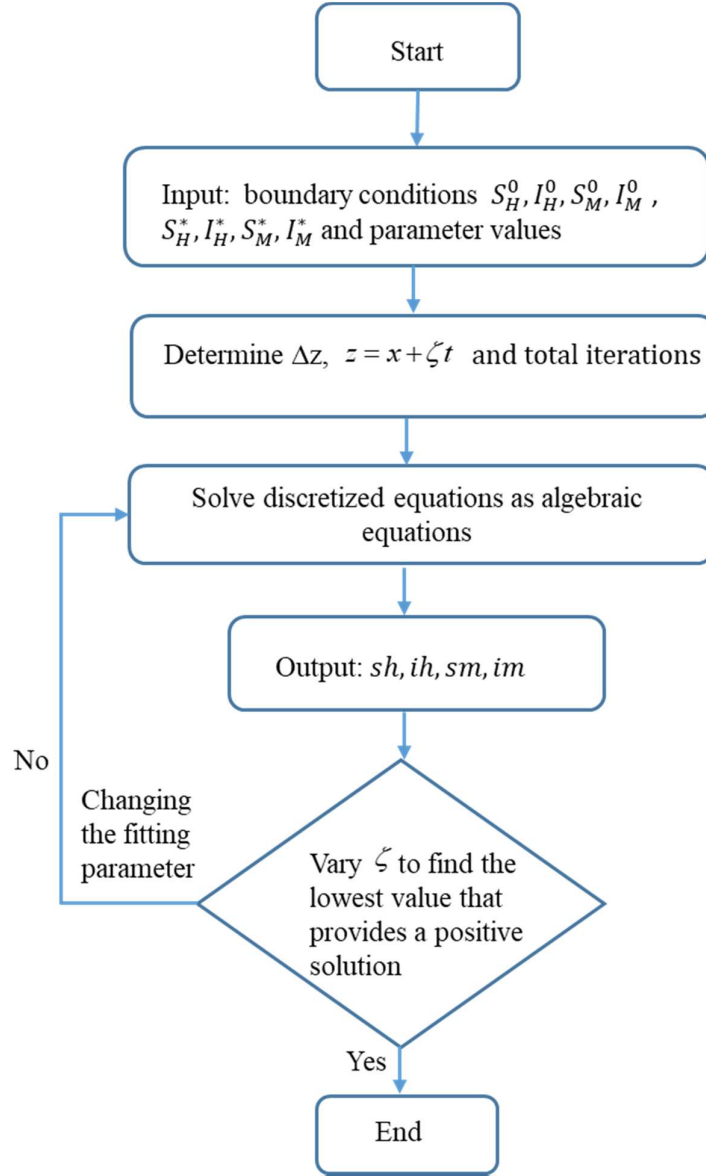


Figure 4.7: Flowchart of the MATLAB numerical procedure to traveling wave solution.

if $R_0 < 1$ and unstable if $R_0 > 1$ (Wang & Zhao, 2011). This means that when $R_0 > 1$, a disease will invade a population or else the disease will die out (Choisy, Guegan & Rohani, 2007). Therefore, to find out whether the increment of human diffusion, D_H and spatial heterogeneity p will contribute to the prevalence of the disease in the population, the

sensitivity of R_0 is studied numerically, parameters used are mainly taken from Wang and Zhao (2011) as in Table 3.3 and $\lambda = 1, r = 0.5 \text{ day}^{-1}, b(x) = 0.0682(1 + \cos(\pi x))$ and $c(x) = 0.1364(1 + \cos(\pi x))$. The effect of spatial heterogeneity is to be observed using parameter values from Wang and Zhao (2011) except for mosquito recruitment rate which is not available. It is found that when $\Lambda = 0.006$ and the transmission probability is varied according to the simpler form of sinusoidal wave (Choisy, Guegan & Rohani, 2007), transmission probability per bite from $I_M \rightarrow S_H$ is $c(x) = 0.1364(1 + p \cos(\pi x))$ and transmission probability per bite from $I_H \rightarrow S_M$ is $b(x) = 0.0682(1 + p \cos(\pi x))$, both taken from Wang and Zhao (2011), the shift from $R_0 < 1$ to $R_0 > 1$ can be clearly seen. This means that the shift can be seen from the steady state where the disease does not exist in the population to the state where the disease invades the population. The parameter p is the magnitude of infection heterogeneity. Increasing p means the higher the heterogeneity for disease spread. In Figure 4.10, it is shown in the graph that when p increases from 0 to 1, R_0 rises and $R_0 = 1$ when $p \approx 0.4$. The disease dies out when $p < 0.4$. This shows that transmission probability which is spatially heterogeneous aggravate the risk of infection.

Next, the influence of human diffusion coefficient D_H on the transmission of the disease is observed numerically. It is found that R_0 is a decreasing function of D_H which is in agreement with the conclusion drawn by Wang and Zhao (2011). However, for the given Λ and set of parameter values, $R_0 > 1$ thus the disease prevails for all values of D_H . The result is not shown here as the interest is in the shift from $R_0 > 1$ to $R_0 < 1$ because that indicates the disease will eventually extinct from the population. Since the interest here is to study the transition of R_0 from above 1 to below 1 and the value for Λ is unavailable, the

value for Λ is reduced until there is a clear result of the conversion. It is found that at 0.00385, a clear depiction of the transition can be seen. From Figure 4.11, it can be observed that $R_0 < 1$ when $D_H > 0.021$. As $R_0 < 1$ indicates that the disease-free equilibrium is stable, this means that the disease dies out as D_H increases after 0.021. Hence, given the set of parameter values, the disease dies out with the increment of diffusion of humans. This agrees with Wang and Zhao (2011) that random mobility of humans can reduce infection.

In addition, to inspect the influence of spatial heterogeneity, transmission probability as mentioned $c(x)$ and $b(x)$, are applied, Λ is kept at 0.00385 and it is clear in Figure 4.12 that the disease does not exist as $0.68 < R_0 < 0.88$ meaning that $R_0 < 1$ for all values of p . Hence when recruitment of mosquitoes is reduced to a certain value, the disease will eventually cease to exist. This shows that if mosquito breeding area can be reduced to a certain level, the disease can be eradicated.

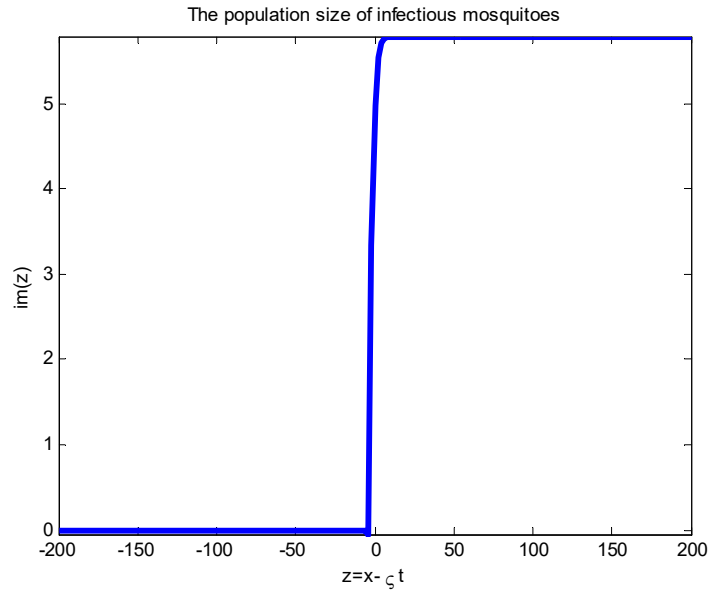


Figure 4.8: The existence of traveling wave front for infectious mosquito population when speed $\zeta = 0.005\text{km/day}$.

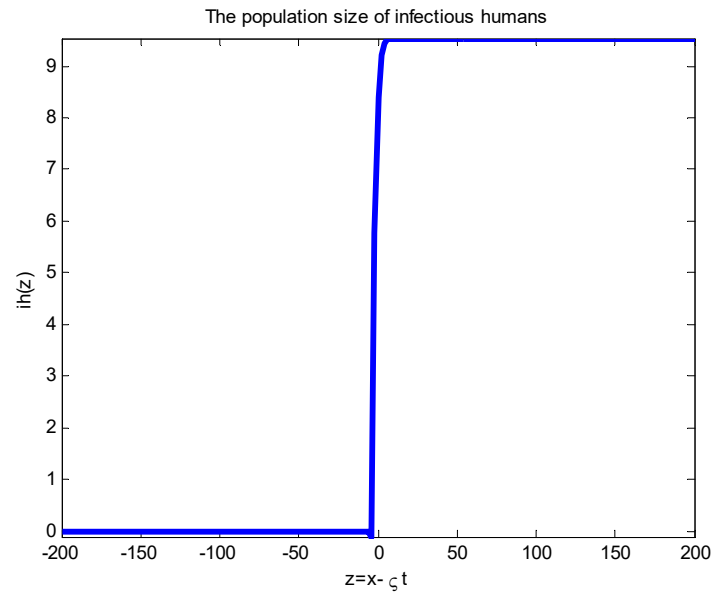


Figure 4.9: The existence of traveling wave front for infectious human population when speed $\varsigma = 0.005\text{km/day}$.

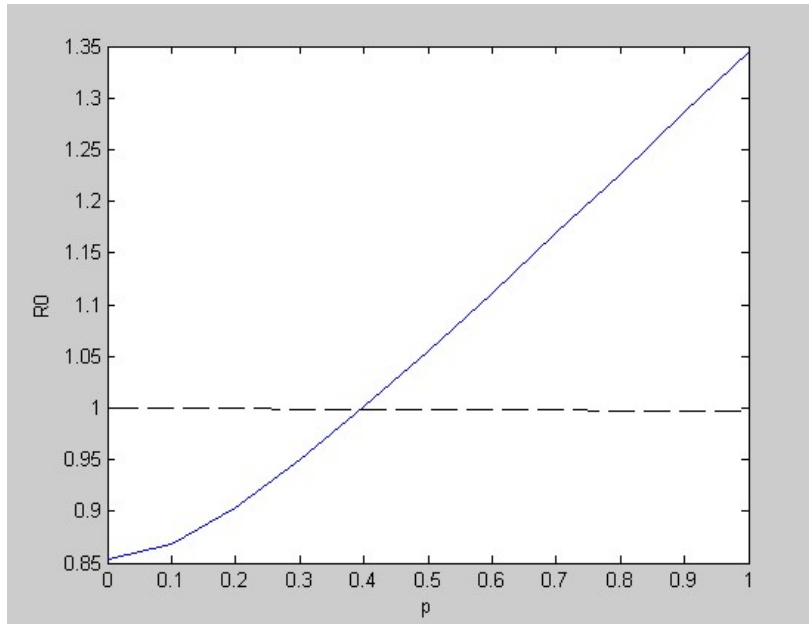


Figure 4.10: R_0 is an increasing function of p

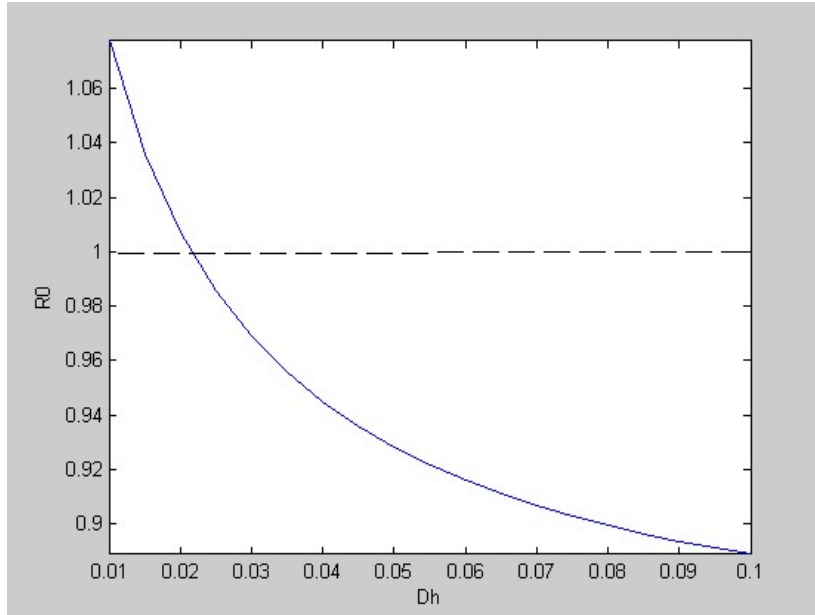


Figure 4.11: R_0 is a decreasing function of D_H

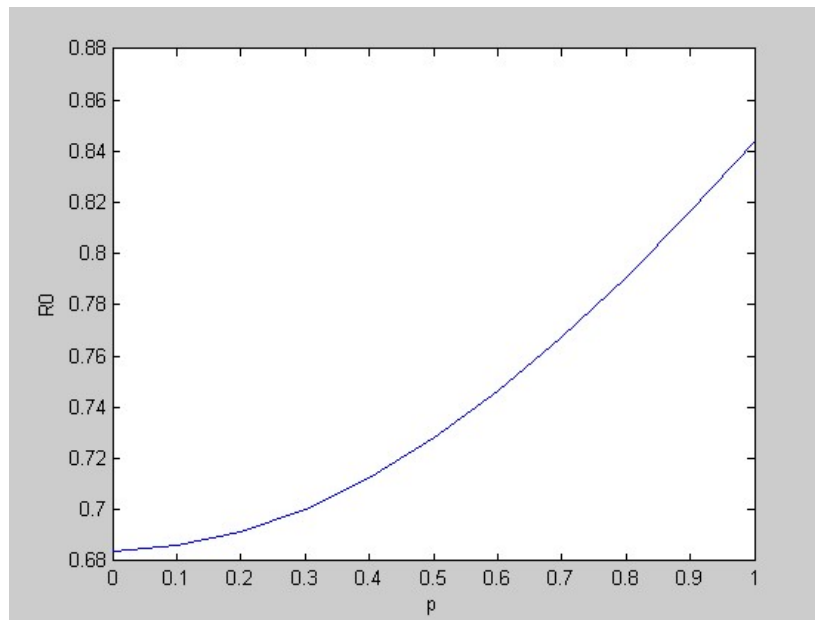


Figure 4.12: R_0 is an increasing function of p and the disease dies out when $\Lambda = 0.00385$.

4.3 Discussion

The spatio-temporal generic model for mosquito-borne diseases is analyzed theoretically by investigating the stability of the disease-free equilibrium point for the system when basic reproduction number $R_0 < 1$ and unstable when $R_0 > 1$. Furthermore, the existence of endemic equilibrium is inspected. Using parameter values from Wang and Zhao (2011), simulation results for both density of human and mosquito population for the generic model are found to be almost identical to that of Wang and Zhao's dengue model (2011). The generic model can also be reduced to the initial model when $g = \frac{\beta}{N_H}$ and $\lambda = 0$ are set therefore the results by Lou and Zhao (2011) are reproduced. By setting diffusion rates as zero, the reaction-diffusion model can immediately be converted to a temporal model. Simulation results from the generic model depict behavior which is similar to the ordinary differential equations model for malaria (Chitnis, 2005) and dengue (Esteva & Vargas, 1998). The generic model is able to reproduce result by Chitnis (2005) if acquired immunity is included. Comparison with Esteva and Vargas (1998) shows that numerical simulation displays similar behavior for both populations. In addition, taking into account density dependent death rate for human and mosquito, the generic model produces results which are complementary to Chitnis (2005). It is shown numerically that the traveling wave front exists and the minimum spread speed for the set of parameter values (Wang & Zhao, 2011) is found to be 0.005 km/day. Simulation shows that increment of human diffusion decreases the basic reproduction number hence the number of secondary cases from an infectious individual dwindles. Thus, the result entails that random movement of human causes the infection risk to reduce. This is likely because when an individual moves randomly, the contact between a susceptible and infectious individual is reduced thus the reduction in the

risk. However, spatially heterogeneous transmission of disease contributes to the hike in the basic reproduction number thus increasing the risk of infection. In the next chapter, the generic model is validated by exploring its ability to reproduce actual cases for three different mosquito-borne diseases. Firstly, the simulations from the generic model for transmission of mosquito-borne diseases are compared with actual malaria and dengue cases in four different districts in Sarawak without considering the diffusion rate. After that, the speed of random movement of human and mosquito populations are included and numerical results compared once more with the actual incidences in the different districts. Moreover, the predicted Zika virus cases are compared with actual incidences in the Rio de Janeiro, and several different neighborhoods in Brazil.

CHAPTER 5

VALIDATION OF REACTION-DIFFUSION GENERIC MODEL

5.0 Introduction

In the previous chapter, the stability of the disease-free equilibrium, existence of endemic equilibrium and the basic reproduction number are examined. The generic model is found to be able to produce simulations which are in good agreement with Lou and Zhao's (2011) and Wang and Zhao's (2011) reaction-diffusion models for malaria and dengue respectively. Moreover, the generic model's numerical results resemble the temporal models' simulations by Chitnis (2005) for malaria and Esteva and Vargas (1998) for dengue. Existence of traveling wave front for the generic model was analyzed numerically. Through numerical simulations, it is shown that random movement of humans contributes to the reduction in the spread of mosquito-borne diseases. Besides, spatial heterogeneity in the transmission of diseases increases the risk of infection.

In this chapter, the validation of the generic model is carried out by investigating its ability to reproduce the actual cases of three different mosquito-borne diseases. A good estimator would be able to estimate as close as possible to the true value. To evaluate the accuracy of the generic model, Root Mean Square Error (RMSE) and Mean Absolute Percentage Error (MAPE) for each comparison is determined. Firstly, notified weekly malaria cases in four districts in Sarawak, Malaysia, are collected from data provided by Sarawak Health Department (2012). Data for notified weekly dengue cases in four districts in Sarawak are also from same health department (2012). For the third mosquito-borne

disease, Zika virus, weekly cases in Rio de Janeiro and four neighborhoods in Brazil are from a research discussion with Artificial Intelligence in Medical Epidemiology (AIME) (research engagement, September 7, 2016). The districts in Sarawak are chosen for the highest overall reported malaria and dengue cases in the state during the specific duration. Likewise, the four neighborhoods in Brazil have the highest reported Zika virus cases during the outbreak of the disease in 2016. The study areas and duration of the actual reported cases are shown in Table 5.1.

Table 5.1: Summary of properties for actual data for malaria, dengue and Zika virus

Mosquito-borne disease	Location	Duration
Malaria	Sarawak: Kapit, Song, Belaga, Marudi	Temporal & Spatio-temporal : Week 39, 2012-Week 22, 2013
Dengue	Sarawak: Kuching, Sibu, Bintulu, Miri	Temporal: Week 39,2012 – Week 9 ,2015 Spatio-temporal: Week 39- Week 47, 2012
Zika Virus	Brazil: Rio de Janeiro, Guaratiba, Campo Grande, Santa Cruz, Bangu	Temporal & Spatio-temporal : Week 52, 2015-Week 24, 2016

5.1 Results of Simulation with Actual Malaria Cases

Malaria is a life threatening disease caused by *Plasmodium* parasites and spread to human beings by *Anopheles* mosquito bites. Nearly half of the world's population was at risk of malaria in 2015 (World Health Organization, 2016a). Symptoms of malaria start appearing typically seven days after an infective bite. The common symptoms of malaria are fever, shivering, joint pain, vomiting, anemia and convulsions. *Plasmodium falciparum* malaria can cause death if not treated. Controlling transmission by mosquito is one of the most important way to reduce and prevent malaria. The usage of insecticide-treated mosquito nets, spraying with insecticide and mosquito repellent are some examples of vector control.

Since the generic mosquito-borne diseases model is formulated to model different types of mosquito-borne diseases, the capability of this model in reproducing a particular mosquito-borne infection cases, is examined. In this section, numerical results from the generic model are compared with 36 weekly notified malaria cases. Notified malaria cases in Sarawak are reported in Sarawak Weekly Epid News and all malaria cases are notified within 24 hours as reported by the Vector Borne Disease Control Section (Sarawak Health Department, 2012). Simulation results from the generic model are compared with actual prevalence in four districts in Sarawak, namely Kapit, Song, Belaga and Marudi from week 39 in 2012 to week 22 in 2013.

In this initial step of validation, movement of both human and mosquito population are not taken into account thus, diffusion rates for human and mosquito population are set to zero. Therefore, the system of PDEs will be reduced to an ODEs model. The subsequent steps taken are discussed in Section 3.2. Parameters used are stated in Table 5.2. Most of these parameter values are taken from literature, unless unstated. This means that the value

is determined when the best fit comparison is obtained. As there is lack of information for mosquito population in the districts in Sarawak, the initial data for susceptible and infectious mosquito are estimated to fit the actual prevalence since the actual values are unavailable. Parameter values for mosquito recruitment rate, Λ is assumed by fitting the simulated result to actual cases as it depends on the birth rate of mosquitoes multiplied by total female mosquitoes in the particular district and the actual number of female mosquitoes is unknown. If the average lifespan of mosquito in ideal situation is considered, mosquito death rate, d_M is 0.333-0.5 week⁻¹ (Malaria site, 2015). Furthermore, Bruce-Chwatt (1985) discussed that the parasite needs time to develop in a mosquito (8–35 days). This indicates that the longer the mosquito life span, the more effective the mosquito becomes as a vector. Ndoen et al. (2012) studied the effect of mosquito longevity to malaria incidences in West Timor and Central Java. They concluded that longevity of mosquitoes in West Timor is higher hence the higher incidences. This suggests that *Anopheles* mosquitoes may live longer than 35 days and that longevity differ in different places. However, the result which is obtained using this range of value differs from the actual cases. According to an article by Centers for Disease and Prevention on *Anopheles* mosquitoes, it is not possible to measure directly the life span of mosquitoes in nature (Centers for Disease Control and Prevention, 2015). Hence the value is varied until the best fit curve is obtained. The values for mosquito death rate in the four locations differ and are lower than the predicted value for ideal situation. This means that fewer mosquitoes die in a week in comparison to the ideal situation. As the number of mosquitoes in the population is inconclusive, there might be fewer mosquitoes than predicted in real life or the actual lifespan of mosquitoes are longer than reported.

The value of the total human population for Kapit, Song, Marudi and Belaga in 2012 are estimated from Sarawak Facts and Figures 2012 (State Planning Unit, 2012). The

estimated values are calculated using exponential growth (World Health Organization, 2017a) formula, $x_t = x_0(1 + q)^t$ where x is population size, t is time and q is growth rate.

The q values for each district is shown in Table 5.2.

Table 5.2: Values of parameters used for Kapit, Song, Marudi and Belaga for simulation of model.

Parameter	Kapit	Song	Belaga	Marudi	Source
diffusion rate for humans, D_H	0	0	0	0	NIL
diffusion rate for mosquitoes, D_M	0	0	0	0	NIL
human recruitment rate, γ	201 week ⁻¹	201 week ⁻¹	201 week ⁻¹	201 week ⁻¹	Department of Statistics Malaysia Sarawak (2013)
time for a mosquito to consume blood per bite, λ	3.5 week	3.5 week	3.5 week	3.5 week	Wang and Zhao (2011)
searching rate of a mosquito, g	2.8 week ⁻¹	2.8 week ⁻¹	2.8 week ⁻¹	2.8 week ⁻¹	Chitnis (2005)
transmission probability per bite from $I_M \rightarrow S_H$, c	1.2×10^{-2}	1.2×10^{-2}	1.2×10^{-2}	1.2×10^{-2}	Nedelman (1984)
human death rate, d_H	8.27×10^{-5} week ⁻¹	8.27×10^{-5} week ⁻¹	8.27×10^{-5} week ⁻¹	8.27×10^{-5} week ⁻¹	Department of Statistics Malaysia Sarawak (2013)
recovery rate, r	1.4×10^{-2}	1.4×10^{-2}	1.4×10^{-2}	1.4×10^{-2}	Williams and Boland (2002)

Table 5.2 continued

mosquito death rate, d_M	$5.5 \times 10^{-2} \text{week}^{-1}$	$1.0 \times 10^{-1} \text{week}^{-1}$	$1.1 \times 10^{-1} \text{week}^{-1}$	$1.1 \times 10^{-1} \text{week}^{-1}$	
incubation period in humans, τ_H	1.4 week	1.4 week	1.4 week	1.4 week	Anderson and May (1992)
incubation period in mosquitoes, τ_M	1.4 week	1.4 week	1.4 week	1.4 week	Cox (2002)
Average annual growth rate (%), q	0.19	0.41	4.83	-1.25	State Planning Unit (2012)

To examine the quality and predictability power of the generic model, the measure used is RMSE. An error is the difference between the real value and the predicted value, thus the lower the errors, the better the model. RMSE is utilized to compare the difference between values predicted by a model and the values actually observed. The usage of RMSE is typical as it makes an appropriate common purpose error metric for numerical predictions. The RMSE of a model prediction is defined as the square root of the mean squared error:

$$\text{RMSE} = \sqrt{\frac{\sum_{i=1}^n (\tilde{X}_i - X_i)^2}{n}} \quad \text{where } \tilde{X}_i \text{ is observed or real values and } X_i \text{ is modelled values}$$

at time i . To compare RMSE with different units, non-dimensional forms of the RMSE are beneficial. Normalized RMSE can be obtained by normalizing the RMSE to the range of the

observed data, $\text{NRMSE} = \frac{\text{RMSE}}{\tilde{X}_{\max} - \tilde{X}_{\min}}$. Another way to assess forecast accuracy is MAPE.

MAPE expresses the size of the error in generic percentage term therefore easily interpreted.

The formula is: $\frac{100}{n} \sum_{i=1}^n \frac{|Actual - Forecast|}{Actual}$.

The initial data used for Kapit district is $S_H = 57768$, $I_H = 8$, $S_M = 165000$ and $I_M = 3000$. In Figure 5.1, it can be seen that the simulation result is complementary to the actual prevalence in Kapit for 36 weeks. The number of malaria cases increases from the initial state until week 35. The estimation of error incurred in this comparison of the observed and modelled cases is measured in terms of normalized root mean square error (NRMSE). The NRMSE for this particular comparison is 0.033 and accuracy percentage, 97.3%. The comparison between actual prevalence and numerical result of malaria cases in Song district is shown in Figure 5.2 and there is a close resemblance in terms of behavior and the magnitude of cases where the disease prevails until the end of the 35 weeks shown. Initial condition for Song is $S_H = 20211$, $I_H = 4$, $S_M = 30000$, $I_M = 1800$, the NRMSE is 0.06 and accuracy percentage, 94.91%.

As shown in Figure 5.3, the numerical simulation shows similar behavior to that of the weekly notified malaria cases in Belaga and the initial data is $S_H = 37325$, $I_H = 6$, $S_M = 1200000$ and $I_M = 3000$. However, from week 9 to week 23, the number of predicted cases is higher than actual. NRMSE is found to be 8.0×10^{-2} and accuracy percentage 92.14%. In Figure 5.4, the number of actual weekly cases in Marudi and the predicted cases depict rise from week 0 to week 35, the initial data is $S_H = 61731$, $I_H = 7$, $S_M = 400000$ and $I_M = 2300$. From week 0 to week 7 the number of actual cases and predicted are almost identical but from week 7 to week 25, the number of predicted cases is slightly higher than the actual cases in the range of 3 to 9 cases. The number of cases is the same from week 26 to 28. From week 29 to 35, the number of actual cases is more than predicted in the range from 3 to 5. It is imperative to note that the overall

pattern of the cases is similar. NRMSE for this particular set of data is 0.07 and percentage accuracy, 93.12%.

To obtain the best fit comparison for each location, the mosquito death rate, d_M is varied and the value is found to be different (see Table 5.2). This coincides with the study carried out by Ndoen et al. (2011) that there are large differences in the mosquito longevity between two locations which is a major contributor in the transmission of malaria. There appears to be slight drop in the actual cases from week 10 to week 25 for both Belaga and Marudi which the generic model could not capture accurately. Hence, there appear to be a pattern where the time span considered could be split into every ten weeks to increase prediction accuracy.

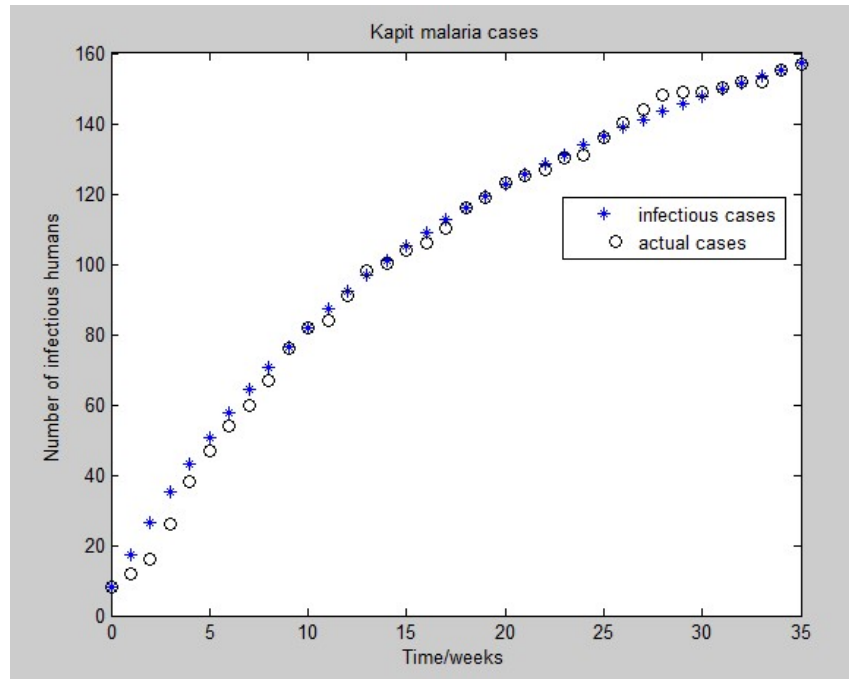


Figure 5.1: Weekly malaria cases in Kapit from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model.

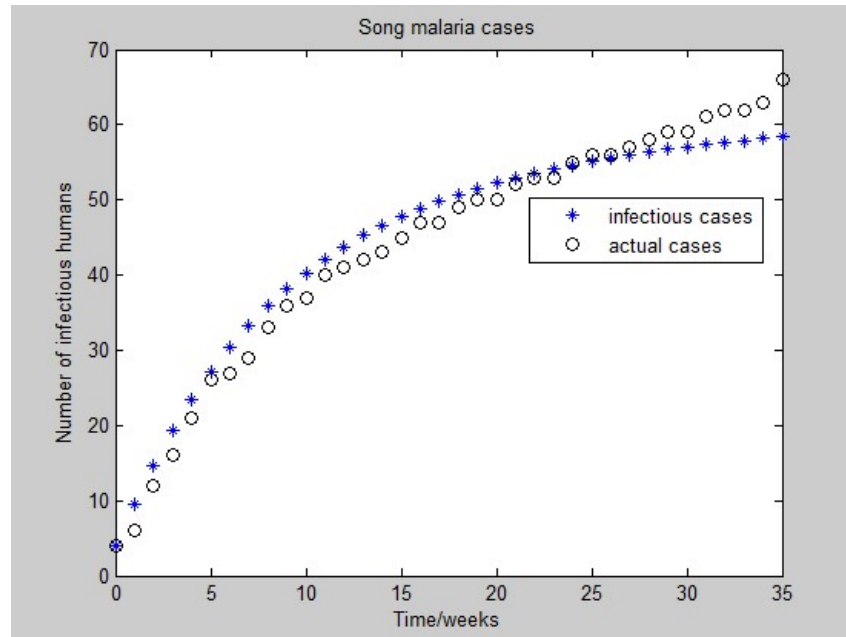


Figure 5.2: Weekly malaria cases in Song from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model.

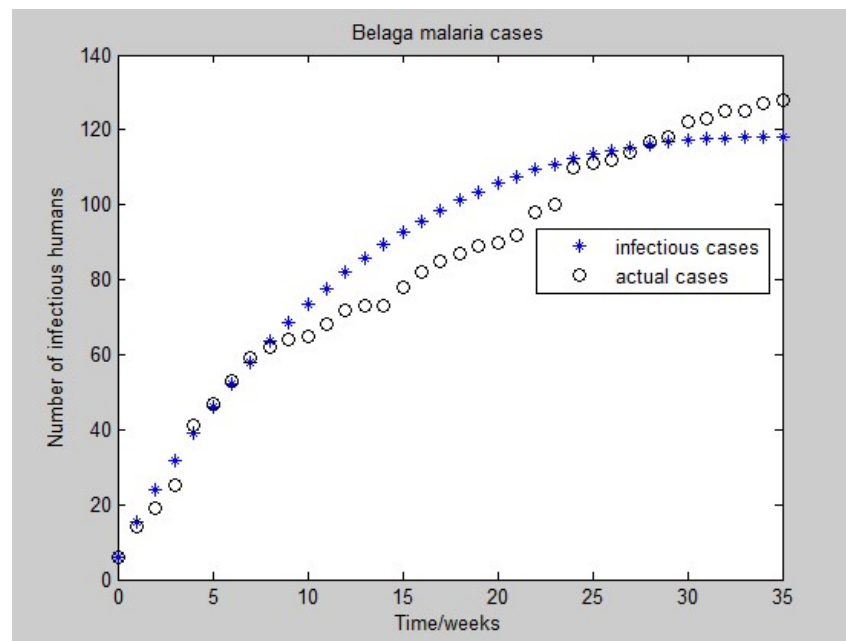


Figure 5.3: Weekly malaria cases in Belaga from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model.

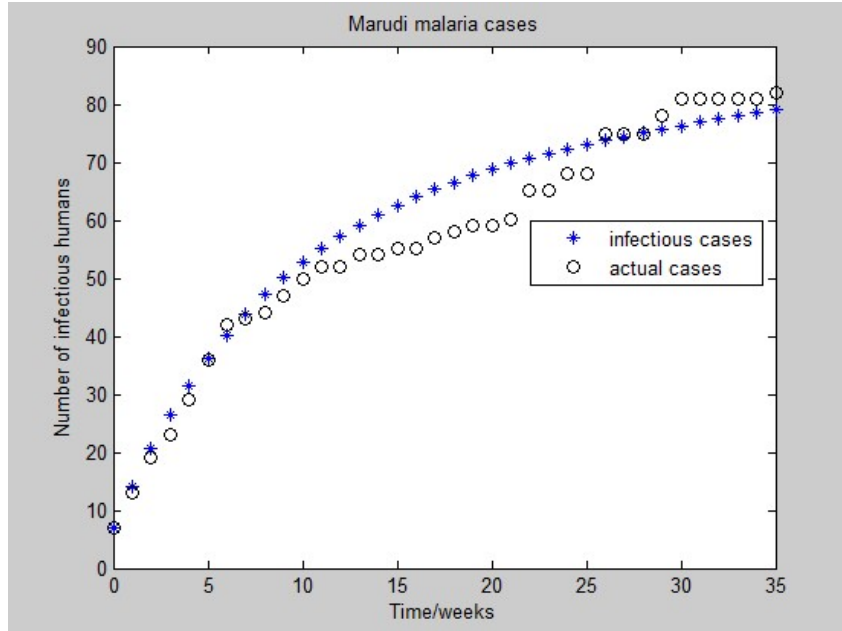


Figure 5.4: Weekly malaria cases in Marudi from week 39 in 2012 to week 22 in 2013 and predicted cases from temporal generic model.

Subsequently, the ability of the spatio-temporal generic model to reproduce malaria cases in these four districts in Sarawak for the same period is investigated. This time the movement of both human and mosquito population is considered. Diffusion rate for human and mosquito population are assumed to be $10\text{km}^2\text{week}^{-1}$. The values for the recruitment and death rate of mosquitoes are considered the same for all locations as the main interest is to keep all parameter values as constant across locations. This is because data availability can be an issue thus it is practical to not consider location dependent parameters unless necessary. New parameter values used are stated in Table 5.3.

The initial data for susceptible and infectious compartments for both human and mosquito population is represented by polynomial function. To obtain the actual density of infectious human in Song, Kapit, Belaga and Marudi, the prevalence of malaria is divided by the area of each district. The values of each area is shown in Table 5.3. In general,

parameter values are kept constant across locations to maintain the genericity of the model. The reason is to reduce the need of different parameter values for each location as accurate parameter values are difficult to obtain.

Table 5.3: New parameter values used for Kapit, Song, Marudi and Belaga for simulation of model.

Parameter	Kapit	Song	Belaga	Marudi
diffusion rate for humans, D_H	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$
diffusion rate for mosquitoes, D_M	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$	$1 \times 10^1 \text{ km}^2 \text{ week}^{-1}$
mosquito recruitment rate, Λ	1.056×10^3	1.056×10^3	1.056×10^3	1.056×10^3
mosquito death rate, d_M	$4.85 \times 10^{-2} \text{ week}^{-1}$	$4.85 \times 10^{-2} \text{ week}^{-1}$	$4.85 \times 10^{-2} \text{ week}^{-1}$	$4.85 \times 10^{-2} \text{ week}^{-1}$
area	$1.56 \times 10^4 \text{ km}^2$	$3.94 \times 10^3 \text{ km}^2$	$1.94 \times 10^4 \text{ km}^2$	$2.20 \times 10^4 \text{ km}^2$

The distances between these locations are calculated according to the latitude and longitude; thus the locations, $x = (\text{Song, Kapit, Belaga, Marudi}) = (0, 43, 200, 375)$ is acquired. The unit is in kilometres. Polynomial functions are found to be better to represent the density data for each of these locations.

Hence, the initial data used are:

$$\begin{aligned}
S_H(\varphi, x) &= -1.55 \times 10^{-7} x^3 + 1.453 \times 10^{-4} x^2 - 3.891 \times 10^{-2} x + 5.135, \\
I_H(\varphi, x) &= -1.229 \times 10^{-11} x^3 + 8.003 \times 10^{-8} x^2 - 1.454 x + 0.001, \\
S_M(\psi, x) &= -8.067 \times 10^{-6} x^3 + 3.249 \times 10^{-3} x^2 - 5.605 \times 10^{-2} x + 7.624, \\
&\text{and} \\
I_M(\psi, x) &= -1.697 \times 10^{-8} x^3 + 1.193 \times 10^{-5} x^2 - 2.807 \times 10^{-3} x + 0.3, \\
\forall \varphi &\in [-\tau_H, 0], \psi \in [-\tau_M, 0], x \in [0, 375].
\end{aligned}$$

Neumann boundary condition is applied where

$$\begin{aligned}
\frac{\partial S_H(0, t)}{\partial x} &= 0, \frac{\partial I_H(0, t)}{\partial x} = 0, \frac{\partial S_M(0, t)}{\partial x} = 0, \frac{\partial I_M(0, t)}{\partial x} = 0 \quad \text{and} \\
\frac{\partial S_H(375, t)}{\partial x} &= 0, \frac{\partial I_H(375, t)}{\partial x} = 0, \frac{\partial S_M(375, t)}{\partial x} = 0, \frac{\partial I_M(375, t)}{\partial x} = 0.
\end{aligned}$$

As mentioned earlier, the data for mosquito population in the districts in Sarawak is not available, therefore the initial data for susceptible and infectious mosquito are estimated to fit the actual prevalence. To obtain best fit, the objective is to attain a very low RMSE. The parameter value for mosquito such as death rate d_M is determined by finding the best fit numerical result compared to prevalence in the four districts. As it is not possible to measure directly the life span of mosquitoes in nature, the value is varied until the best fit curve is acquired. The values for mosquito death rate in the four locations differ and are lower than the predicted value for ideal situation. It is challenging to decide the value of the speed of the random movement of both human and mosquito populations, henceforth the diffusion rate for human population, D_H and mosquito population D_M are decided upon comparison of actual and simulation of the infectious human density. Figure 5.5 depicts the actual infectious human density, taking into account the cases in Song, Kapit, Belaga and Marudi from

locations $[0,375]$ in kilometers and time $[0,35]$ weeks. It is clear from the numerical result produced from the generic model displayed in Figure 5.6 that the magnitude and behavior of the infectious human density is in good agreement with the illustration in Figure 5.5.

Next, the simulated infectious human density in each of the four districts is compared with that of the actual notified cases. The initial conditions used are the same except for:

$$I_M(\psi, x) = -6.857 \times 10^{-8} x^3 + 4.192 \times 10^{-5} x^2 - 7.141 \times 10^{-3} x + 0.4, \forall \varphi \in [-\tau_M, 0], x \in [0, 375].$$

This is because the change in the initial data for infectious mosquito population actually increases the accuracy of the model in producing simulated cases which are similar to actual cases. Hence, the initial condition plays a vital role in getting a good approximation. The simulated density is graphed on the same axis as the actual cases to compare them visually and the Root Mean Square Error (RMSE) is calculated. In Figure 5.7, it can be seen from the graph that the density of weekly actual malaria cases in Song and the predicted cases increases from week 0 to week 35. The disease prevails in the population and displays similar behavior for both the actual and simulated cases. RMSE for this particular set of data is 6.2334×10^{-4} and accuracy percentage, 95.21%.

The numerical result of the generic model's density of malaria infectious humans in Kapit resembles the actual notified cases closely as depicted in Figure 5.8. The RMSE is a low 4.5217×10^{-4} and accuracy percentage is 94.63%. Malaria cases surge from week 0 to week 35 and are alike in both cases. As shown in Figure 5.9, the actual density of infectious humans in Belaga is slightly higher but both display similar growth of the disease until week 35. The RMSE and accuracy percentage are calculated to be 4.1168×10^{-4} and 92.33% respectively. Finally, the comparison of actual prevalence and simulated cases in Marudi can

be seen in Figure 5.10. The actual cases are higher than the simulated cases from the first week to fifteenth week. After that, the actual cases are lower from week 18 onwards. In general, the growth of the simulated cases is higher in comparison to the actual cases. Although the result is visually inaccurate, the RMSE for this comparison, 8.0379×10^{-4} and accuracy percentage is found to be 80%. This may be due to the low infectious human density. As the accuracy for Marudi is lower than the rest, the parameter recruitment rate of mosquito Λ is slowly increased until the best fit is obtained. The time span is reduced to 5 weeks to allow a better fit. The motivation is to find out the number of weeks ahead that the generic model can accurately predict. It is found that when $\Lambda = 2.2 \times 10^5$, the infectious human density for the first two weeks are met as shown in Figure 5.11. However, the predicted cases are higher than the actual ones from weeks 3 to 5. The ability of the generic model to predict two weeks ahead accurately is significant to public health and policymakers. Having an accurate prediction of two weeks ahead, enables authorities to focus their control measures in specific locations. Thus, it is more effective than carrying out a general large scale control strategy in the state or national level. This indicates that the admission of susceptible mosquito is higher in Marudi, suggesting that there may be more breeding sites in this district. Movement can be carried out to reduce mosquito breeding grounds such as alerting the community to dispose old tires, empty containers, and fix drainage issues.

The temporal and spatio-temporal generic model is found to be able to reproduce actual cases in the four locations. The disease is endemic in all four districts for period studied. The simulated cases for Song and Kapit are found to be in good agreement with that of the actual notified cases. Numerical results for Belaga and Marudi shows similar behavior that is the disease prevails in the population nevertheless the magnitudes differ slightly.

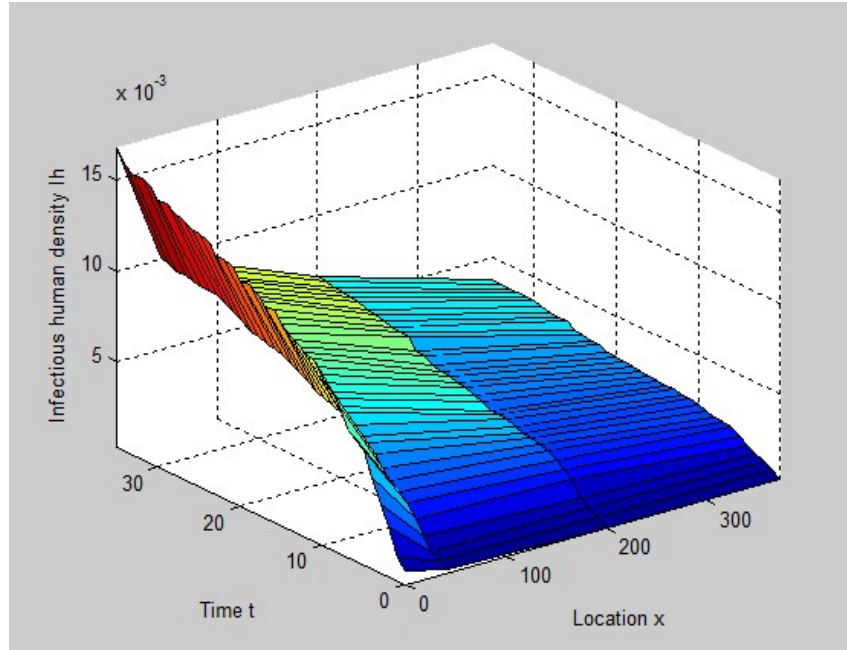


Figure 5.5: The actual density of infectious humans in time and space.

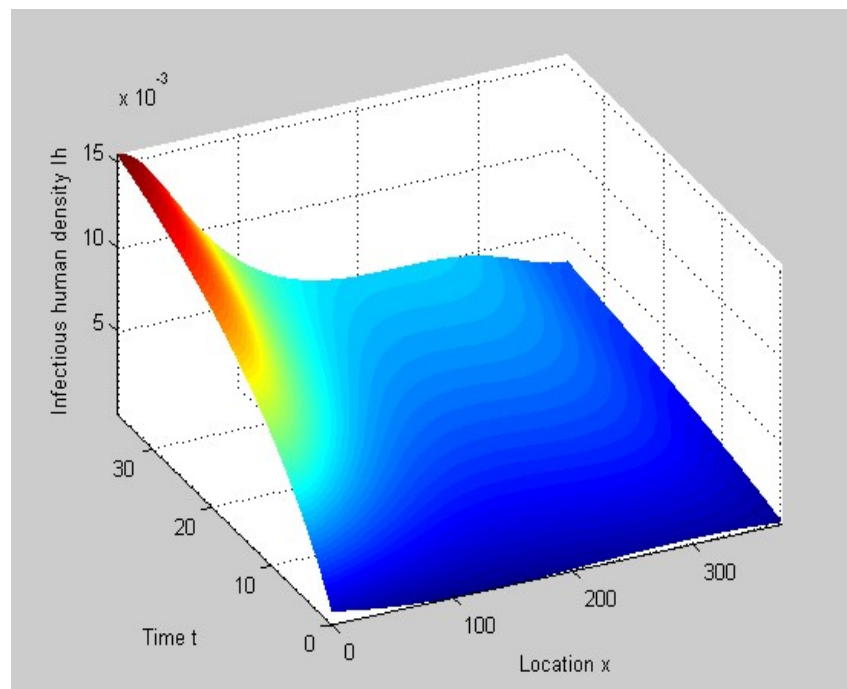


Figure 5.6: The simulated density of infectious humans in time and space

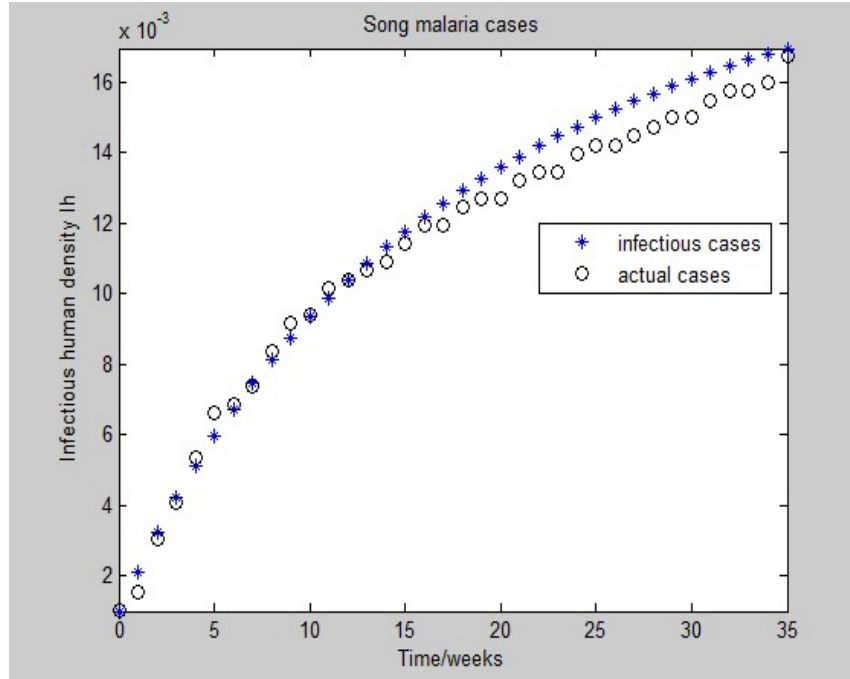


Figure 5.7: Weekly actual malaria cases in Song from week 39 in 2012 to week 22 in 2013 and simulated cases from the spatio-temporal generic model.

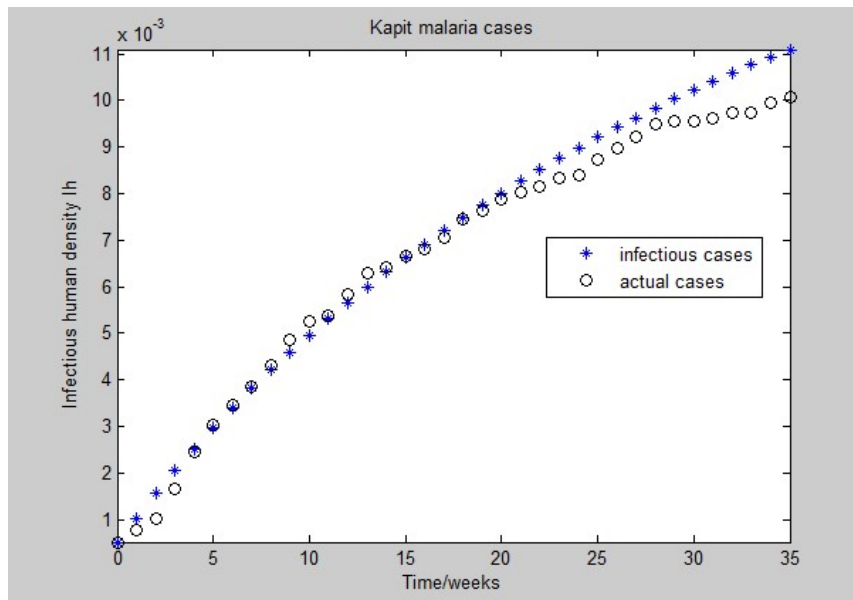


Figure 5.8: Weekly actual malaria cases in Kapit from week 39 in 2012 to week 22 in 2013 and simulated cases from the spatio-temporal generic model.

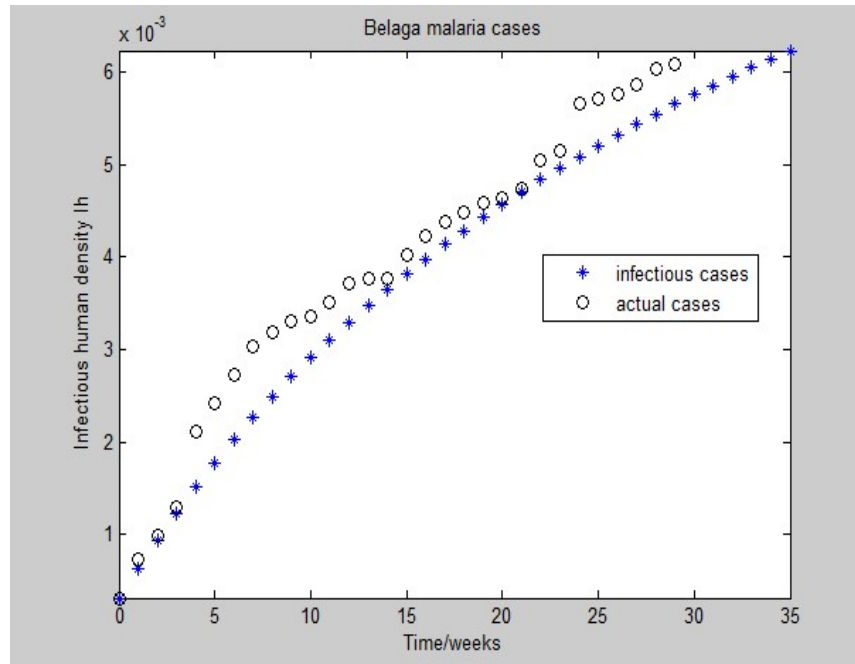


Figure 5.9: Weekly actual malaria cases in Belaga from week 39 in 2012 to week 22 in 2013 and simulated cases from the spatio-temporal generic model.

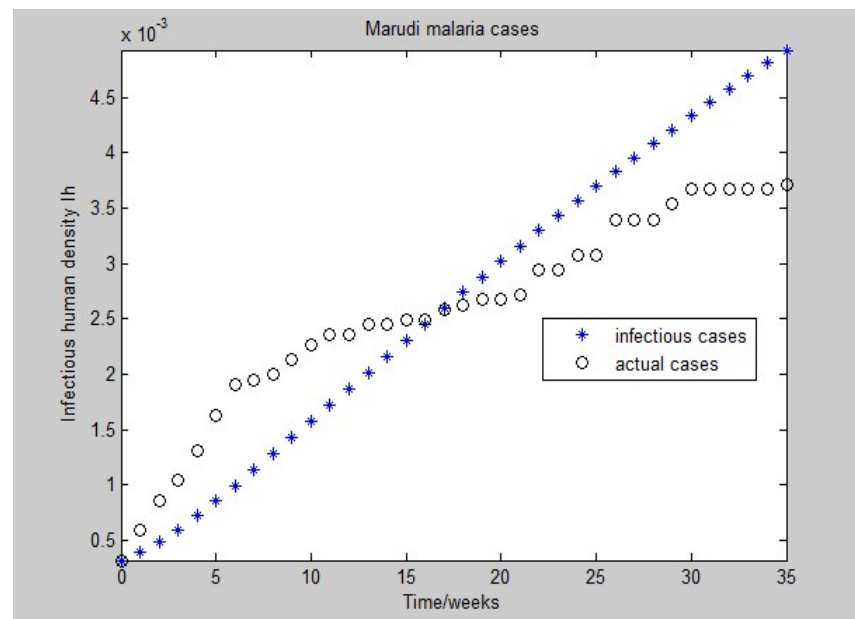


Figure 5.10: Weekly actual malaria cases in Marudi from week 39 in 2012 to week 22 in 2013 and simulated cases from the spatio-temporal generic model.

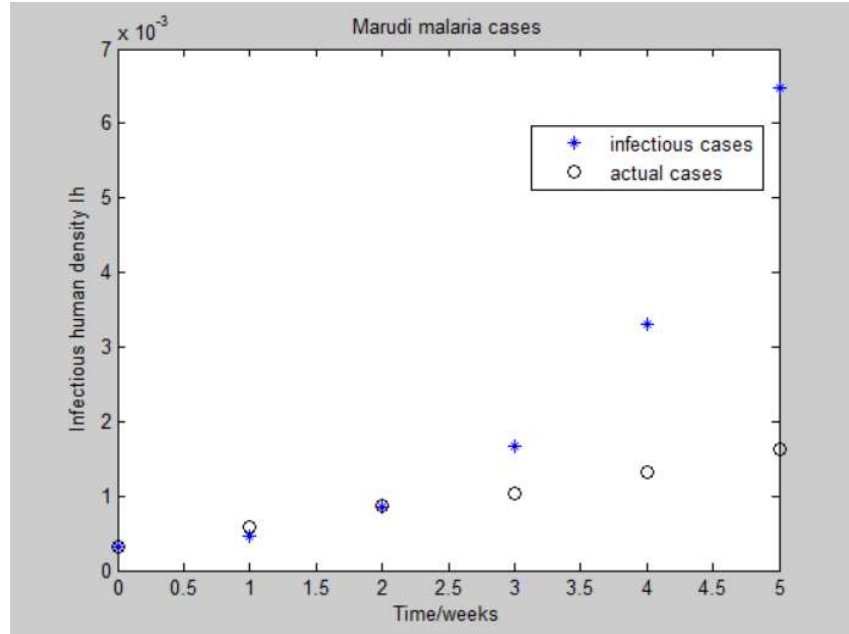


Figure 5.11: Weekly actual malaria cases in Marudi from week 39 in 2012 to week 44 in 2012 and simulated cases from the spatio-temporal generic model.

5.2 Results of Simulation with Actual Dengue Cases

Dengue is a mosquito-borne disease caused by virus and found mostly in urban and semi-urban areas, in many regions of the world. *Aedes* mosquitoes spread the disease and normally bite during daytime. According to World Health Organization (2016b), the number of dengue cases reported increased from 2.2 million in 2010 to 3.2 million in 2015. There are four typical serotypes of dengue virus namely DEN-1, DEN-2, DEN-3 and DEN-4. However, a fifth serotype which demonstrated sylvatic cycle has been discovered (Mustafa et al., 2015). Sylvatic cycle means that the disease is transmitted to non-human primates. Therefore, the virus is transmitted to humans when humans are working in the forests. Normally the first dengue infection is asymptomatic; nonetheless individuals who are later exposed to one of the other serotypes have higher chance to develop severe dengue. The

symptoms of non-severe dengue illness include rash, high fever, headache, muscle, joint pains and vomiting. Symptoms of severe dengue are for example, severe abdominal pain, blood in vomit, rapid breathing, bleeding gums, respiratory distress, severe bleeding, or organ impairment.

In this section, the simulations from the generic model are compared with 127 weekly notified dengue cases which are reported in Sarawak Weekly Epid News (2012). As the actual results fluctuate drastically, the general behavior of the spread of dengue is obtained by finding the best fit curve. This is relevant as the generic model describes the average trend of the transmission of diseases and it is unable to capture rapid and stochastic changes in the behavior. Dengue prevalence in four districts in Sarawak namely Kuching, Sibu, Bintulu and Miri are compared with simulations from the temporal and spatio-temporal generic model respectively. The time span is 127 weeks, from week 39 in 2012 to week 9 in 2015.

Firstly, the actual cases will be compared with numerical results from the temporal model hence diffusion rates of both human and mosquito population are set to zero. Parameters used are shown in Table 5.4. As discussed in Section 5.1, since the data for mosquito population in Sarawak is sparse, the initial data for susceptible and infectious mosquito are estimated to fit the actual prevalence. The parameter values for mosquito population such as recruitment rate, Λ and mosquito death rate, d_M are unknown therefore they are determined when the best fit curve is acquired. In addition, the initial values of human population for each district, namely Kuching, Sibu, Bintulu and Miri in 2012 are estimated using exponential growth formula as discussed in Section 5.1. The value for q , growth rate for each district is shown in Table 5.4.

For Kuching district, the initial data used is $S_H = 615719, I_H = 14, S_M = 1.3 \times 10^5$ and $I_M = 9$. The initial values of the actual cases might not be precisely the initial value of the simulation as the former is represented by the best fit curve. The simulation in Figure 5.12 shows an almost accurate depiction of the general behavior of the actual dengue prevalence in Kuching for 127 weeks. The number of infectious humans drops drastically from the beginning to week 8 and then increases steadily until week 126. The normalized root mean square error (NRMSE) is 7.7×10^{-3} and accuracy percentage is 98.24% for this comparison. In Figure 5.13, the simulated weekly dengue prevalence and actual cases are shown. Initial condition for Sibuluan is $S_H = 247814, I_H = 1, S_M = 242500, I_M = 8$, plus the NRMSE is 2.41×10^{-2} and accuracy percentage, 93.85%. The number of infectious humans for both predicted and actual resembles in terms of behavior and magnitude as both grows exponentially from the first week until week 126.

Next, comparison of simulated and actual cases of Bintulu district is displayed in Figure 5.14 and the initial data is $S_H = 194326, I_H = 5, S_M = 1000$ and $I_M = 5$. From the first week to fiftieth week, the discrepancy is noticeable and the actual prevalence is higher than simulated cases. However, after that, both actual and simulated cases are similar until week 126. The decrement of the actual cases is at a slower rate in comparison to simulated cases in the first five weeks. The reason of the deterioration in the simulation in the first few weeks is the low initial value of infectious mosquito in this data set. The NRMSE and accuracy percentage for this set of comparison is 0.25 and 61.16%. As the simulated result is not in good agreement with the actual from week 1 to 50, the value of r , recovery rate is varied to get a better fit. It is found that when $r = 0.245$, the number of infectious human is complementary to the actual cases for the first three weeks as illustrated in Figure 5.15. In

addition, the accuracy percentage increases to 97.45%. The duration of infectious period is about four weeks. The dissimilar infectious period indicates that the strain of dengue in Bintulu may be different. Different genotypes of dengue causes different infectious period. Average infectious period of dengue as reported by Andraud et al. (2012) is 3 to 14 days.

Finally, it is clear in Figure 5.16 that the simulated number of infectious humans in Miri is in good agreement with the actual cases. The initial data used is $S_H = 311934$, $I_H = 2$, $S_M = 10$ and $I_M = 8$. The infectious human population shows an exponential growth from the initial state to week 126. The NRMSE is 3.45×10^{-2} and accuracy percentage, 94.73%. The mosquito death rate for this simulation is $d_M = 8.0 \times 10^4 \text{ week}^{-1}$ as this value enables the best fit curve to be acquired. In summary, the generic model is able to reproduce numerical results of actual dengue cases in four districts in Sarawak.

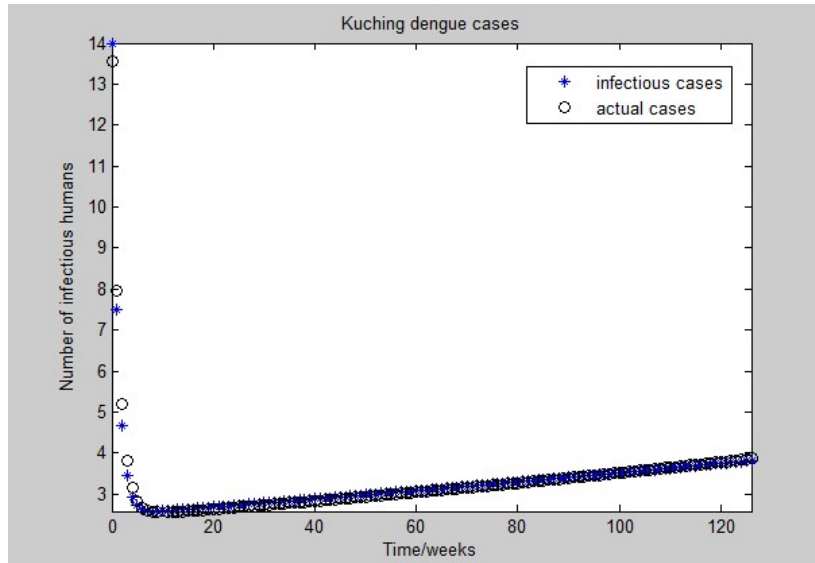


Figure 5.12: Weekly dengue cases in Kuching from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model.

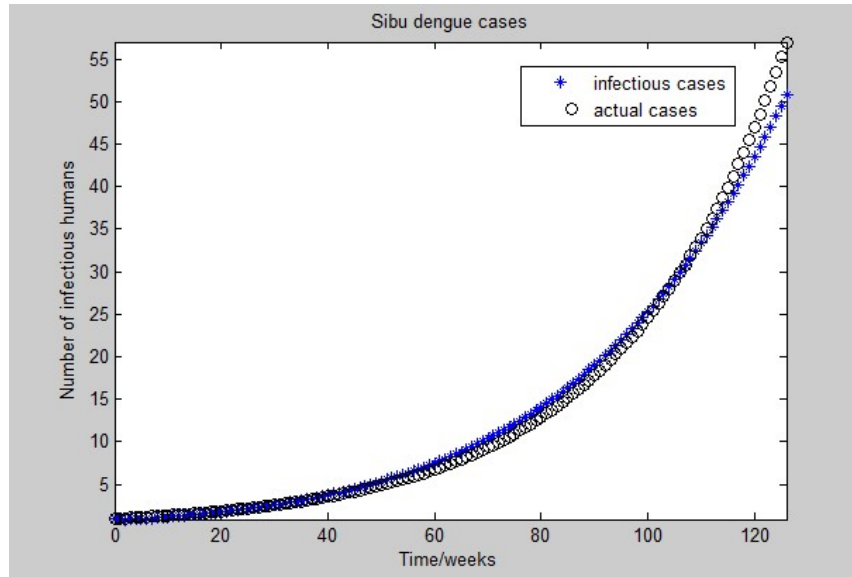


Figure 5.13: Weekly dengue cases in Sibu from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model.

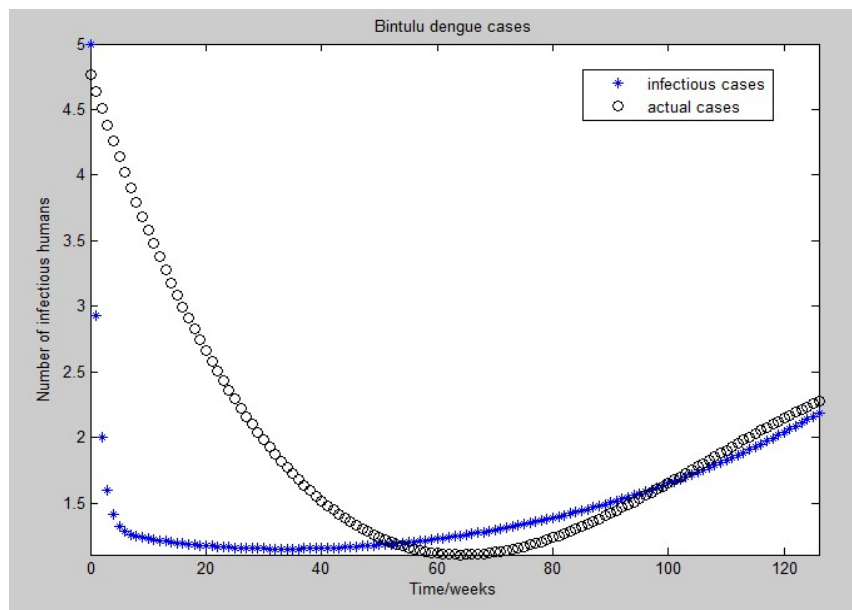


Figure 5.14: Weekly dengue cases in Bintulu from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model.

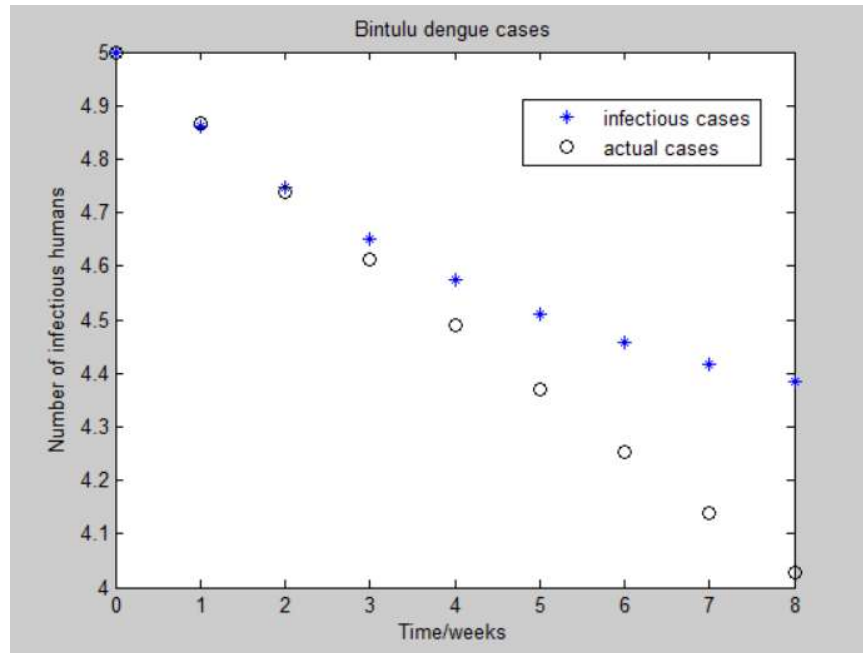


Figure 5.15: Weekly dengue cases in Bintulu from week 39 to 47 in 2012 and predicted cases from temporal generic model.

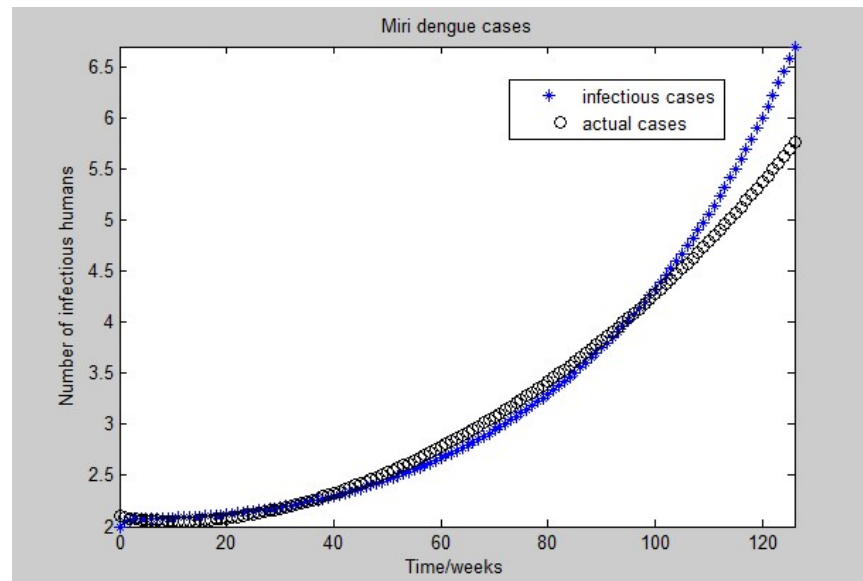


Figure 5.16: Weekly dengue cases in Miri from week 39 in 2012 to week 9 in 2015 and predicted cases from temporal generic model.

Subsequently, to compare simulations from spatio-temporal generic model with actual cases in the mentioned districts, locations are obtained by finding the distance using each latitude and longitude, $x = (\text{Kuching, Sibul, Bintulu, Miri}) = (0, 178, 345, 517)$. Taking into account the actual density of infectious human, the best fit mathematical functions could not be determined as negative values are obtained. Therefore, initial values for each location and population is interpolated. The value of the total human population in these locations in 2012 are estimated from Sarawak Facts and Figures 2012 (State Planning Unit, 2012) as discussed in Section 5.1. Hence, the initial data of population is:, $S_H = (330.53, 111.14, 26.91, 66.27)$, $I_H = (7.5 \times 10^{-3}, 4.5 \times 10^{-4}, 6.9 \times 10^{-4}, 4.2 \times 10^{-4})$, $S_M = (69.79, 108.75, 0.1385, 2.1 \times 10^{-3})$ and $I_M = (4.8 \times 10^{-3}, 1.3 \times 10^{-3}, 6.9 \times 10^{-4}, 1.7 \times 10^{-3})$. The time span is 8 weeks. Particularly, movement of both human and mosquito population is considered this time. As the actual diffusion rate for human and mosquito population are not known, it is assumed to be $2\text{km}^2\text{week}^{-1}$ as this enables the best representation of the actual cases. The values for the recruitment and death rate of mosquitoes are considered the same for all locations. New parameter values used are stated in Table 5.3. Changing the values of time for a mosquito to consume blood per bite, λ and mosquito death rate d_M allows a depiction of the actual scenario. The value for recovery rate, r is different for each district to obtain the best curve that represents the real cases.

From the graph in Figure 5.17, it can be seen that the density of infectious human procured from the generic spatio-temporal model resembles that of the actual cases in Kuching for all eight weeks. The cases decreases in an exponential manner. The RMSE and percentage accuracy for this comparison is 1.5077×10^{-4} and 97.05%. Next, as shown in Figure 5.18, the infectious human density increases steadily with time and is similar to the

actual prevalence in Sibuluan for the considered period. The RMSE and accuracy percentage by comparing the model's predicted and actual value is 6.4551×10^{-6} and 98.93% .

The generic spatio-temporal model is able to predict the infectious human density in Bintulu for week 1 as displayed in Figure 5.19. Unfortunately, after week 1, the modelled values shows an upward trend while the actual infectious cases decline slowly. The RMSE is 5.5303×10^{-4} and accuracy percentage, 36.59%. The recovery rate, r is the lowest among the districts studied as shown in Table 5.5. The infectious period which coincides with this recovery rate is 2.9 weeks. The best fit of the generic temporal model's simulation (shown in Figure 5.15) also displayed a recovery rate lower than other districts, the corresponding infectious period is found to be 4 weeks. This shows that temporal generic model underestimates the recovery rate in comparison to the spatio-temporal generic model. From this observation, the serotype of dengue in Bintulu may differ from the other districts hence the longer period needed for those who are infected to recover from dengue. According to Gubler et al. (1981) studies in dengue epidemic showed that there is variation in different serotypes.

Furthermore, for Miri, it is displayed in Figure 5.20 that the generic spatio-temporal model's infectious human density coincides closely with the actual values from week 2 to week 5. The actual dengue cases decreases slowly over time while the predicted density decreases drastically from week 6 to week 8. It is notable that the model is able to reproduce density of infectious human up to 5 weeks for this particular district. The RMSE and percentage accuracy for this set of comparison is 9.88×10^{-6} and 98.71%. In a nutshell, the spatio-temporal generic model is able to generate results of infectious human density which resembles the actual cases in three out of four districts in Sarawak. The result for Bintulu

district is unsatisfactory and from numerical analysis, the recovery rate is lower than the other districts studied.

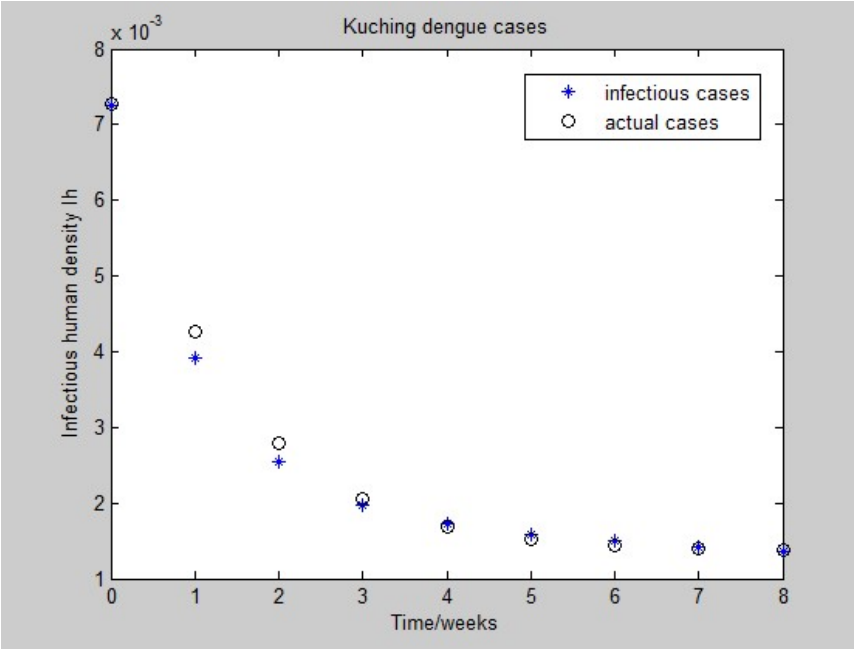


Figure 5.17: Weekly dengue cases in Kuching from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model.

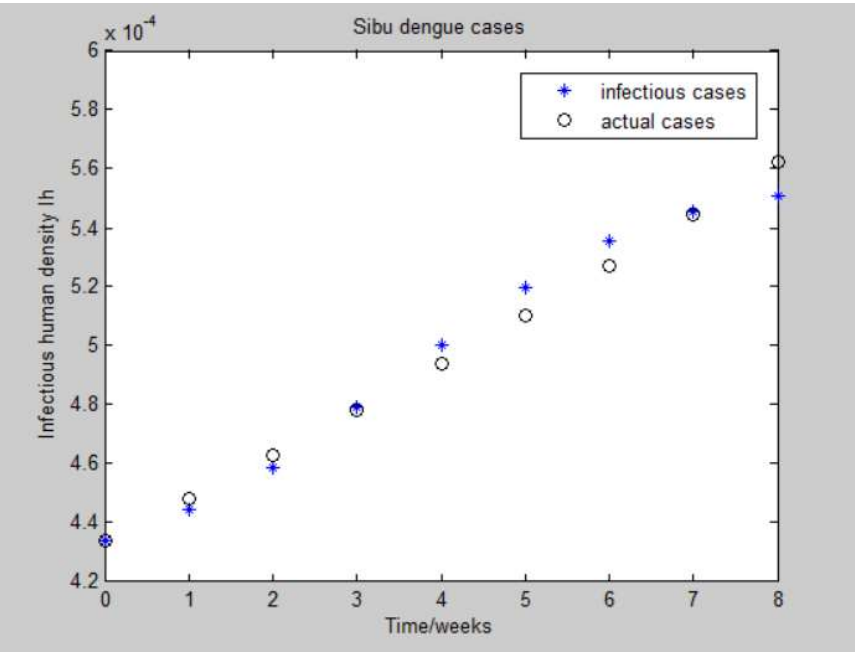


Figure 5.18: Weekly dengue cases in Sibu from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model.

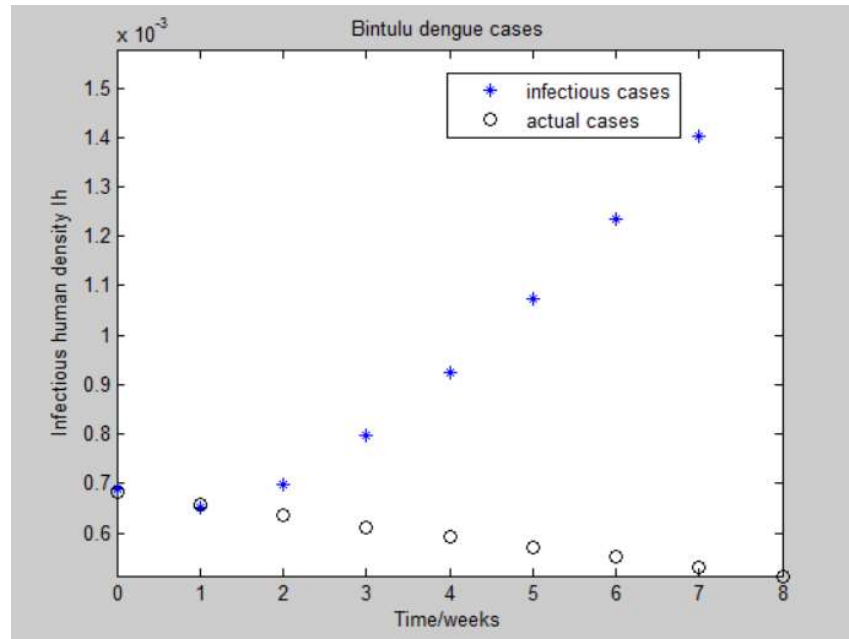


Figure 5.19: Weekly dengue cases in Bintulu from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model.

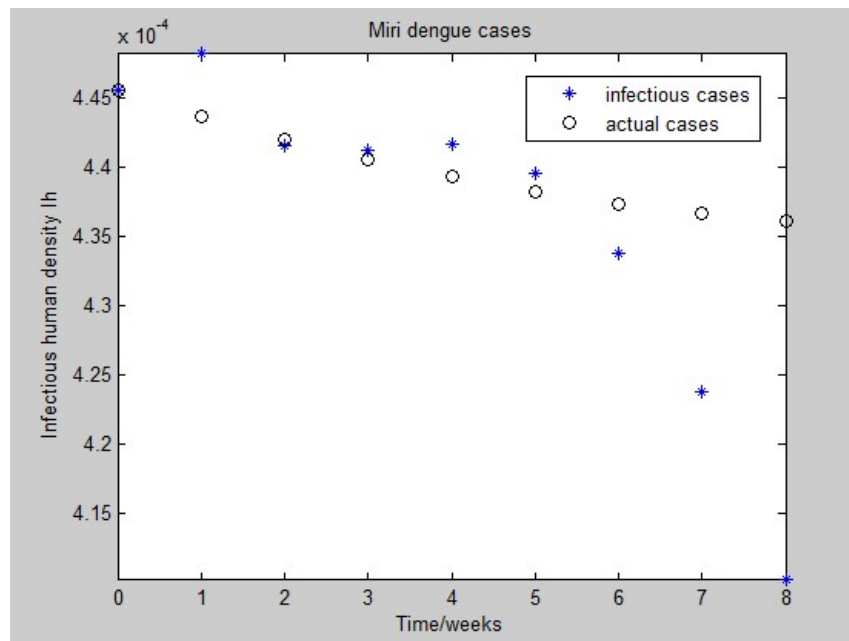


Figure 5.20: Weekly dengue cases in Miri from week 39 to 47 in 2012 and predicted cases from the spatio-temporal generic model.

Table 5.4: Values of parameters used for Kuching, Sibü, Bintulu and Miri for simulation of model.

Parameter	Kuching	Sibü	Bintulu	Miri	Source
diffusion rate for humans, D_H	0	0	0	0	NIL
diffusion rate for mosquitoes, D_M	0	0	0	0	NIL
human recruitment rate, γ	$2.01 \times 10^2 \text{ week}^{-1}$	$2.01 \times 10^2 \text{ week}^{-1}$	$2.01 \times 10^2 \text{ week}^{-1}$	$2.01 \times 10^2 \text{ week}^{-1}$	Department of Statistics Malaysia Sarawak (2013)
time for a mosquito to consume blood per bite, λ	3.5 week	3.5 week	3.5 week	3.5 week	Wang & Zhao (2011)
searching rate of a mosquito, g	2.8 week^{-1}	2.8 week^{-1}	2.8 week^{-1}	2.8 week^{-1}	Chitnis (2005)
transmission probability per bite from $I_M \rightarrow S_H$, c	7.5×10^{-1}	7.5×10^{-1}	7.5×10^{-1}	7.5×10^{-1}	Derouich & Boutayeb (2006)
human death rate, d_H	$8.27 \times 10^{-5} \text{ week}^{-1}$	$8.27 \times 10^{-5} \text{ week}^{-1}$	$8.27 \times 10^{-5} \text{ week}^{-1}$	$8.27 \times 10^{-5} \text{ week}^{-1}$	Department of Statistics Malaysia Sarawak (2013)
recovery rate, r	8.24×10^{-1}	8.24×10^{-1}	8.24×10^{-1}	8.24×10^{-1}	Andraud <i>et al.</i> (2012)
mosquito recruitment rate, Λ	1.0×10^3	1.0×10^3	1.0×10^3	1.0×10^3	
transmission probability per bite from $I_H \rightarrow S_M$, b	7.5×10^{-1}	7.5×10^{-1}	7.5×10^{-1}	7.5×10^{-1}	Derouich & Boutayeb (2006)
mosquito death rate, d_M	$8.0 \times 10^{-3} \text{ week}^{-1}$	$8.0 \times 10^{-3} \text{ week}^{-1}$	$8.0 \times 10^{-3} \text{ week}^{-1}$	$8.0 \times 10^{-4} \text{ week}^{-1}$	

Table 5.4 continued

incubation period in humans, τ_H	1 week	1 week	1 week	1 week	Gubler (1998)
incubation period in mosquitoes, τ_M	1.4 week	1.4 week	1.4 week	1.4 week	Gubler et al. (1981)
Average annual growth rate (%), q	1.84	1.53	2.8	2.88	State Planning Unit (2012)

Table 5.5: New parameter values used for Kuching, Sibul, Bintulu and Miri for simulation of model.

Parameter	Kuching	Sibu	Bintulu	Miri
diffusion rate for humans, D_H	2km ² week ⁻¹	2km ² week ⁻¹	2km ² week ⁻¹	2km ² week ⁻¹
diffusion rate for mosquitoes, D_M	2km ² week ⁻¹	2km ² week ⁻¹	2km ² week ⁻¹	2km ² week ⁻¹
time for a mosquito to consume blood per bite, λ	3.3 week	3.3 week	3.3 week	3.3 week
recovery rate, r	8.24×10^{-1}	6.39×10^{-1}	3.4×10^{-1}	8.58×10^{-1}
mosquito death rate, d_M	2.0×10^{-1} week ⁻¹	2.0×10^{-1} week ⁻¹	2.0×10^{-1} week ⁻¹	2.0×10^{-1} week ⁻¹
area	1.86×10^3 km ²	2.23×10^3 km ²	7.22×10^3 km ²	4.71×10^3 km ²

5.3 Results of Simulation with Actual Zika Cases

Zika virus is caused by a virus which is primarily transmitted by infectious *Aedes* mosquitoes. Additionally, Zika virus can spread through blood transfusion and from mother to child. The symptoms include fever, skin rashes, conjunctivitis, headache, muscle and joint pain. The virus can be detected through blood or urine test. World Health Organization declared a public health emergency of international concern in February 2016 and ended it in December 2016, stating that Zika is here to stay and it is still of high priority. Clustering of cases of microcephaly in Brazil has been linked to the virus as there is a hike in the number of children being born with unusually small heads. Furthermore, Zika triggers a neurological condition Guillain-Barré syndrome in adults which causes paralysis. At the moment, there is no medicine or vaccine for Zika. Researches on the virus, vaccine and potential complications are carried out to better understand this mosquito-borne disease.

First of all, prediction from temporal generic model are compared with actual notified weekly Zika virus cases. However, the data chosen is actual Zika prevalence in Rio de Janeiro, Brazil from week 52 in 2015 to week 24 in 2016 (research engagement, September 7, 2016). The intention is to investigate the ability of the temporal generic model to reproduce historical data for a municipality. As comparisons of results for both temporal and spatio-temporal generic model have been carried out for all district locations for malaria and dengue, only spatio-temporal would be focused here. Subsequently, the values of infectious human density generated by the spatio-temporal generic model and actual cases in four different neighborhoods namely Guaratiba, Santa Cruz, Campo Grande and Bangu, are examined.

Similar to the practice in Section 5.2, it is not viable to acquire a mathematical function to represent the initial data for human and mosquito population. Therefore interpolation method is applied using the available set of data. To make comparison of the generic temporal model cases with that of real Zika cases, the initial values for each population in Rio de Janeiro is $S_H = 6469760, I_H = 6871, S_M = 1.7 \times 10^7$ and $I_M = 18500$. All parameter values are displayed in Table 5.5. The searching rate of mosquito, g is unknown therefore the parameter is gradually increased until the best fit is obtained at $g = 7$. Hence, a mosquito encounters seven human per unit of human density per week. The graph in Figure 5.21 shows that the number of infectious human increases to 11490 from the beginning to week 6 for both the modelled and observed cases. From week 7 to week 25, there is a fall in the number of infected cases. It is notable that simulation from generic model is in good agreement with actual Zika cases. The NRMSE for this comparison is 0.0779 and accuracy percentage, 93.75%.

The next intention is to compare simulations from spatio-temporal generic model with actual cases in different neighborhoods. Thus, locations are obtained by finding the distance between the neighborhoods using each latitude and longitude, $x = (\text{Guaratiba, Santa Cruz, Campo Grande, Bangu}) = (0, 1991, 4545, 5727)$. Initial values for each location and population is interpolated because the best fit mathematical functions fail to capture the actual density of infectious human. The population in the municipality of Rio de Janeiro are obtained from City Population (2017). The area of the neighbourhood can be retrieved from the same website and the values are in Table 5.7. The initial density of population is: $S_H = (908.98, 264.79, 6046, 7086.1), I_H = (0.8, 0.72, 2.12, 0.78),$
 $S_M = (600, 200, 600, 5 \times 10^4)$ and $I_M = (10.2, 12, 10.25, 4.3).$

The values for mosquito population are not known therefore the values which give the best fit curve are used. Diffusion rate for human and mosquito population are assumed to be $2\text{km}^2\text{week}^{-1}$ as this enables the best representation of the actual cases. New parameter values used are stated in Table 5.7. The aim is to use the same value across locations for all parameters in the model if possible, as it is challenging to acquire data for different locations. Recovery rate, r and mosquito death rate d_M are changed to acquire the best fit comparison.

Lessler et al. (2016) discussed that there is uncertainty regarding the duration of viremia of Zika virus therefore research to determine it is essential as control measures and necessary protection can be decided. Viremia is a process where virus enter into the bloodstream. The current recommendation is that Zika viremia lasts about a week after the onset of infection (Centers for Disease Control and Prevention, 2016). The best fit value obtained for r is 0.8235 which means the infectious period is about 1.2 weeks. This corresponds with the understanding of the duration of viremia. Apart from that, mosquito death rate, d_M is varied to obtain the best fit and it is determined to be 0.27 week^{-1} , corresponding to lifespan of 26 days which is within the range reported by Andraud et al. (2012).

The graph in Figure 5.22 illustrates the infectious human density for Guaratiba from week 52 in 2015 to week 24 in 2016. It can be seen that both infectious human density from the generic spatio-temporal model and real cases appear to be of complementary behavior. The simulated infectious human density increases to a peak in week 3 and then decreases gradually onwards. Similarly, the observed infectious human density displays similar trend except that it peaks in week 4 instead. The RMSE and accuracy percentage for this comparison are 0.2075 and 87.2%. Next, as shown in Figure 5.23, the modelled infectious

human density is able to capture the general trend of Zika cases in Santa Cruz for 25 weeks. Both show similar behavior in the time span studied as the density rises significantly and then reaches a peak and gradually drops. However, the modelled cases peak at week 5 while the actual cases at week 9. The RMSE and accuracy percentage are found to be 0.5025 and 88.11% respectively.

It can be seen from the graph in Figure 5.24 that the modelled and observed density of infectious humans for Campo Grande are in good agreement up to week 4. Then, the actual infectious human density dropped gradually from week 3 to week 10, 2016. After that, it increases for four weeks, reaches a peak and decreases until week 25. On the other hand, the simulated cases decreases slowly after week 4. Simulated and observed data show a similarity in terms of behavior but the simulated cases are higher than observed cases. For this set of comparison, RMSE is 0.5775 and accuracy percentage, 68.06%. The parameter value for mosquito recruitment rate, Λ is 1.5×10^4 to obtain the best fit comparison. This value is higher than in other neighborhoods which signifies that there might be more breeding sites in Campo Grande. Moreover, the increase in Λ indicates that there is an increment in the density of infectious mosquitoes. This observation agrees with the discussion by Tesla et al. (2017) that the level of pathogen differs in hosts which can lead to the variation in the infectious mosquito population.

Finally, in Figure 5.25, the comparison of simulated and observed infectious human density in Bangu for the same 25 weeks is displayed. As shown, the behavior of the Zika cases is similar for the first seven weeks. After that, the generic model's infectious human density decreases drastically while the actual cases increases for the next seven weeks before dropping rapidly. The RMSE and accuracy percentage are 0.5455 and 53.85%. The spatio-temporal generic model could not capture the fluctuations after week 7. A suggestion would

be to explore seasonality by considering a forcing mechanism such as transmission parameter to take the sinusoidal wave form. Nonetheless, this method is not investigated in this study as it is not within the research scope.

To summarize, the temporal generic model is able to reproduce the number of infectious human cases which closely resembles the magnitude and behavior of Zika virus in Rio de Janeiro from week 52, 2015 to week 24, 2016. The spatio-temporal generic model simulations managed to capture the overall trend of infectious human density in the first two neighborhoods, namely Guaratiba and Santa Cruz. However, the simulations met the actual cases for both Campo Grande and Bangu, for the first four and seven weeks respectively. It is notable that the distance between these neighborhoods in Rio de Janeiro are in thousands of kilometres as opposed to hundreds for the districts in Sarawak. This may contribute to the lack of accuracy in the last two neighborhoods. Moreover, location dependent parameters may need to be considered for certain situations to acquire better prediction.

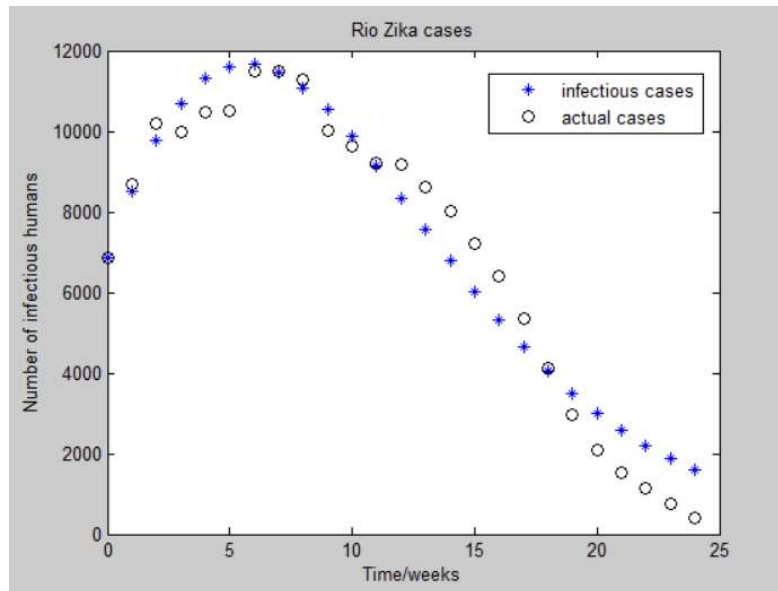


Figure 5.21: Weekly Zika cases in Rio De Janeiro from week 52 in 2015 to week 24 in 2016 and predicted cases from the temporal generic model

Table 5.6: Values of parameters used for Rio de Janeiro, Brazil for simulation of temporal generic model.

Parameter	Rio de Janeiro, Brazil	Source
diffusion rate for humans, D_H	0	
diffusion rate for mosquitoes, D_M	0	
human recruitment rate, γ	$6.1 \times 10^2 \text{ week}^{-1} \#$	City Population (2016)
time for a mosquito to consume blood per bite, λ	3.5 week^{-1}	Wang & Zhao (2011)
searching rate of a mosquito, g	7	
transmission probability per bite from $I_M \rightarrow S_H, c$	7.5×10^{-1}	Andraud et al. (2012)
human death rate, d_H	$2.56 \times 10^{-4} \text{ week}^{-1}$ 1/life expectancy	World Health Organization (WHO)
recovery rate, r	$3.0 \times 10^{-1} \text{ week}^{-1}$	Research Engagement (September 7, 2016)
mosquito recruitment rate, Λ	5.0×10^3	
transmission probability per bite from $I_H \rightarrow S_M, b$	7.5×10^{-1}	Andraud et al. (2012)
mosquito death rate, d_M	$2.0 \times 10^{-1} \text{ week}^{-1}$	Zika Virus Net (2016)
incubation period in humans, τ_H	3 weeks	Research Engagement (September 7, 2016)
incubation period in mosquitoes, τ_M	3 weeks	Research Engagement (September 7, 2016)

Table 5.7: New parameter values used for Guaratiba, Santa Cruz, Campo Grande and Bangu for simulation of model.

Parameter	Guaratiba	Santa Cruz	Campo Grande	Bangu
diffusion rate for humans, D_H	2km^2 week^{-1}	2km^2 week^{-1}	2km^2 week^{-1}	2km^2 week^{-1}
diffusion rate for mosquitoes, D_M	2km^2 week^{-1}	2km^2 week^{-1}	2km^2 week^{-1}	2km^2 week^{-1}
recovery rate, r	8.24×10^{-1}	8.24×10^{-1}	8.24×10^{-1}	8.24×10^{-1}
mosquito death rate, d_M	2.6×10^{-1} week^{-1}	2.6×10^{-1} week^{-1}	2.6×10^{-1} week^{-1}	2.6×10^{-1} week^{-1}
mosquito recruitment rate, Λ	5.0×10^3	5.0×10^3	1.5×10^4	5.0×10^3
area	1.48×10^2 km^2	1.25×10^2 km^2	1.39×10^2 km^2	$6.2 \times 10^1 \text{ km}^2$
population	1.35×10^5	3.32×10^4	8.42×10^5	4.39×10^5

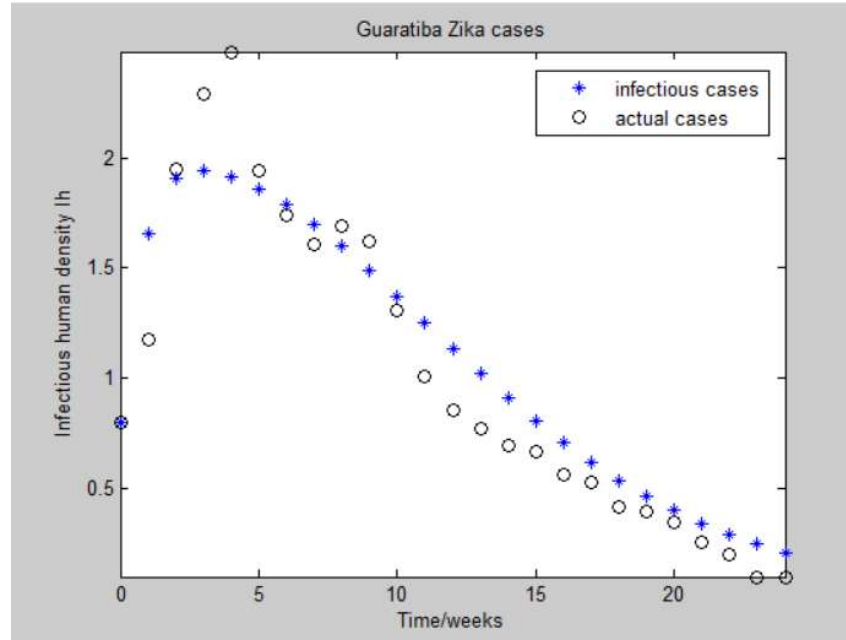


Figure 5.22: Weekly Zika cases in Guaratiba from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model.

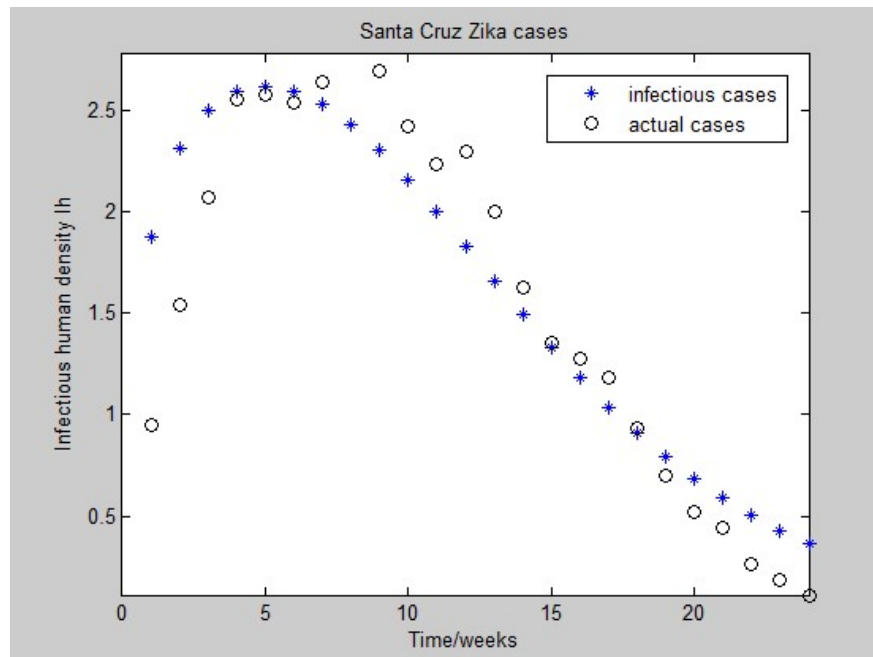


Figure 5.23: Weekly Zika cases in Santa Cruz from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model.

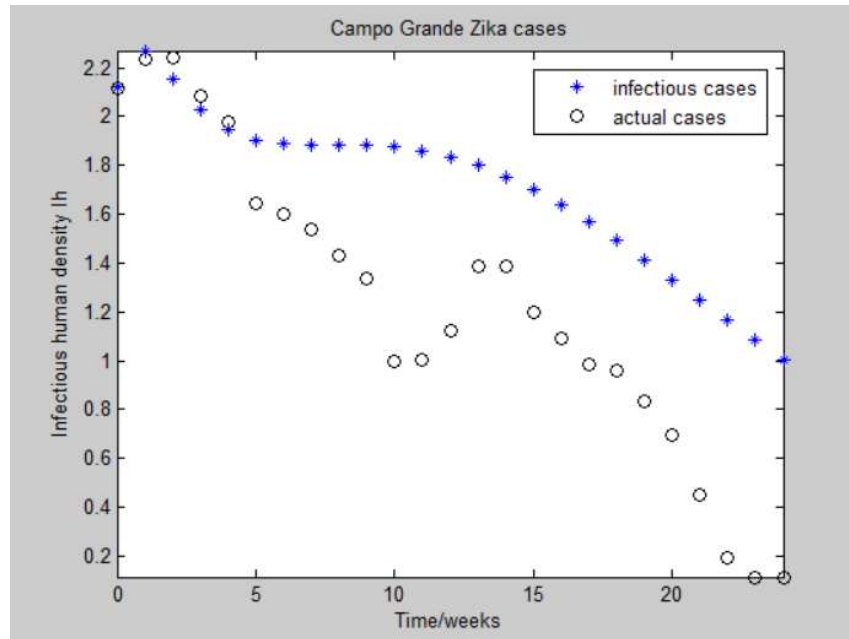


Figure 5.24: Weekly Zika cases in Campo Grande from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model.

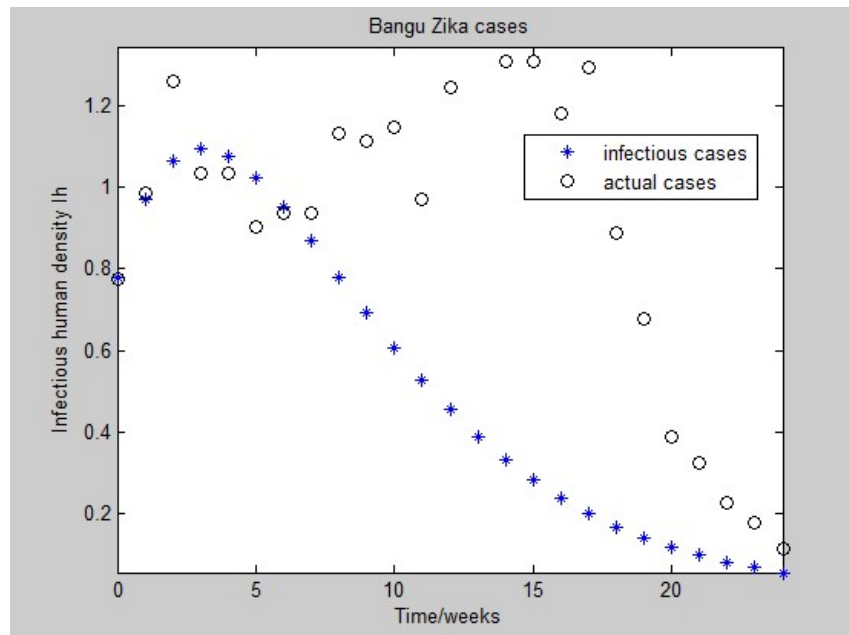


Figure 5.25: Weekly Zika cases in Bangu from week 52 in 2015 to week 24 in 2016 and predicted cases from the spatio-temporal generic model.

5.4 Discussion

Validation of the generic spatio-temporal generic model for transmission of mosquito-borne diseases is implemented by examining its ability to reproduce actual cases of malaria, dengue and Zika virus. The temporal generic model is found to be able to generate the number of infectious humans which is similar in terms of behavior and magnitude for thirty six weekly notified malaria cases in Kapit, Song, Belaga and Marudi. The actual cases in Marudi and Belaga are lower from weeks 7 to 25 and 9 to 23 respectively but the behavior of malaria is comparable. The disease is found to prevail in all four districts in the 36 weeks. After that, locations are incorporated, hence diffusion rate is included. The spatio-temporal model is found to be able to reproduce actual cases in the four locations. The disease remains endemic in all four districts. The simulated cases for Song and Kapit are found to be in good agreement with that of the actual notified cases as the accuracy is 94.63% and 95.21%. Numerical results for Belaga and Marudi show similar behavior that the disease prevails in the population over time although the magnitude differ slightly.

From the comparison of dengue prevalence in Kuching, Sibul, Bintulu and Miri districts in Sarawak, it can be concluded that the temporal simulations closely resembles the general behavior of actual prevalence in the four locations. The spatio-temporal generic model produced values of infectious human density which coincides with the actual cases in Kuching, Sibul and Miri. For Bintulu, the first week result was predicted by the generic model, however, results for the rest of the weeks are not in good agreement. The rate for an infectious human to recover in Bintulu district is found to be the lowest among the districts, suggesting a different dengue serotype may be present. Moreover, from observation, the

temporal generic model underestimates the recovery rate in comparison to the spatio-temporal generic model.

In addition, for Zika virus, the temporal generic model's numerical result corresponds to actual cases in Rio de Janeiro for 25 weeks. The spatio-temporal generic model simulations of infectious human density in Guaratiba and Santa Cruz are in good agreement with the observed cases. Numerical result of infectious human density in Campo Grande coincides with actual data from the first week to fourth week. In addition, Bangu's modelled and observed infectious human density are complementary for the first seven weeks. As a conclusion, the generic model is able to reproduce the data observation of malaria, dengue and Zika virus at specific period using initial values for different locations at an average of 88% accuracy. Parameter values used remain constant for all locations in this study, however, location dependent parameters are encouraged to be adopted for better accuracy. If the generic model is unable to reproduce actual cases, time span studied should be reduced to increase accuracy of the estimated result. In addition, it is observed that there is a pattern that the generic model is able to reproduce historical data for the first fifteen weeks accurately. Therefore, it is suggested that prediction be repeated every fifteen weeks to increase the performance of the generic model.

CHAPTER 6

CONCLUSION

6.0 Research Summary

In this study, the motivation of modeling mosquito-borne infectious diseases is examined and studied in the beginning. The inadequacy that is focused here is the lack of spatial factor in the existing disease models. To model the geographic spread of diseases, different types of spatio-temporal models such as metapopulation, reaction-diffusion models, cellular automata and geographic information system (GIS) are developed. These models are effective tools to analyze the effect of spatial heterogeneity on the transmission of diseases. After reviewing the different types of spatial models, reaction-diffusion modeling is selected to satisfy the research objective. The aim is to incorporate the movement of both human and mosquito population, hence to gain insight from analytical and numerical approach. Furthermore, to validate the generic model with actual mosquito-borne diseases cases at district to national (meso to macro) spatial scale.

In the preliminary stage, an initial reaction-diffusion generic model for transmission of mosquito-borne diseases was formulated. It is made up of a system of partial differential equations which considers movement of human and mosquito similar to Brownian motion. Then, the initial model is analyzed theoretically. The threshold dynamics of the model is discussed and explicit basic reproduction number, R_0 defined. It is shown that disease-free equilibrium point for the system is stable when $R_0 < 1$ and unstable when $R_0 > 1$. After that, the numerical computation of implicit R_0 is deliberated. Existence of endemic equilibrium when $R_0 > 1$ is also proven. Besides that, the initial generic model is analyzed numerically.

The effect of human diffusion was studied numerically and the result showed that increment in human random movement causes disease risk to reduce. In addition, in a numerical simulation, it is found that migration of individuals from rural to urban area (urbanization) is responsible for the rise in disease risk. However, the initial generic model is modified to refine its ability in reproducing literature simulation.

The changes implemented is that biting rate of mosquito is changed from constant to dependent on density of total human population. As a result, the reaction-diffusion generic model for transmission of mosquito-borne diseases is obtained as it is able to reproduce the literature numerical results. Similar to the initial generic model, this model was analyzed theoretically. The stability of the disease-free equilibrium point for the system was explored and existence of endemic equilibrium discussed. Besides, the generic spatio-temporal model can be converted to a temporal model by setting diffusion rate to zero. The temporal generic model could reproduce infectious population results for malaria and dengue deterministic temporal models. Furthermore, the existence of traveling wave front and the minimum spread speed is shown numerically. In the same way as the initial model, numerical simulation from the generic model showed that the hike in diffusion of human decreases disease risk. Nevertheless, spatially heterogeneous transmission of disease worsen spread of infection.

As the generic model is formulated for multiple types of mosquito-borne diseases, the intention is to explore its capability to portray real infectious cases. This model is validated by comparing simulations with actual cases of three different mosquito-borne diseases namely malaria, dengue and Zika virus. In the beginning, numerical results from the temporal and spatio-temporal generic model were compared with notified malaria cases

for thirty six weeks, in Kapit, Song, Belaga and Marudi, districts in Sarawak, Malaysia. The number of infectious human from the temporal generic model displayed resemblance to the actual prevalence in the four districts. Additionally, the spatio-temporal model's infectious human density coincided with the actual malaria cases in Kapit, Song and Belaga. For Marudi district, the infectious human density corresponded to the behavior of the observed cases, however, the magnitude differs, the accuracy percentage is 80%. Continuing, temporal and spatio-temporal simulations from the generic model were compared with 127 weekly actual dengue cases in Kuching, Sibü, Bintulu and Miri, districts in Sarawak. From the comparisons, it was deduced that simulations from the temporal generic model is in good agreement with the general behavior of real dengue prevalence in the four districts.

Furthermore, the spatio-temporal generic model's infectious human density is similar to the actual cases in Kuching, Sibü and Miri. As for Bintulu, the generic model could predict only the first week's infectious human density. After the recovery rate is changed, the accuracy percentage increases from 61.16% to 97.45%. One reason that the recovery rate differs is because the dengue strain in Bintulu is different. For the third mosquito-borne disease, Zika virus, simulations from the temporal generic model coincides with 25 weekly actual cases in Rio de Janeiro. Infectious human density from the spatio-temporal generic model for Guaratiba and Santa Cruz are in good agreement with actual cases with 87.2% and 88.11% percentage accuracy respectively. However, for Campo Grande and Bangu, infectious human density only depicted similarity with actual data for the first four and seven weeks. The percentage accuracy are 68.06% and 53.85%. Summing up, the generic model is capable of reproducing infectious human cases for malaria, dengue and Zika virus for various locations for a certain time span. As the purpose is to maintain the genericity of the model, the preferred parameter values for the model are constant for all locations. The reason

is because parametrization of data can be challenging thus maintaining simplicity ensures data availability. Nevertheless, in situations where the simulated best fit curve is not satisfactory when compared with the actual cases, parameters which incorporate spatial heterogeneity can be considered. Parameters which incorporate spatial heterogeneity or temporal forcing can improve the percentage accuracy of results.

6.1 Contribution of Research

The results presented in this study recommend that a spatio-temporal generic model for transmission of mosquito-borne diseases based on reaction-diffusion equations can be developed, confirming the hypothesis of this study. The governing equations for this generic model is a system of PDEs. However, this system can be changed to ODEs by setting the diffusion rates, $D_H = D_M = 0$. Therefore, this generic model is a spatio-temporal and also temporal model. Moreover, when time for a mosquito to complete bloodmeal, $\lambda = 0$, the biting rate becomes β which reduces the generic model to initial model. The spatio-temporal generic model is able to reproduce numerical results from literature: reaction-diffusion models for malaria and dengue. Furthermore, when the spatio-temporal generic model is transformed to a temporal generic model, it is capable of reproducing results from literature: deterministic temporal models for malaria and dengue. Hence, the generic model simulations are in good agreement with literature, namely dengue and malaria, answering part of the research question.

To validate the spatio-temporal generic model, simulated cases are compared with actual prevalence of malaria, dengue and Zika virus, and it is summed up simulations are in good agreement with historical data of mosquito-borne diseases. This answers the other part

of the research question. In the validation of malaria cases, it was observed that, for the temporal model, the best fit values for mosquito death rate d_M in the four locations differ (0.055-0.11 week⁻¹). This suggests that mosquito longevity is distinct in different locations as mosquito lifespan = $1/d_M$. From the spatio-temporal model comparison, in procuring the best fit, it is found that admission of susceptible mosquito into the population is at 1056 weekly. High recruitment rate of mosquito, $\Lambda = 2.2 \times 10^5$ in Marudi suggested that there may be more breeding grounds in this area and community awareness needs to be promoted to reduce them. Furthermore, in the validation of dengue cases, the temporal generic model is able to reproduce the cases in Kuching, Miri and Sibul. The best fit of the simulation for Bintulu was obtained with a low recovery rate, $r = 0.245$, the corresponding infectious period is 4 weeks. However, for the spatio-temporal generic model, the infectious period which coincides with the recovery rate, $r = 0.34$ is 2.9 weeks. Thus, in this situation, the temporal model may underestimate the recovery rate in comparison with the spatio-temporal model. In the validation of Zika virus cases, by obtaining the best fit for the temporal generic model to Rio de Janeiro actual cases, the searching rate of mosquito is found to be $g = 7$. This means a mosquito encounters one human per unit of human density per day. Through the validation of spatio-temporal generic model to actual cases in Guaratiba, Santa Cruz, Campo Grande and Bangu, the best fit value obtained for r is 0.8235. As the viremia of Zika virus is indefinite and it is recommended to be about a week, the value found means the infectious period is 1.2 weeks. This value means that an infectious person is able to transmit the Zika virus during that period hence should be quarantine. Besides that, *Aedes* mosquito death rate, d_M is found to be 0.27 week⁻¹, corresponding to lifespan of 26 days which is as reported in literature (Andraud et al., 2012). The best fit for Campo Grande, revealed that mosquito recruitment rate, Λ is 15000 which is higher than in other districts, hence there are more

breeding sites in this neighborhood. The results are not in good agreement for Campo Grande and Bangu, as the percentage accuracy are 68.06% and 53.85%. It is observed that the distance between districts in Rio de Janeiro are in thousands kilometres as opposed to hundreds in Sarawak.

From numerical analysis, it is confirmed the increment in human diffusion rate lowers the disease risk and that urbanization aggravates disease spread. In addition, spatial heterogeneity in transmission probability worsens the spread of infection. It was found that parameter p , magnitude of infection heterogeneity increases the risk of infection. When $p \geq 0.4$, it was numerically shown that $R_0 \geq 1$ depicting that when transmission probability which is spatially heterogeneous goes beyond a certain threshold, a disease-free state can switch to an endemic state. As mentioned before, increment in human movement decreases the risk of infection. However, whether the population will remain in an endemic state or otherwise depends on the recruitment rate of mosquito. If the recruitment rate is low enough, in the simulation, $\Lambda = 3.85 \times 10^{-3}$ meaning every week the population admits less than density of susceptible mosquito $3.85 \times 10^{-3} \text{ km}^2 / \text{week}$, the disease will cease to exist. This indicates that reducing the breeding sites by clearing tires, containers or drains which collects water would help in preventing the spread of mosquito-borne diseases. The existence of traveling wave solution is investigated numerically and the minimum spread speed obtained is $5.0 \times 10^{-3} \text{ km/day}$. This means that the least distance the disease invades geographically is $5.0 \times 10^{-3} \text{ km}$ in a day.

Theoretical analysis for the generic model provide general insights of the behaviour of the spread of disease. The standard analysis is implemented by defining the basic reproduction number, R_0 for the generic model. From R_0 , transmission probability from infectious human to susceptible mosquito, b and transmission probability from infectious

mosquito to susceptible human, c contributes to the infection risk. Therefore, it is essential to prevent transmission by using insect repellent, bed nets and wearing long sleeved and long pants. Moreover, reducing infectious period decreases infection risk. This means treatment should be administered as early as possible to enable those infected to recover faster, thereby eventually eradicating the disease.

Different initial values of population gives different spread of disease behavior hence it plays an influential role. As data availability is not always adequate, it can be challenging to estimate the parameter values. In a broader perspective, the temporal and spatio-temporal generic model for transmission of mosquito-borne infectious diseases has been kept as simple and general as possible to cater for the ease of using parameterizable data for different types of infection across states and countries. Parameter values are assumed as constant across locations, using national value unless results are not in good agreement. Although a complex model may encompasses most processes of a disease, but without sufficient data to obtain reliable parameter value, it is not practical. From numerical analysis, the parameters recovery rate r , mosquito death rate d_M and time taken for a mosquito to complete a blood meal for each bite taken λ , greatly affect the behavior of the spread in simulations. In addition, it is observed that the generic model is able to predict historical data accurately up to 15 weeks. Therefore, it is suggested that, to predict cases of periods longer than 15 weeks, the time span should be divided into every 15 weeks to maintain accuracy.

6.2 Limitations of Research

As it is impossible to develop a perfect model which shed light on transmission of diseases and provide accurate forecast of future infection, limitations exists. In real life, transmission

of disease might occur from a different location, however, nonlocal transmission is not considered in this study. To formulate a precise model for mosquito-borne diseases, variations in climate and temperature need to be taken into account. Inevitably, temperature and rainfall affect the life cycle of mosquito population. The maturation rate of immature mosquitoes is dependent on temperature and mosquito species. In the generic model, only adult mosquito is included as considering the egg, larva and pupa form of mosquito would make obtaining parameterizable form of available data difficult. Furthermore, population size of mosquito is not known in most research thus the value is decided by the best fit comparison. The historical infections of human population which contributes to immunity for some mosquito-borne diseases are also not included as this factor may or may not occur for different types of infection. As the interest in this study is to come up with a generic model to cater for as many mosquito-borne diseases as possible, conflicting factors are not incorporated. This generic model uses all constant parameters across locations to conserve its simplicity. From validation of the generic model, there are situations where the model can reproduce observed cases for most locations but one or two. This is because a certain parameter value in the particular location may differ from the rest.

6.3 Future Studies

From this study, a generic reaction-diffusion model for mosquito-borne diseases has been formulated, analyzed and validated. This generic model can be further developed to be a software which can be utilized by authorities in public health. With a prediction tool, the health of public can be improved and protected. The performance of the generic model in terms of computational time, error estimation and precision can be further study. The

accuracy of the generic model in predicting Zika virus can be further explored as research on the characteristics of this virus is still ongoing. Incorporating locations and random movement of human and mosquito population allow the effect of spatial heterogeneity and human diffusion rate on spread of diseases to be explored. Despite that, there are some ways to attain more progress in understanding the disease spread, predicting future outcomes and making decision on control measures. Location-dependent parameters which takes into account spatial heterogeneity can be considered to increase precision. As not all transmission cases occur in the same location, nonlocal transmission can be included in the formulation of the disease model. In addition, control measures such as vaccination and quarantine can be incorporated to the system to analyze the impact on the spread of the diseases. For mosquito population, the full lifecycle can be compartmentalized and temperature can be included as a function in the system of equations as it influences the maturation of aquatic mosquitoes. Collection of mosquito data could be enhanced as there is lack of parameterizable information.

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