Simulation Modeling and Forecasting of Dengue Spread using Agent-based Modeling

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ISLAMABAD

AUGUST 2019

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A thesis submitted in partial fulfillment of the requirements for the degree of
MS Information Technology

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AUGUST 2019

Approval

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Acknowledgment

First and Foremost, praises and thanks to Allah almighty for His blessings throughout my research work, to complete the research successfully, and without His guidance I couldn’t complete this task.

I would like to express my deep and sincere gratitude to Dr. Imran Mahmood for guiding and encouraging me to complete my thesis. His vision, sincerity and motivation have deeply inspired me. It was a great privilege and honor to work and study under his guidance.

I am also thankful to my GEC members, Dr. Faisal Shafait, Dr. Sharifullah and Dr. Moazzam Ali Khan Khattak for their help and valuable comments. I offer my tribute to Department of Computing, National University of Science and Technology NUST, for providing me opportunity to complete my study here.

My family provided unconditional love and support throughout this journey. I am extremely grateful to my parents, siblings and In-laws for their love, prayers, support and encouragement, and made it possible for me to complete this thesis.

Most importantly, I would like to thank my husband, for understanding, motivation and support that made me reach where I am today.

Lastly, Hanzalah – my son for always bringing up the positive energy in me.

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List of Abbreviation

DF	Dengue Fever
DHF	Dengue Hemorrhagic Fever
ABM	Agent-based Modeling
SEIR	Susceptible, Exposed, Infectious, Recovered.
SLI	Susceptible, Latent, Infectious
GIS	Geographical Information System
WHO	World Health Organization
NIH	National Institute of Heath
CDC	Centers for Disease prevention and Control
LASSO	Least Absolute Shrinkage and Selection Operator
ARIMA	Autoregressive Integrated Moving Average
LR	Linear Regression
MAPE	Mean Absolute Error Percentage
CA	Cellular Automata
MAS	Multi agent Systems

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Abstract

Dengue Fever a “mosquito-borne” viral disease is also known as “break bone Fever”, with the symptoms of sudden commencement of fever (for>3 days and <10 days), aches, nausea, severe joints pain, rashes, leukopenia (Platelets<150,000), and thrombocytopenia. It is instigated by one of four Dengue viruses or serotypes (belonging to Flavivirus group), DENV-1, DENV-2, DENV-3 and DENV-4. It is challenging to control and prevent epidemic disease such as dengue in Pakistan because of its complex dynamics. There is a need to develop a simulation framework that models the population dynamics of both humans and mosquitoes and their interactions to analyze the transmissibility and forecast the spread of dengue disease in a given area. This research work is based on computational epidemiology, in which we aim to explore the mathematical model SEIR, across space and time. Our goal is to develop an Agent-based simulation model, based on a mathematical framework of SEIR (Susceptible, Exposed, Infectious, Recovered), compute the vector density based on the reproductive behavior of vector, by studying the complex dynamics of existing epidemic disease to simulate the spread of Dengue Fever. The simulation results with respect to real data are analyzed. Through vector density estimation and the rate of disease transmission, we aim to generate graphs that can be used for forecasting and analyzing the dengue outbreak risks. The graph peaks identify the expected Dengue cases and their direction of spread, which eventually detect epidemic outbreaks. We have proposed a framework that provides visualization and forecasting capabilities and flexibility to modeler to add features that assist stakeholders to study the epidemiology of the region to make prediction. This simulation tool can be used to help the Public Health field to formulate and apply different strategies to cater the risk of Dengue in regions with a high prevalence of Aedes Aegypti and dengue virus infection.

Keywords: *Computational epidemiology, Outbreak forecast, Public Health, Agent-based modeling and Simulation, SEIR model.*

Chapter 1

Introduction

This chapter provides the information about the topic which is being studied. It describes the definitions and concepts of crowd simulation and some preliminaries to get understanding about this thesis.

Dengue Fever is considered to be one of the most significant “mosquito-borne” disease, which is also known as “break bone Fever”. Dengue fever is a viral infectious disease with the symptoms of sudden commencement of high fever, nausea, myalgia, headache, arthralgia, muscle ache, joints pain, rashes, leukopenia(Platelets count<150,000), and thrombocytopenia [1]. The fever lasts for>3 days and <10 days as stated by healthcare provider [2]. Four primary dengue viruses (Flavivirus group) DENV-1, DENV-2, DENV-3 and DENV-4, are responsible to cause the deadly disease of Dengue. These viruses are genetically related but antigenically distinct. Among these, the “Asian” genotypes of DENV-2 and DENV-3 causes secondary dengue infections, with serious diseases [3]. According the age, the of Dengue symptoms vary for each patient. They generally begin 4-7 days (on an average) after the infective mosquito bite and lasts 3-14 days [2]. Severe dengue also known as Dengue Hemorrhagic Fever (DHF) is defined as dengue fever with one or more cautionary symptoms such as abdominal pain, obstinate vomiting, extravascular fluid accumulation, hemoconcentration, mucosal bleeding, liver enlargement >2 cm, thrombocytopenia. It was first recognized in 1950’s during dengue outbreaks in Philippines and Thailand. Currently it has become primary cause of hospitalization amongst children and adults in countries like Asia and Latin America. [4].

1.1 Modeling and Simulation in Epidemiology

For disease surveillance, multiple methods and approaches had been used by researchers. Modeling and simulation is widely used to understand epidemic dynamics and helps in planning and decision making processes.

Besides prediction, modeling has multiple uses in healthcare field such as training, treatment and disease modeling [5]. Modeling uses set of mathematical expression in order to predict the spread of disease.

Simulation formulize new theories and models and helps in predicting future actions and behavior.

Through modeling and simulation, a better understanding of transmission process is done in order to monitor the dengue spread. It helps in understanding the problems by diagnosing the interactions among system agents/variables/components. Modeling and simulation welcomes the change and allows incorporating change and provides ability to explore possibilities and choose correctly through testing each possible scenario. Simulation helps in visualizing the plan through animations and helps understand the operation and organization of the system.

Furthermore, Agent-based modeling allows observing dynamics at larger scales and describing structures and behaviors at smaller scales.

1.1.1 Computational epidemiology

Our work is based on computational epidemiology, which is a combination of multidisciplinary field of geography, mathematics, computer science, and public health. It usually caters the epidemiological issues like disease transmission with the help of public health. In computational epidemiology, two key modeling approaches are commonly used for studying the vector population dynamics, namely: Empirical modeling and Mathematical modeling. Empirical approach is based on data collection, analyzing co-dependence between different input variables and using statistical learning techniques for predicting results. This approach has primarily been used by public health for study. However, it has overcome by mathematical modeling in the past few decades and has started to gain increasing popularity in public health due to its suitable nature of studying the behavior and characteristics of a certain phenomenon and ability to specify its mathematical formula (or computable model). The phenomenon in this case is the vector's reproductive behavior based on the input parameters (i.e., the climatic and regional conditions) and its influence on the transmission of dengue disease. We aim to study the population dynamics of the vector in depth, using a mathematical model, a state-of-the-art simulator is developed for the simulation of the reproductive lifecycle of the mosquitoes. The model is simulated with multiple parameter values explained in Chapter 4, and it will compute the vector density based on the reproductive. behavior over a period. Once the model simulates for a suitable period, an output dataset is generated for analysis and visualization. In the next step the vector density is used to compute the dengue spread and predict the locations of dengue high risk. Estimation of vector density and the rate of disease transmission is an important part of forecasting outbreaks of vector born diseases. These estimations will help us to generate a spatiotemporal visualization that can be used for analyzing the dengue outbreak risks and forecasting the number of Infectious patients at a given time in future for a given area location. This forecast is meant to providing insights to government officials for strategic decision making and planning/devising effective countermeasures against future dengue outbreaks.

1.1.2 Existing control strategies.

There exists only single licensed dengue vaccine (Dengvaxia®, CYD-TDV, Sanofi Pasteur, Lyon, France), developed in mid of 2016, with modest protection for individuals above age of nine years [6] [7] [8]. To prevent the dengue transmission, multiple strategies and approaches such as introduction of other pathogens into vectors [9], plummeting vector population [10], averting vector-human contact [11] etc., have been proposed. Furthermore, research is still going on to solve this health issue, since none of them can be used as an immediate cure.

1.2 Challenge

Focalization of Dengue Fever DF and Dengue Hemorrhagic Fever still need to be elucidated, so, there is a need to share mutual interests and queries between dengue experts and hypothetical epidemiologists to explore future research directions [12]. Our research is Practical Applied Research which has a very small Gap in local industry

It is identified from local industry that a visualization and forecasting framework is needed which cater the spread of disease and behavior of agents using ABM

1.3 Problem Statement

It is challenging to control and prevent epidemic disease such as dengue in Pakistan because of its complex dynamics

There is a need to develop a simulation and forecasting framework that models the population dynamics of both humans and vectors and their interactions to analyze:

- The transmissibility
- Forecast and
- Spread of epidemic disease in a given area.

1.4 Solution Statement

Modeling and simulation play essential role to model the real-world scenarios with micro details.

Our proposed solution is (i) to develop an Agent-based simulation model, based on a mathematical framework of SEIR (Susceptible, Exposed, Infectious, Recovered), and compute the vector density based on the reproductive behavior, (ii) the simulation results with respect to real data are analyzed, (iii) through vector density estimation and the rate of disease transmission, we aim to generate graphs that can be used for forecasting and analyzing the dengue outbreak risks.

1.5 Key Contributions

To the best of our knowledge no simulation model consisting of three separate interacting compartments (Humans, Mosquitoes, and Eggs), using agent-based modeling that combines the visualization and forecasting capabilities have been implemented so far. Therefore, our simulation model can help Public health, devise plans and take in time counter measures to detect the future outbreaks. It is identified from local industry that a visualization and forecasting framework is needed which cater the spread of disease and behavior of agents using ABM. Our proposed framework is open-ended that allows flexibility to the modelers to add features and human-vector behavior to make predictions.

The impetus for this study is to analyze the transmissibility, predict the density of mosquito population and its consequence on dengue spread in time and space, visualize the population dynamics of Humans and Aedes Aegypti mosquito and forecasting the outbreaks using graphs in Swat region

1.6 Research Impact

Our proposed Simulation framework consists of both Humans and Mosquitoes along with a separate compartment for eggs. To better understand the Dengue spread, we have used Agent-based approach that depicts the micro-behavior and interactions of the agents (humans and mosquitoes). Instead of classical approaches, we intend to provide a dynamic and physical implementation model to our Public Health. Through simulation we can predict future actions and behavior of the epidemic disease Dengue.

In epidemic modeling, Human and Vector population dynamics and behavior is modelled using Agent-based paradigm by adding mosquito vector dynamics as a layer (egg layer) and combining it with spatiotemporal resolution using exogenous parameter such as temperature.

Furthermore, the proposed simulation model can be used by Clinicians, Micro-biologists and Public Health.

1.7 Thesis Organization

Rest of the thesis is organized in following chapters

1.7.1 Chapter 2: Background

Chapter 2 provides brief overview of Dengue Fever, its transmission, Global burden and epidemiology of Dengue, Mosquito’s ecology, factors affecting mosquito’s lifecycle, Vertical and Horizontal Transmission of Dengue. Moreover, few preliminary concepts, used in methodology chapter, have also been discussed.

1.7.2 Chapter 3: Literature

This chapter explains the work done so far related to modeling simulation and forecast of dengue spread and agent-based modeling.

1.7.3 Chapter 4: Methodology

Our proposed simulation framework and its analysis has been presented in this chapter along with the discussion of approaches used in methodology section.

1.7.4 Chapter 5: Simulation and Results

This chapter explains the functionality of our proposed framework and is concluded by results and their detailed discussion.

1.7.5 Chapter 6: Model Validation

This chapter deals with the evaluation of the model by validating the results with the actual data, which has been presented in chapter 5.

1.7.6 Chapter 7: Conclusion and Future work

The work accomplished in this thesis has been concluded in this last chapter. Moreover, this chapter also describes the future directions which can be done ahead to this work.

Chapter 2

Background

This chapter provides the information about the topic which is being studied. It describes the definitions and concepts of Dengue Fever and some preliminaries to get understanding about this thesis.

2.1 Dengue Transmission

Dengue is principally transmitted by either of two types of female mosquitoes named Aedes aegypti and Aedes albopictus. Humans attain virus via the infective bite of a Female mosquito. The virus is further passed on to the mosquitoes through biting an infective human. Within mosquito, the virus infects the mosquito in the intestine and spreads to the salivary glands for a period of 8 to 12 days. The virus is transferred to a human, after completing its incubation period, upon probing or subsequent feeding [4]. Dengue transmission can take place under two scenarios. In scenario A: A susceptible mosquito can only attain a DENV infection after it has taken its meal (blood) from a infectious person. This virus is further transmitted to susceptible humans after incubation of 8-10 days. [13]

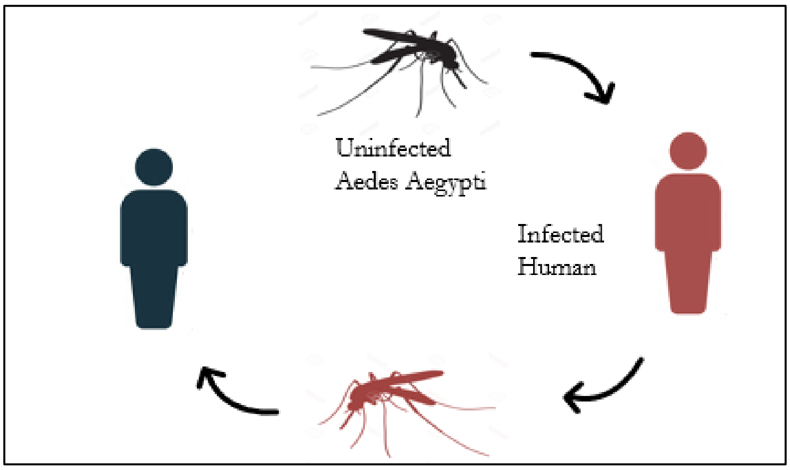


Figure 1: Human to Mosquito Transmission

While in scenario B, Human gets infection from the bite of already Infectious vector Aedes Aegypti (in this case virus is transmitted via eggs).

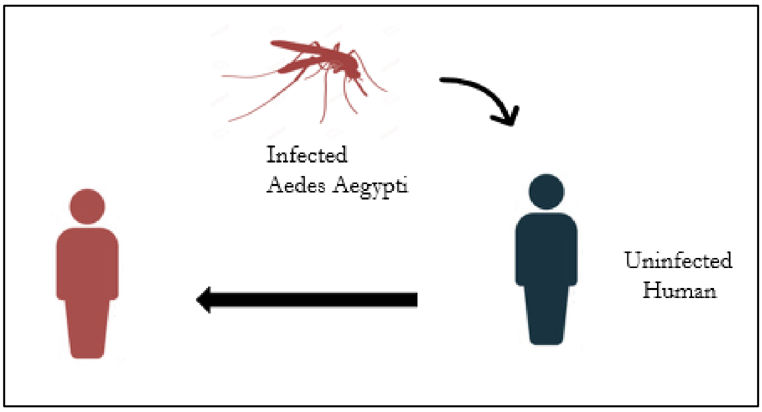


Figure 2: Mosquito to Human Transmission

Flight distance studies show that Aedes Aegypti spends its lives around or inside houses , becomes adult and typically fly 400 meters [4]. It shows that people are primarily responsible to move virus inside and between communities and places, instead of mosquitoes.

2.2 Dengue- Global burden

The global pervasiveness of dengue has grown intensely in recent decades and around half of the World’s population is at risk [4]. “WHO estimates 50 - 100 million dengue infections worldwide, every year, with 10000-20000 deaths, which is quite alarming [14]. The Asia-Pacific region accounts for about 2/3rd of the global weight of dengue and covering about 70% of the 2.5 billion individuals in the world [15]. In tropical and sub-tropical regions, Dengue fever is emerging at the fastest pace and is prevalent in at least 100 countries around the world.

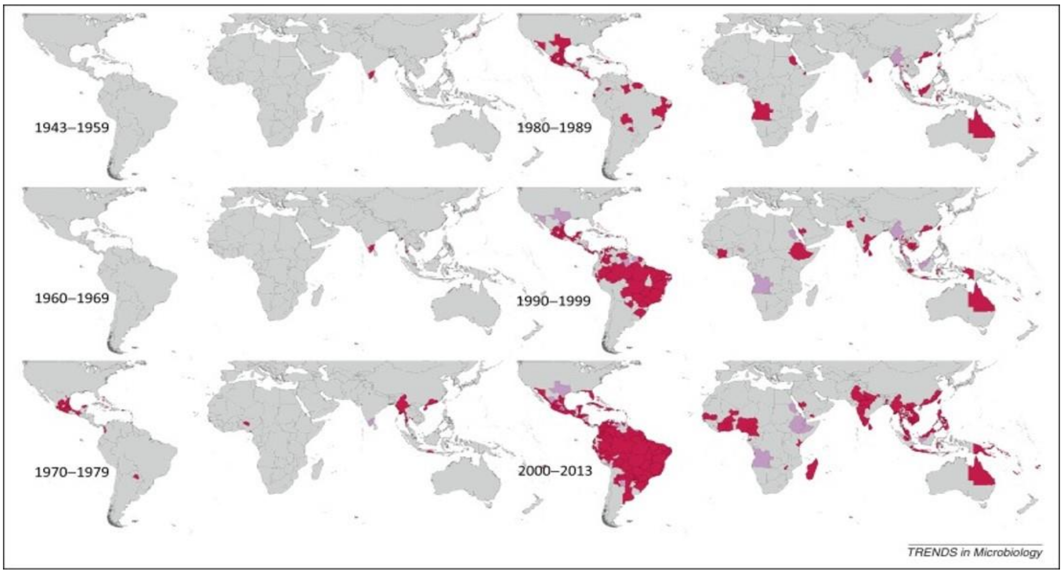


Figure 3: Worldwide Dengue hotspots estimation, WHO

Worldwide, WHO estimated 390 million dengue infections per year [16].

Southeast Asia Cases		
2011	Philippines	18885
2012	Thailand	52008
2013	Bangladesh	21324
South Asia cases		
2011	Pakistan	14000
2013	China	15-fold increase
2013	Taiwan	10-fold increase
South America cases		
2008	Rio de Janeiro	55000
2009	Bolivia	13000
2010	Latin America	1.5 million
2013	Brazil	205000
2013	Paraguay	70000
Australia		
2003	Cairns	503

Table 1: WHO Dengue cases

Rapid population growth, unplanned city development, inadequate public health infrastructures, increased international movement and ineffective vector control programme as well as climate change have been said to contribute to the spread of the disease [17]. Dengue has spread intensively over the tropical and subtropical areas and is causing infection among travelers from other countries. In comparason to malaria, dengue fever has more risk in urban areas than malaria. [18]

Worldwide Dengue deaths are reported in Table 2 as stated in GIDEON [19].

1990	1996	1998	1999	2008	2010	2015
11,400	138,000	15,000	13,000	12,300	14.700	18,400

Table 2: Dengue deaths Worldwide

Recent reports of dengue cases from official, newspaper and other media sources are shown in the form of map in which the larger circle shows the presence of Dengue disease at country level and the smaller circle shows its presence at city level, with 1716 alerts from sept 2018-March 2019, as reported by Centers for Disease Control CDC. [20].

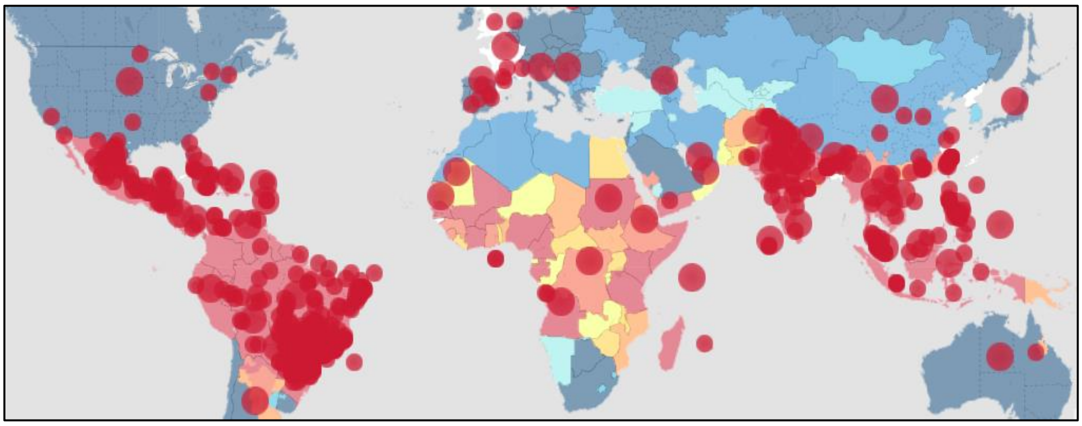


Figure 4: Dengue Map with 1716 alerts from sept 2018-March 2019, CDC

2.3 Dengue Epidemiology

Epidemiology is the study of models, causes, effects of diseases and risk factors in a particular population. Dengue is one of the most important public health problems in Pakistan. According to WHO, Dengue outbreak in Pakistan took place in 1994 with the confirmed infectious cases [13]. Furthermore, in November 2005, a dramatic increase in dengue cases took place in Karachi [2]. Since 2010, dengue infection cases have risen dramatically causing thousands of fatalities. It is, therefore, a matter of national emergency to employ every possible means for preventing this disaster. In 2011, there were more than 20,000 confirmed cases with 300 fatalities. It was the worst strike of Dengue Pakistan has suffered. [3].

Year	Area	Cases	Deaths
1995	Hubb, Baluchistan	75	57
2003	Haripur	1000	7
	Khushab, Nowshera	2500	11
2004	Islamabad and Karachi	25	-
2005	Karachi	500	13
2006	Sukkar , Karachi, Rawalpindi Nawabshah, and Islamabad [22] [23]	5400	55
2007	Lahore, Hyderabad, Karachi, Haripur, Rawalpindi, Islamabad and Mirpurkhas	2700	24
2008	Lahore	1800	-
2009	Lahore [24]	570	
2010	Lahore, Sheikhpura and Gujranwala	320	-
	Islamabad	35	1
	Khyber Pakhtunkhwah	25	3
	Azad Jammu Kashmir [25]	5	
2011	Lahore, Faisalabad, Rawalpindi, Sargodha, Karachi [26]	20000	300

Table 3: Dengue infection reported cases and deaths in Pakistan

Their graphical presentation is shown in the Figure 5.

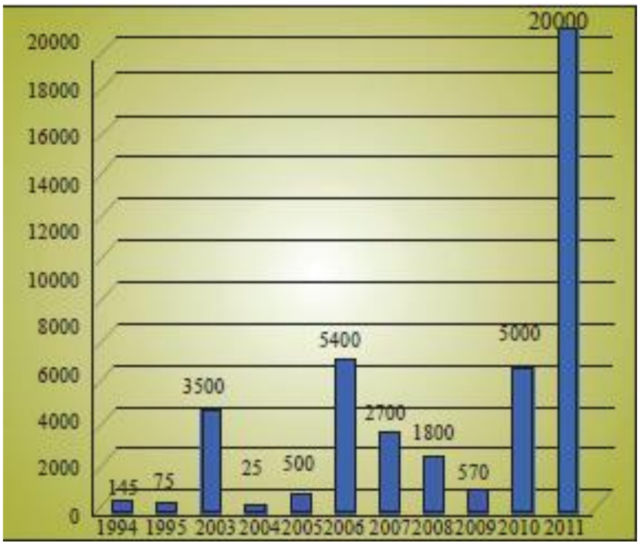


Figure 5: Evolution of Dengue cases in Pakistan

2.3.1 Seasonality

Rainfall is one of the main drivers that play a vibrant role in the growth of mosquitoes and Dengue transmission. There is an increase in dengue cases during and after rainy seasons. Relatively humidity, temperature and rain remained noteworthy prognosticators of dengue occurrence in Pakistan. Surge of cases occurred from September to October [27]

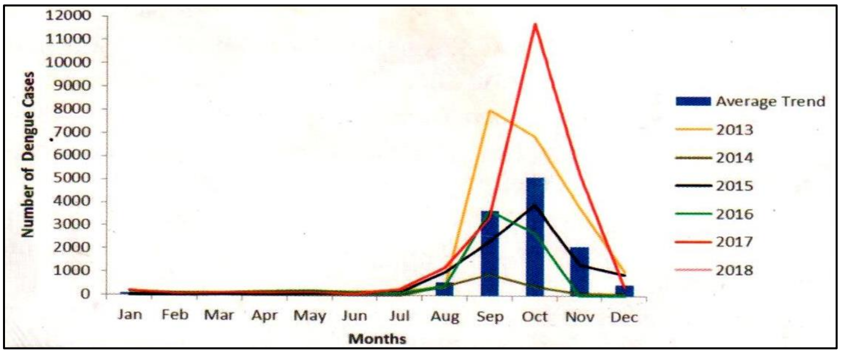


Figure 6: Dengue Cases From 2013-2018 [89]

2.3.2 Geographical Distribution*:*

During 2013-2018, KP followed by Sindh and Punjab remained most affected areas with Dengue in Pakistan. [28]

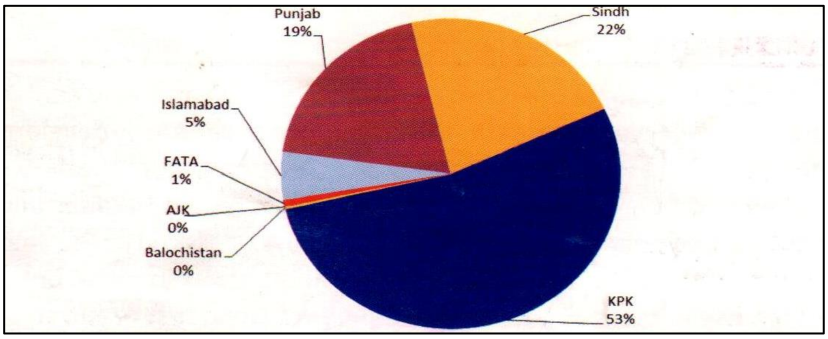


Figure 7: Provincial Dengue Cases From 2013-2018

2.4 Mosquito Ecology

Dengue virus is transferred to an individual via two of infectious female mosquitoes named, Aedes Aegypti and Aedes Albopictus. Aedes Aegypti lives near (closely or inside) residential areas, while Aedes Albopictus is found mostly in outside.

2.4.1 Aedes Albopictus

Aedes Albopictus is generally known as “Asian Tiger Mosquito”. Dengue Fever is also attributed to Aedes Albopictus, which is principally a forest specie adapted to rural, and urban regions. It has spread from Asia to Africa, America and Europe, through international trade, mainly in used tires, with the Aedes deposited eggs, when they contain rainwater, in recent decades. Eggs of Aedes Albopictus remain viable in dry conditions and even if water is unavailable. Ae. Albopictus can it is vastly adaptable to different climatic conditions. It survives in lower temperatures, and its eggs diapause – i.e., undergoes a period of delayed development – during cold winters [29] and hatch in spring. This diapause is reduced during winter months [4]**.**

2.4.2 Aedes Aegypti

Aedes Aegypti is the primary vector that spreads the viruses causing Dengue. Aedes Aegypti surpassed numerous changes in its name since its original portrayal as Culex Aegypti by Carl Linne [30]. It is also known as yellow-fever mosquito. As the result of many observations, it is found that Dengue is carried by A. aegypti in different parts of the world. In Australia where Bancroft in 1906 proved A. aegypti as the vector as it infected two volunteers, in an area where infection might have been otherwise contracted [31]. Figure 8 presents an overview of Aedes Aegypti, the “Yellow Fever Mosquito”.

Figure 8: Aedes Aegypti

2.4.2.1 Aedes Aegypti developmental stages

A reaction–diffusion–advection model has been proposed by Takahashi et al. [32] in which the mosquitoes are alienated into two inhabitants: the winged form (adult female mosquitoes), and an aquatic form (eggs, larvae and pupae). The life expectancy of Aedes Aegypti can fluctuate from two-weeks to one month depending on the conditions**.** Climate has a great influence on the development, survival, population density, feeding, and imitation of Aedes Aegypti. The lifecycle proceeds from eggs to larva then pupa and adult. Mosquito’s lifecycle can be prolonged or shortened depending upon availability of water, and temperature. According to Mengyun [33] low rate of oviposition and high death rates increases the extermination of the Aedes aegypti mosquitoes.

Aedes Aegypti lifecycle is composed of four stages as shown in Figure 9.

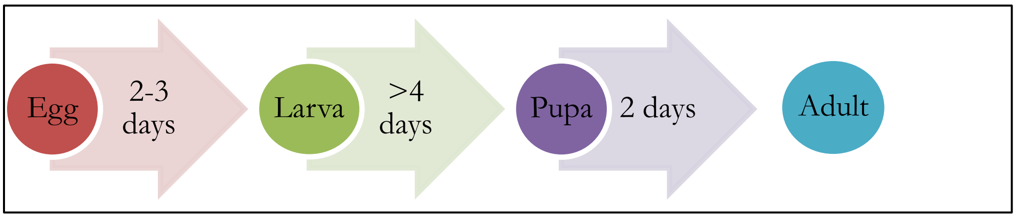


Figure 9: Life-cycle of Dengue vector (Aedes Aegypti)

2.4.2.1.1 Egg

Female Aedes Aegypti can lay three-five clutches of eggs during her lifetime with 100-200 eggs per clutch, depending on blood meal. Aedes Aegypti breed indoors, with the typical habitats such as domestic containers, discarded receptacles, flower pots, Canvas/plastic sheet gully traps/roof gutter, trash cans, ground depression etc. [34]. According to Jacintho [35] egg is the most resilient state of Aedes Aegypti life cycle. They can be hatched within 2-3 days in favorable conditions and can remain viable for 6-8 months. Aedes does not produce eggs at once but separately over hours and days unlike other species. Egg hatch rate depends on the climate; in summers they can be hatched within two days while it can take several months in winters to get hatched. Eggs can hatch immediately if exposed to water while they can sustain dry conditions for years. [36]

2.4.2.1.2 Larva

Larva feeds on organic substances like algae and other microorganisms like bacteria fungi and protozoa, after hatching [35]. The mosquito remains in this stage for 5-10 days, in suitable conditions, but they may take up to few weeks. This stage is temperature dependent and is spent on water surfaces. Larva passes through four instars; among which it spends its maximum time in the fourth instar. In cool temperatures and adequate water supply, Aedes Aegypti can remain in larva state for months [36].

2.4.2.1.3 Pupa

In this stage, mosquitoes neither eat nor move, they just breathe. Larva and pupa are both active states but only larva eat. They remain in this state for about 2 days if favorable conditions are provided.

2.4.2.1.4 Adult

Adult mosquitoes feed on plant juices and nectar [35]. Furthermore, females require blood for breeding, so that eggs can get mature. The density of adults directly depends on rain and temperature.

Female Aedes Aygepti is the principal vectors for the spread of Dengue. They inject the virus from human blood, which develops inside the mosquito and is reinjected with saliva into the blood stream [37]. Proliferation of Aedes Aygepti takes place around temperature of 30-32 C. The number of eggs laid per batch depends on the weight of mosquito and other factors.

2.5 Factors affecting mosquito’s lifecycle

Various meteorological factors influence the frequency of dengue fever. Temperature influence the incidence of dengue fever by modifying adult feeding behavior, larval development and mosquito survival [38].

2.5.1 Temperature

The typical life-time of Aedes mosquito is 25 days, with a range from one day to 76 days. [39] As the temperature increases, the incubation period of mosquitoes become shorter and they take less time to emerge from eggs to adults. Since high temperatures reduce the incubation period for dengue virus, so the probability of high rate of infection increases. The mortality rate of mosquitoes increases at high temperatures. For temperatures >15 C, the feeding frequency of mosquitoes increases which increases the risk of Dengue transmission [40].

Population density of Aedes Aegypti rapidly increases in summers due to shorter incubation period, which increases the risk of dengue transmission.

2.5.2 Rainfall

Mosquito’s lifecycle consists of two stages one of which is aquatic i-e they require stagnant water in order to develop and reproduce. Rainfall is one of the main drivers that play a vigorous role in mosquitoes development and Dengue transmission. After rainfall, due to stagnant water, there is increase in breeding places, which in turn increases the density of mosquitoes. Rainfall forms many artificial and natural places into breeding habitats, which results in a rapid increase in mosquito’s population after rainfall. However, recent studies have shown that heavy rainfall can help in the cleaning of mosquito breeding sites by increasing the mortality rate of mosquitoes by flushing out the aquatic stages [41].

Heavy rainfall may destroy the immature stages of Aedes mosquito, but it increases the breeding places which hypothetically impact the Dengue transmission.

2.6 Vertical and Horizontal transmission

Dengue transmission can take place in two ways i-e vertical and horizontal transmission.

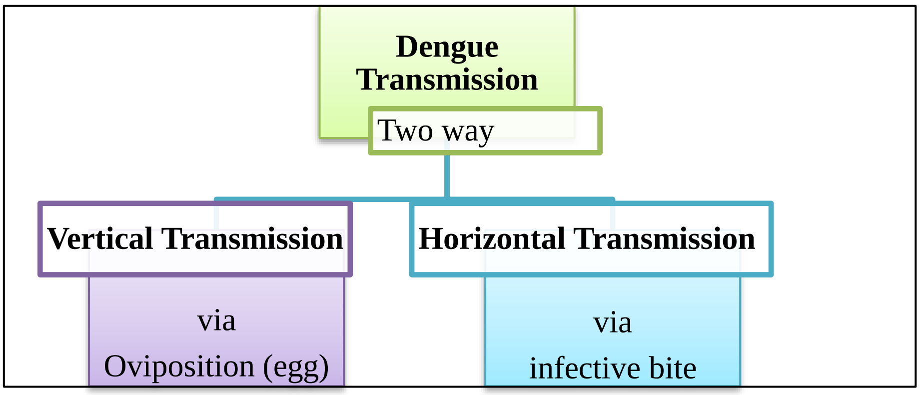


Figure 10: Two-way Dengue Transmission

Dengue can be transmitted within female Aedes mosquito via egg. This transmission is known as vertical transmission (Infectious female adult-Infectious egg).

The second way of dengue transmission is through bite. When an uninfected mosquito bites an infectious person (with dengue virus), it gets the virus into saliva and becomes infectious. This type of transmission is known as horizontal transmission(human-mosquito-human).

The horizontal transmission mostly determines the disease epidemiology [42].

2.7 Mathematical Modeling

Mathematical models can help project the evolution of infectious diseases to show the expected outcome of an epidemic. Models use several conventions and mathematics to find parameters for different infectious diseases and use them to find their effects. Mathematical models can be classified into Deterministic and Stochastic models. Deterministic models are those who have no chance of uncertainty. These models are used for large population and they account for mean trends. While Stochastic or Non-Deterministic models are used where there is a chance of uncertainty and variance. They are like statistical models, usually used for small population. Mathematical models focus on prediction of future events grounded on assumptions and past event’s data.

2.7.1 Classic Epidemic Spread Models

Classic or traditional epidemiology models uses a non-spatial, population-based approach to represent epidemics of communicable disease. These models are deterministic models. The simplest epidemic model is classified into two population groups: "Susceptible" (individuals, receptive to be influenced by disease), and "Infectious" (those individuals who can transmit the disease). So, the model is called "SI", because of this division of the population. SI models, based on total population, can further be extended as (SIR i-e Susceptible-Infectious-Recovered, SEI i-e Susceptible-Exposed-Infectious, and SEIR i-e Susceptible-Exposed-Infectious-Recovered). [43]

2.7.1.1 An SEIR model for Humans (Host-component)

An SEIR (Susceptible, Exposed, Infectious, Recovered) model is an epidemiological model that describes the transmission process of an infectious disease.

“S” represents the Susceptible Humans in the Human Population. “E” represents the individuals who have received infection, but they have not showed the symptoms of infection yet. “I” denotes the number of Infectious individuals and “R” represents the number of individuals who have recovered from infection.

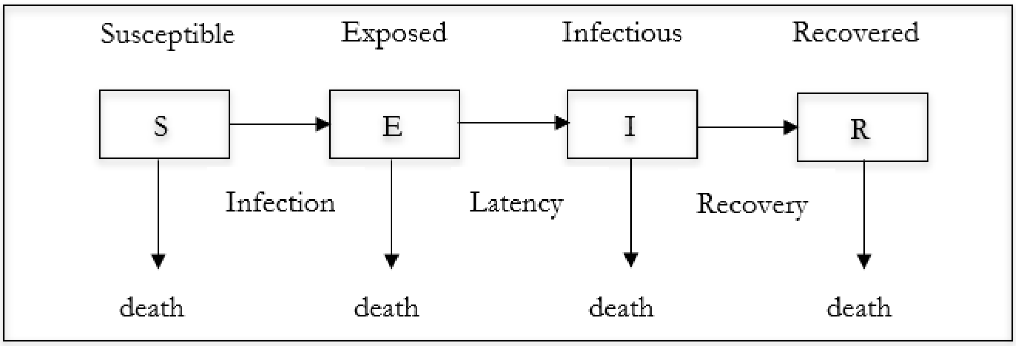


Figure 11: A basic SEIR model

This is a basic Human model containing individuals in each compartment, with total population T= S+E+I+R. The individual enters or leave the compartment based on flow rates defined. There is a decrease in Susceptible individuals when individuals get infection, or they die. Individuals in the Exposed compartment increases when they get infection and decreases as soon as they show the symptoms of infection and decreases with the death rate. The infection compartment increases by the infection events of Exposed and decreases by the death and recovery rate. There is an increase in Recovered compartment with the recovery rate and decreases with the natural death.

2.7.1.2 An SIS model (Humans and Vectors)

SIS model shows that the agent is Susceptible, Infectious and becomes Susceptible again. This model consists of four compartments with “S” and “I” compartment for both Humans and Vectors respectively. This model assumes that Infectious mosquito after getting infection, remains infectious for lifetime.

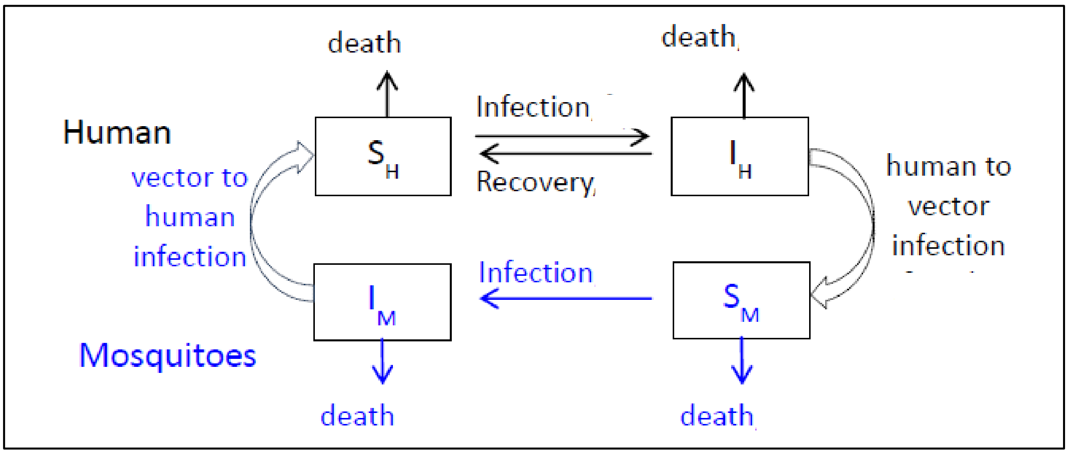


Figure 12: Human and Mosquitoes Infection

The upper row depicts the disease transmission for humans and the lower row represents the disease transmission for vectors. The susceptible humans leave the compartment as soon as they receive infection or through death and they leave the infectious compartment as they get recovered or die. Same goes for mosquitos’ vector.

2.7.1.3 A combined SIR model for Humans, Vectors and Eggs

This model contains three components i-e Humans, Vectors and Eggs. “L” represents the number of Latent mosquitoes (similar to “Exposed” state in Human component) who are in incubation period. The subscript $_H$ represents Humans, $_M$ represents Mosquitoes and $_E$ represents Eggs.

At first a Susceptible human gets infection from a vector's bite and moves to the Infectious compartment. While at infectious state, a human may get recovered and move to the Recovered state or may die. An Infectious human may spread infection to a Susceptible vector which would move to the Latent compartment, where it stays for the time between getting Infection and becoming infectious, called latency period; the vector then moves to the Infectious compartment. A susceptible mosquito if lays eggs increases the population of susceptible vectors, whereas an Infectious mosquito if lays eggs would increase the population of Infectious vectors. It is also possible that an Infectious mosquito lays normal eggs (which contribute to the susceptible population). The main goal of modeling the lifecycle of mosquitoes is to estimate the growth of the vector density at a place and time; and the interaction with the hosts (humans in this case) to predict the rate of spread of disease.

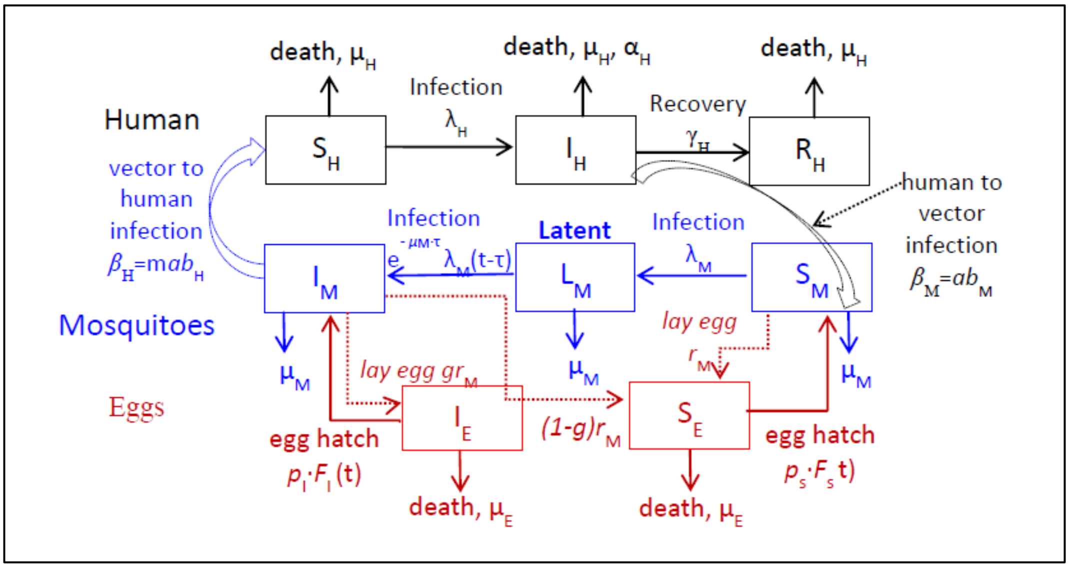


Figure 13: Humans, mosquitoes and eggs infection.

Based on this mathematical model proposed by Jing [44], we aim to develop an agent based simulation model of Humans and Vectors in addition with egg, larva, pupa and adult, submerged in vector's component, further discussed in detail in chapter 4.

2.7.2 Complex System Approaches for Epidemic Spread Models

To cater the probabilistic behavior of disease transmission, stochastic approach known as Cellular automata (CA) theory has been used. It models the location-specific features of susceptible populations [45] [46] However, CA does not cater the individual's interactions spatially, so an new approach known as Agent based modeling (ABM) emerged. Agent-based modeling (ABM), is similar to CA but has the cutting-edge of tracing the disease transmission and spread and the interactions between Autonomous agents located in a geographic area. [35]

2.8 Agent-based Modelling and Simulation

Mathematical models emphasis on macro-level aspects of the system instead of micro-level behavior, therefore our proposed model focuses on Agent-based modeling to cater the micro-level aspects of our agents.

An agent-based model consists of agents (autonomous decision making entities), with a capability of perceptively assessing the situation and make decision according to the set of defines rules. ABM is decentralized i-e the individual agents produce collective behavior by communicating and interacting with each other in their environment.

In Agent based modeling each distinct agent has its own goals and behaviors. Agents are self-sufficient software modules with the ability to plan, adapt and change their behavior through perception and social skills. They can perform knowledge processing aimed at people in time and communicate with their environment using sensors and effector Agents possess the ability of reasoning, planning, and decision making.

Agent-based modeling is a state of the art for simulation modeling of complex epidemic systems. Agent-based modeling offers a higher degree of freedom with more possibilities of adjustment. It focuses on behavior and interactions among agents that helps in decision making based on particular set of rules [47]. Since agents hold multiple characteristics which helps in examining the behaviors in a better way that further results in the better decision making. In ABM, agent's behavior depends on the rules defined for them along with the learning mechanisms they possess. [48].

Traditional modeling approaches uses aggregated average quantities ignoring the individual properties and relationships. Agent-based modeling (ABM) is used to study endemic as well as non- endemic diseases as well as transmissible and non-transmissible diseases.

Simulation is a tool that helps us to study the dynamics of a system, even if its not been developed by providing a virtual environment to perform experiments that are difficult to perform in real scenarios. It saves time, effort and money by finding out the working of a system before it is developed [49].

ABM is best suitable for environment where decentralized solutions are required, and a central control solution method is not valid. It focuses on modeling a system at local level through agents and their interactions, agents are planned to be modeled in a simple way, and complexity is the product of their interactions. Intelligence is embodied in each individual agent, so they can take initiative themselves being active agents. ABM can offer a better understanding of a real scenario. It is very suitable for modeling systems with heterogeneous, autonomous and proactive actors, such as people-oriented systems. It has been applied to numerous fields successfully and is now paving its path towards Epidemiology. Besides ABM is based on some key assumptions which needs to be validated to remove the uncertainties and improve the model applicability and reliability.

Meanwhile our thesis aims to model the behavior of the individuals in a diverse population, having dynamic relationships having geo-spatial behavior, therefore Agents-based modeling fits best to our case scenario.

Chapter 3

Literature Review

This chapter helps in explaining how similar the work with that of others is. Moreover, it contributes in the understanding and development of the area of research.

Over the years, many methods have been proposed to view the problem from different angles. Epidemiological models are divided into three classes: statistical, mathematical, and machine learning models. Statistical methods are used to monitor epidemics and identify real epidemic spatial patterns, mathematical models, to predict the progression of an epidemic spread while machine learning methods to predict the sequence of an enduring epidemic. To develop epidemic disease policies in order to eradicate the emerging epidemics, these models are used by Public health organizations. The simulation enables quick valuation and decision making and offers insight into space-time dynamics of a spread. A classification figure of mathematical models for infectious diseases is shown below [50]

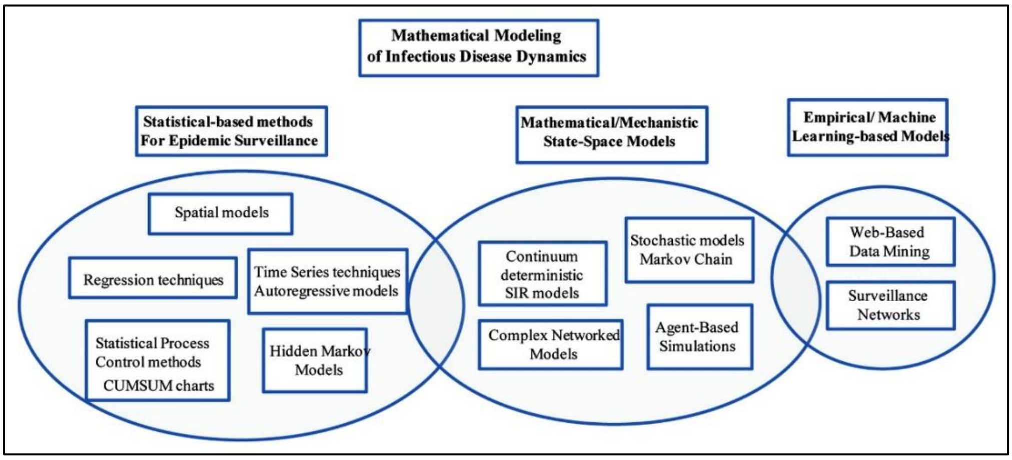


Figure 14: Classification of mathematical models for infectious diseases

The table below précises the literature work into three major categories based on the approaches mentioned above. Besides literature work based on Dengue Fever and factors affecting Dengue, is also mentioned.

Author (s)	Paper Description	Key Features
Dengue Fever		
[51]	Study of dengue Fever and its progression towards Dengue Hemorrhagic Fever	Using differential equations, explained the compartmental modelling of Human and Mosquitoes.
[52]	Optimized the vector control program	Multiple feasible approaches for dengue control (Environmental, Biological and Chemical) are explained
[53]	Explained the vector and virus distribution based on seasonal pattern and temperature variation	It was found that climatic factors along with virus virulence, exposure to it, vector population, its habitat, trade and transport are also significant aspects in dengue spread
Dengue in Pakistan		
[54]	Discussed the progression from disease free to highly endemic state of Pakistan	Starting from 75 cases and 57 deaths in 1995, dengue cases reached to its peak in 2011 with more than 20,000 cases in Pakistan.
[55]	Conducted a descriptive study about children having Dengue and other fevers at Dow, Medical College Hospital Karachi	Aimed to identify dengue fever among undifferentiated fever (in children) in Karachi
[56]	Discussed four modes of Dengue prevention	To eradicate the deadly dengue disease, an early warning system that forecasts the outbreaks must be developed for Pakistan
[57]	Explored dengue vectors and their introduction to Pakistan	According to results, frequency of dengue was high in southern coastal area in mild winters and humid summers
[58]	Conducted a survey of multiple locations of Swat city during 2013 outbreak	Found 9036 confirmed dengue cases with high proportion of males as compared to females. The outbreak occurred from August to November, showing the highest peak in September. Besides favorable temperature, there is heavy rainfall in these months, so the dengue transmission increases also.
[59]	Developed a geostatistical model to study dengue	Through Ordinary Least Squares and geographically weighted regression analysis to perform dengue analysis.
Statistical methods		
[60]	Compared ARIMA model with Knorr-Held two-component model	Both models reliably predicted future DF growth in Singapore, while ARIMA performed better. The ARIMA models were implemented quickly, while the K-H model was sensitive to the choice of assumptions.

[61]	Autoregressive integrated moving average (ARIMA) was applied to make predictions on the Aedes egg populations in three selected dengue hotspots of Malaysia.	Improved the management of mosquito control by sending alerts to decrease the likelihood of dengue outbreaks.
[62]	Predicted the onset of dengue hemorrhagic fever (DHF) using the SARIMA model	Dengue hemorrhagic cases showed a seasonal trend with an increase in June, a peak in October and a gradual decrease from 2012-2016
[63]	Compared SARIMA, LR and the LASSO regression	LASSO had accurate forecasting results compared to LR and SARIMA.
[64]	Forecasted the weekly incidence of Dengue notifications in Singapore	Recent case data, meteorological data, vector surveillance data, and population-based national statistics was used.
Mathematical Models		
[44]	Proposed a theoretical framework based on mathematical modeling in which he discussed the relation of temperature and dengue vectorial capacity	Poisson multivariate regression model is used to examine the risks of dengue, relative to temperature. Cross-validation and root mean square errors was used to analyze the Forecast precision. Seasonal results showed Low in winter and high in summer Results showed that dengue risk decreases when T<14 C.
[65]	Presented a time-dependent mathematical model of dengue transmission incorporating human-vector population of two Brazilian cities, considering climatic factors like rainfall and temperature.	The model is directly applicable multiple geographical regions regarding rainfall or temperature variations
[9]	Developed a biological control mathematical model of dengue transmission via infection of wolbachia in the mosquito population in Indonesia	The model showed that the existence of wolbachia infections helps in the control of the spread of dengue disease in humans.
[66]	An SIR-SI model is developed using ordinary differential equations	These equations are solved using Runge Kutta 4 method
Agent-based Models		

[67]	Discussed the comparison of cellular automata (CA) and Multi agent Systems (MAS) approaches with agent-based modelling using Agent-based Modelling	It was found that Agent-based Modelling (ABM) had an advantage over them in terms of high degree of freedom and use of state charts to cater the behavior of agents.
[35]	Proposed an agent-based model of dengue fever spread, using Swarm Platform.	Focused on identifying and modeling the behavioral aspects of microparticles involved in the spread of dengue fever.
[68]	Discussed Dengue as a case study to validate Agent-based Model	Showed that assumptions lead to the uncertainties in ABM which makes model unreliable, so it needs to be validated with real data.
[69]	Developed agent-based SEIR model with small number of agents	Schull case study was used. Behavior of agents in the town was analyzed using simulation.
Machine Learning		
[40]	Discussed dengue fever considering climatic factors like temperature and rainfall based on early warnings.	To analyze risks of dengue, Poisson multivariate regression was used analogous to weekly temperature and rainfall and dengue forecast models were developed via clustering and validated through multiple statistical models
[70]	Influenza web queries processing to a Swedish website	Two models were fitted, one for linking web queries with the influenza lab confirmed cases; and other with people with flu-like symptoms are treated by doctors in Sweden. These models assessed and predict the incidence of the disease within time (evolution of influenza).

Table 4: Literature Review

3.1 Dengue Fever

Dengue has instigated increasing concern in tropical and subtropical regions. According to the NIH, the first Dengvaxia (CYD-TDV) vaccine was registered in many endemic areas at the end of 2015 and early 2016 for use in people having age of 9-45. [52]

WHO commends that the Dengue vaccine CYD-TDV should be introduced to the areas with high risks of dengue. [71]

The paper proposed by M Derouich [51] aimed to study the dynamics of Dengue Fever(DF) and its evolution to Dengue Hemorrhagic Fever(DHF), using MATLAB as a simulation tool. He discussed Dengue epidemics with respect to vaccination program. The results were conferred based on presence and absence of vaccination.

3.1.1 Dengue in Pakistan

Dengue strike Pakistan for the first time in 1985 with 5 cases of Dengue Hemorrhagic Fever among 122 cases in children [55]. It was found that 26% of indistinguishable fever cases was instigated by dengue virus.

Year 1994 had a major outbreak with 15 cases [72].

There were75 reported cases and 57 deaths in 1995, 113 cases in 2006, 232 cases in 2007, 1407 in 2010 [53].

Pakistan has worst strike of Dengue that reached to its peak in 2011 with more than 20,000 cases in Pakistan [54]. The scenario of cases changed during the year of 1995 – 2011 showing high incidences (peaks) in 2003, 2006, 2010 and 2011.

According to Jehangir khan [57] total of 81 reports were acknowledged, with more Dengue cases in 2010, 2011, and 2013. His work was based on dengue incidence and dengue vector using literature searching and analysis protocol. The protocol he used was registered on a database named PROSPERO. He explored dengue vectors and their introduction to Pakistan. The results showed that the frequency of dengue was high in Southern coastal region with normal winters and summers. It was further moved to the areas with hot summers, cold winters ad categorized by slight winters and tropical warm summers.

Bilal etal., [56] discussed preventive measures to be taken against Dengue, such as awareness, usage of vaccine, eradication of vector breeding places, and instant treatment to patients. An early warning system needs to be developed that predicts the dengue outbreaks in Pakistan, like the one, developed in China. Moreover, climatic variability plays a vital role in dengue transmission. China and Pakistan share almost similar climate, in addition, Pakistan is the 12th most vulnerable country to climatic changes.

A survey was conducted by Chaudary [58] at 330 locations in Swat. Among 16000 cases 9036 confirmed dengue cases. Epidemic peaked from August to

November with highest cases in September. Besides favorable temperature, there is heavy rainfall in these months, so the dengue transmission increases also.

Tariq [59] in his paper developed a geostatistical model to study dengue through Ordinary Least Squares and geographically weighted regression analysis to perform dengue analysis.

3.2 Statistical methods for Dengue Epidemic

3.2.1 ARIMA model

ARIMA modeling is a tool which is used to predict cases in order to timely control and guide the disease preclusion. It is also useful for interpreting surveillance data. Autoregressive Integrated Moving Average (ARIMA) model and the Knorr-Held two component (K-H) model were compared using Mean Absolute Percentage Error (MAPE) by Arul [60] . It was found that the K-H model had a relatively low MAPE value, but that the K-H model was much difficult to adapt in terms of parameters specification and more run time is required by the models. Bayesian analysis was performed on different assumptions. Both models reliably predicted future DF growth in Singapore, while ARIMA performed slightly better. In terms of implementation, the ARIMA models were quick, while the K-H model was sensitive to the choice of assumptions.

Autoregressive integrated moving average (ARIMA) is also applied by Nur Aida, H. [61] to make predictions on the Aedes egg populations in three selected dengue hotspots of Malaysia. Is useful tool for health officials to improve the management of mosquito control and alert the public to reduce the possibility of dengue outbreaks.

3.2.2 SARIMA model

To develop a forecast model by analyzing time series data with seasonal patterns, the seasonal autoregressive integrated moving average model is used to predict the incidence of DHF in different countries. [63] [73] Fazidah A Siregar et al [62] predicted the onset of dengue hemorrhagic fever (DHF) using the SARIMA model for Asahan District, North Sumatra province. Version 16.0 of Minitab was used to analyze and determine the best-fitting model. The results showed that dengue hemorrhagic cases showed a seasonal trend indicating an increase in June, a peak in October and a gradual decrease from 2012-2016. SARIMA turned out to be the most suitable predictive model, showing the lowest mean square error. A study in Brazil by Luz etal [63] found that the SARIMA model was most suitable for the dengue incidence data with no seasonal differencing.

A comparison of the performance of the Seasonal Autoregressive Integrated Moving Average SARIMA, the linear regression (LR) and the LASSO regression with a mean absolute error percentage (MAPE) was performed. The results showed that LASSO had improved, and more accurate forecasting results compared to LR and SARIMA. The LASSO approach degrades more slowly over time (in terms of MAPE), from 17% error prediction at 1 week to 24% at 3 months.

3.2.3 LASSO approach

One of the statistical technique known as Least Absolute Shrinkage and Selection Operator (LASSO) has been used by Yuan Shi [64], to weekly forecast the Dengue incidences in Singapore, using existing data, climatic data, vector surveillance data, and population-based statistics.

3.3 Mathematical methods for Dengue Epidemic

In the last few decades, mathematical modeling has started to gain increasing popularity in public health due to its suitable nature of studying the behavior and characteristics of a certain phenomenon and ability to specify its mathematical formula (or computable model). Mathematical models can be categorized into classic or traditional spread models such as SI models and Complex System models such as CA.

3.3.1 SI-Models

Jing Helmersson [44] proposed a theoretical framework based on mathematical modeling in which he discussed the relation of temperature with dengue vectorial capacity. Poisson multivariate regression model is used to examine the risks of dengue, relative to temperature.

Forecast precision was analyzed using cross-validation and root mean square errors. The combined effect involves Seasonal showing low in winter and high in summer and Daily variation (Large in winters and small in summers). Results showed that dengue risk decreases when T<14 C. Cooler regions may have high risk of dengue than warmer ones. But mathematical model neglects the importance of micro-level behavior and focuses on macro-level aspects of the system.

Marcelo Margon Rossi presented a time-dependent mathematical model of dengue transmission incorporating human-vector population of two Brazilian cities, considering climatic factors like rainfall and temperature. Rainfall or temperature variations can be directly modeled in several geographical locations. [65] According to him, the vector density depends on housing density as well as unoccupied locations

Rocha et al. simulated the disease infections that spread and transmits sexually using SI and SIR models. [74]

A biological control mathematical model of dengue transmission via infection of wolbachia in the mosquito population in Indonesia is developed by A. K., Supriatna, and N. Anggriani [9]. The model showed that the presence of wolbachia infections helps in the control of the spread of dengue disease in humans, still it requires more study to release wolbachia Infected mosquitoes ideally into the wild population.

An SIR-SI model is developed by Valdez [66], using ordinary differential equations for the Susceptible, Exposed, Recovered and Infectious Humans as well as Susceptible and Infectious vectors. These equations are solved using Runge Kutta 4 method [75].

3.3.2 Agent-based and Multi agent system Models

Work done by L. F. Jacintho [35] proposes an agent-based model of the dengue spread, using Swarm Platform. Swarm identifies and models the behavior involving the micro- level aspects in the spread and transmission of Dengue Fever.

Stefan Emrich [67] discussed the comparison of cellular automata (CA) and Multi agent Systems (MAS) approaches with agent-based modelling using Agent-based

Modelling. It was found that Agent-based Modelling (ABM) had an advantage over them in terms of high degree of freedom and use of state charts to cater the behavior of agents. But dynamics of mosquito and climatic factors are not considered.

De Almeida [76] developed individual-based model of mosquitoes, considering vectors, humans and objects as agents. A multi-agent system model's results are compared with biological data, which showed some high correlation indices.

The validation of spatially explicit ABMs, using multiple scale patterns is studied by Young Kang [68] using Dengue transmission having agents i-e human and Infectious female mosquitoes. An interactive Agent based Model with human and mosquito agents showing transmission of Dengue is developed. Results showed that assumptions lead to the uncertainties in ABM which makes model unreliable, so it needs to be validated with real data so eight different scenarios were examined.

Hunter [69] developed agent-based SEIR model with small number of agents. Schull case study was used. Behavior of agents in the town was analyzed by simulation using Netlogo software for Agent-based Modeling. Furthermore vector population was not taken into account.

3.4 Machine learning based models

Machine learning uses data extracted from online communication platforms and online search engines Services like Microblogging socializing, web searching platforms that assists search queries are used as tools for prediction in the market.

Yein Ling Hii [37] in his medical dissertation discussed dengue fever considering climatic factors like temperature and rainfall based on early warnings. To analyze risks of dengue, Poisson multivariate regression was used analogous to weekly temperature and rainfall and dengue forecast models were developed via clustering and validated through multiple statistical models. A prediction (forecast) model was used as an early warning, which uses dengue risk calendars to obtain the risk levels, so that right decisions could be made with in time. But for new Dengue virus, statistical methods cannot be used, because of unavailability of data of data of a new serotype.

In US, Ginsberg et al. used search engine queries on the Google platform to immediately detect influenza epidemics [69]. Between 2003 and 2008, editors used approximately 50 million web-based queries about influenza symptoms [45]

Hulth et al. [62] addressed the web queries related to influenza presented between 2005 and 2007 on a Swedish website. Two models were fitted, first for linking web queries with the influenza lab confirmed cases; and the other one with people having flu-like symptoms are treated by doctors in Sweden. These models assessed and predict the incidence of the disease within time (evolution of influenza).

In in Bolivia, Brazil, India, Indonesia and Singapore, a linear model using Google's research on dengue using available public dengue cases between 2003 and 2010 was used by Chan et al. [70].

3.5 Our Position in the State of Art

Our proposed Simulation framework SEIR-SLI comprises of three compartments including Humans (Person), Vectors (Mosquito) and Eggs. To better understand the spread of Dengue, we have used Agent-based approach that depicts the micro-behavior and interactions of the agents (humans and mosquitoes). Instead of classical approaches, we intend to provide a dynamic and physical implementation model to our Public Health.

Chapter 4

Methodology

In this chapter we propose an agent-based simulation framework comprising of three components of Humans, Mosquitoes and Eggs.

In this section we propose a compartmental model, with two-types of agents (Persons, Mosquitoes), distributed over GIS, that represent Aedes aegypti population dynamics, human demography, dengue transmission via bite between humans and mosquitoes, and their graphs.

Our proposed framework is agent-based, which simulates Human (Person) and Vector (Mosquito) separate agents. Person and Mosquito change its appearance (color) as it changes the state. Furthermore, female mosquitoes lay eggs and bite humans. Humans get infection with a certain probability, when bitten by Infectious female mosquito. Mosquitoes become infected upon biting a viremic person. Person either becomes recovered or dies according to assigned probabilities. Mosquitoes become dead after completing their lifespan.

We aim to develop a simulation framework and visualization of the population dynamics of Humans and Aedes Aegypti mosquito. The impetus for this study is to analyze the transmissibility, predict the density of mosquito population and its effect on the rate of spread of dengue in time and space. To express the functionality of the framework i-e proof of concept, the case study of Dengue outbreak in SWAT in 2013 is considered.

4.1 Project tasks

The methodology for simulating spatiotemporal visualization framework and dynamics of transmissible disease of Dengue Fever is discussed in this Chapter 4. Humans (Persons) and Vectors (Mosquitoes) is represented by agents and their environment where they interact with other agents over GIS.

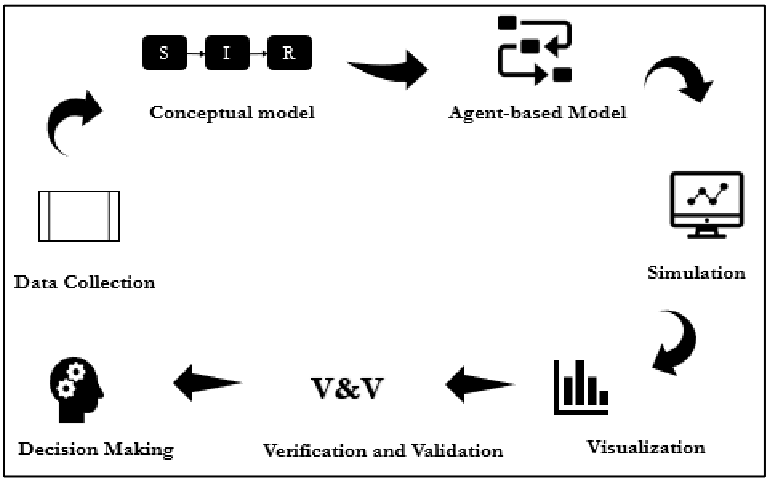


Figure 15: Proposed Methodology

We propose the following tasks in order to achieve the above-mentioned objectives.

4.1.1 Data

Swat, a district of Khyber Pakhtunkhwa, with the area of 5337 km^2 is having a population of 1257602 approx. In 2013, an outbreak occurred in Swat city, with 9036 laboratory confirmed Dengue cases among 12000 suspected ones including 36 deaths. The attack rate was found to be 7.18 out of 1000. The epidemic took place from August to November with the highest ratio of infected individuals in September. In our thesis we chose Swat as our study region and validated our simulated cases with the actual cases of Swat. The geographic location of the area under consideration is shown in Figure 16.

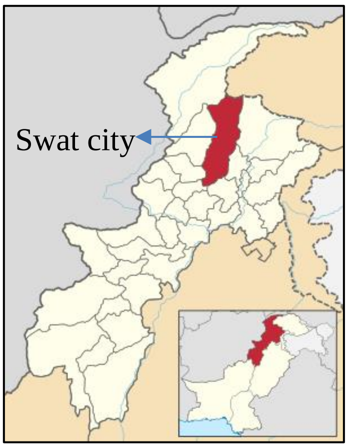


Figure 16: Geographic location of Swat city, KPK

Moreover temperature of Swat (Mingora) is taken from online public source [77], whose graph is shown in Figure 17.

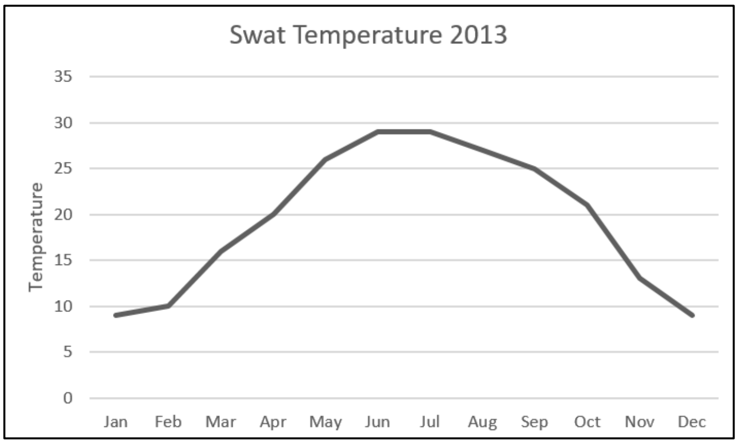


Figure 17: Temperature of Swat city in 2013

In our proposed framework we have used the temperature values from August to November.

4.1.2 Development of conceptual model

We propose to develop an agent based simulation model of Humans and Vectors in addition with egg, larva, pupa and adult, submerged in vector's component using Mathematical model proposed by Jing [44], referred in Section 2.7.1.3.

4.1.3 Development of Executable model and its Simulation

This task aims the development of actual model which is the physical implementation of conceptual model stated by Jing. The model is executed in AnyLogic University Edition, using Agent-based modeling. Agent-based modeling (ABM) approach is used in which we have decentralized autonomous agents. ABM models the behavior of agents at micro level and is used to study communicable and non-transmissible diseases.

Our model is run and simulated in AnyLogic University Edition for person agent population of 5000 and mosquito agent population of 1000, showing the agents behavior over GIS and graphs of the agents.

4.1.3.1 Simulation Platform (AnyLogic)

AnyLogic is a flexible simulation environment in java, providing high level of abstraction and several visual modeling languages. It allows multiple modeling approaches such as Discrete Event, System Dynamics, Dynamic Systems and Agent Based modeling. It runs 2D and 3D animations with refine and increased frame rates and responsiveness.

It allows enabling and disabling of the Run/Pause and speed control button groups at runtime, custom search bounds on GIS.

In agent modeling, AnyLogic supports agent synchronization in form of steps, space such as GIS in our case, mobile and spatial animation and agent connection.

Furthermore, AnyLogic also provides Problem, Search and Console view, and can be customized accordingly.

4.1.3.2 Model portrayal

Our proposed model is comprised of multiple elements described below:

Elements	Description
Main	Specifies the agent's population and their interactions
Mosquito	Specifies the agent's (Mosquito) states and behavior
Person	Specifies the agent's (Person) states and behavior
Simulation: Main	Simulation Experiment used to simulate the model
Database	Provides facility of creating and importing databases (data tables and views).

Table 5: Model Elements

4.1.3.3 Agent-based modeling

ABM can provide a better understanding of a real-world scenario. Besides ABM is based on some key assumptions which needs to be validated to remove the uncertainties and improve the model applicability and reliability.

In Agent-based modeling we defined the active agents of our model i-e Person and Mosquito over GIS map, established connection between them, defined their behavior and interactions and run the simulation. AnyLogic agent library consists of agent components and state chart etc.

4.1.3.4 Proposed framework layers

Our proposed model is composed of two layers as shown in Figure 18.

1. Person (Human) Layer
2. Mosquito (Vector) Layer

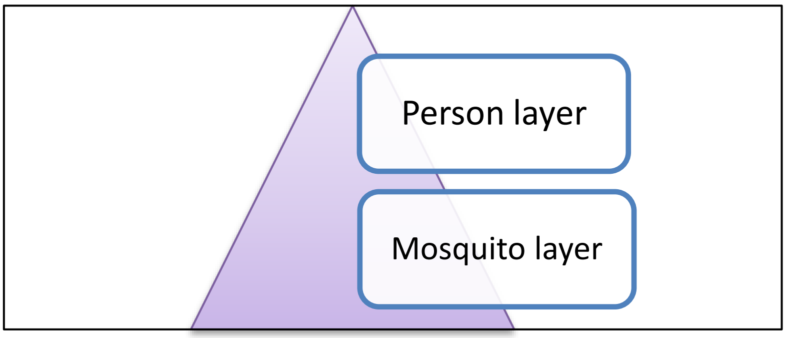


Figure 18: SEIR-SI Framework

The underlying framework is composed of SEIR (for Human population) and SLI (for Vector population) models. There are two types of agents i-e Person and Mosquito. Both agents have their separate state charts with different states. Both layers interact with each other via message passing i-e bite.

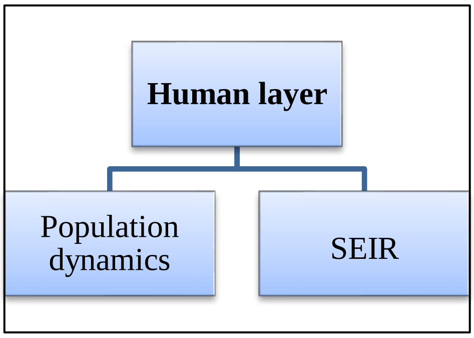


Figure 17: Human Layer

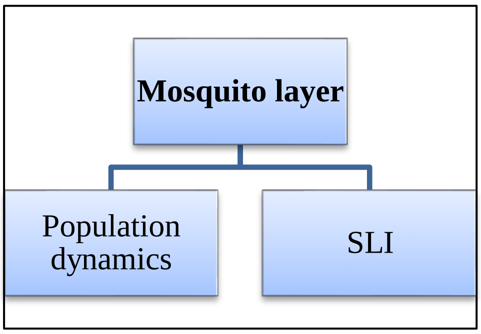


Figure 18: Vector(Mosquito)

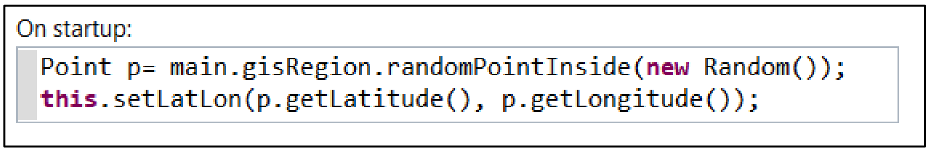
The agents (Person and Mosquito) interact through biting mechanism. Infection can take place via two-way bite, i-e either an Infectious mosquito bites an Infectious Person and takes virus into its saliva, gets Infection and pass infection so on; or an already Infectious mosquito (through vertical transmission or Infectious egg laid by Infectious mosquito) bites an uninfected Person. In our work we have covered both two-way biting mechanisms.

AnyLogic provides built-in functions to send and receive messages from other agents. When an uninfected mosquito (agent) bites an Infectious person (agent), a message (“Infection”) is passed among two agents that an Infectious bite has occurred so declare the current agent (mosquito) as Infectious. Here the state and appearance of mosquito changes to Infectious and the agent becomes red.

Similarly, Person’s state chart starts with a message (“Infectious Bite”), after which the agent moves to the Exposed state and changes its color and further to the Infectious one and become recovered or dead depending upon conditions as described above.

4.1.3.5 Person layer

To initialize an agent population, AnyLogic provides numerous probability distributions. In person layer we have randomly placed agents over GIS map in the region of Swat, having population of 5000 person agents and 1000 mosquito agents



```
Point p= main.gisRegion.randomPointInside(new Random());
this.setLatLon(p.getLatitude(), p.getLongitude());
```

Figure 19: Random distributionof Person agents over GIS

4.1.3.5.1 Person Agent

AnyLogic enables user to create default agents or by creating new type of agents with customized properties. Each agent has its own attributes such as appearance, position and size, points etc. The person agent possesses one of the following states i-e Susceptible, Exposed, Infectious, Recovered and Dead.

4.1.3.5.2 Person Agent's Behavior

It provides the ability to characterize the behavioral states of agents in the form of state charts. The agent's behavior is catered using state charts and transitions such as time triggered, or message triggered transitions**.** Human/ Person behavior is catered using a state chart with states such as Susceptible, Exposed, Infectious, Recovered and Dead and transitions such as bite message, the timeout for being in exposed Infectious, Recovered and Dead state.

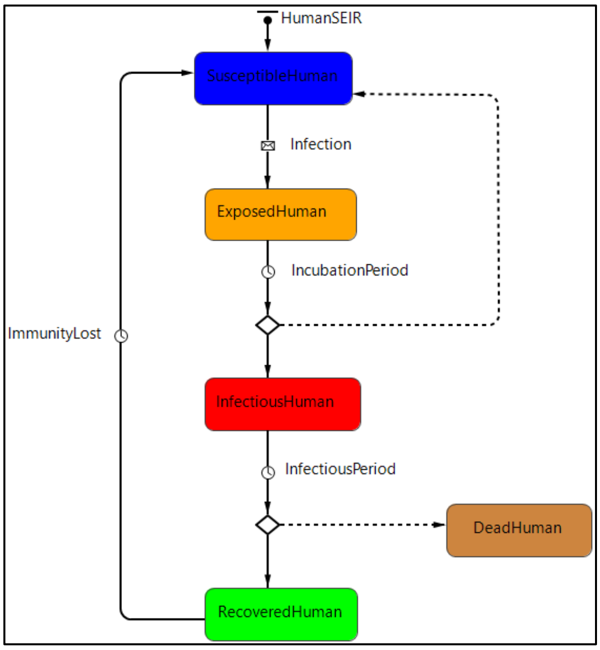
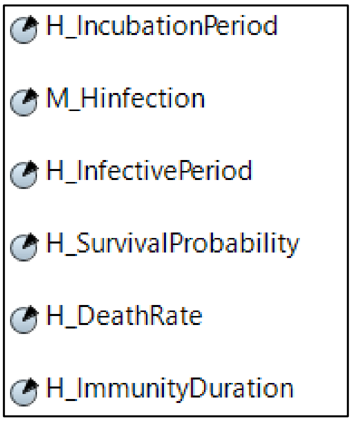


Figure 20: Person agent state chart

Figure 20 describes the agent's (Person) behavior in the form of different states with respect to mosquito's bite. Initially, agent is in Susceptible state with navy in color, as soon as it receives a bite message, the agent's state changes into Exposed and becomes orange in appearance. The agent remains in Exposed state till it is in incubation period i-e approx. 3-8 days**.** During this period if the agent shows the signs/symptoms of infection, it moves to the state of Infectious, otherwise it moves to the Immune stage and becomes gray in color. After getting infection, the color of the agent changes into red. The agent completes its Illness duration. of 20 days in Infectious state [78]. From here it can either get recovered with the rate of Survival probability (0.9) and becomes lime or die with Death probability (0.1) by becoming peru/brown in color and moves to the respective state accordingly.

4.1.3.5.3 Person Agent parameters

The parameters used are shown in Figure below



H_IncubationPeriod
M_Hinfection
H_InfectivePeriod
H_SurvivalProbability
H_DeathRate
H_ImmunityDuration

Figure 21: Person Agent Parameters

It is obtained from multiple sources that the incubation period after a bite of Aedes Aegypti lasts for 4-10 days [14]. In our model we have taken an average incubation period of 5 days [79].

The average duration of infectious period of agent is dependent on temperature. We have applied a mathematical formula used by Jing for the infectious period of person agent.

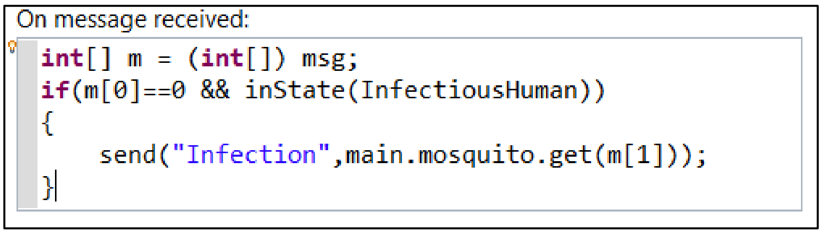
$$\text{Infectious prob} = 0.001044 \times T \times (T - 12.286) \times \sqrt{(32.461 - T)}$$

Here T is temperature. The infection transmission increases when temperature lies between 12.286 <= T <= 27 and decrease sharply from 28 <= T <= 32.461

Agents Survival probability is 0.9 taken from example model of AnyLogic, The Big Book of Simulation [78], with the Death probability of 0.1.

4.1.3.5.4 Person Agent connections

Message passing is done in the Person agent’s connection. Infection is received as a message in the form of an array. The condition checks that if the agent is uninfected mosquito and person agent is Infectious then message “Infection” is sent to the mosquito class along with the index of that mosquito agent, declaring that the particular mosquito agent with that particular index is Infectious now.



On message received:

```
int[] m = (int[]) msg;
if(m[0]==0 && inState(InfectiousHuman))
{
    send("Infection",main.mosquito.get(m[1]));
}
```

Figure 22: Person agent connections

As soon as the Person agent in Susceptible state receives a bite message from Infectious mosquito, Person agent is bitten by the Infectious Mosquito agent and becomes orange in appearance by changing its state to Exposed.

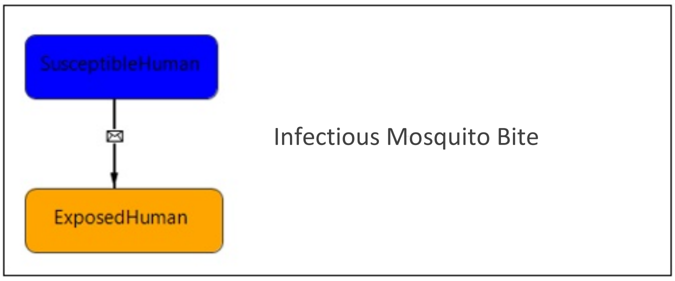
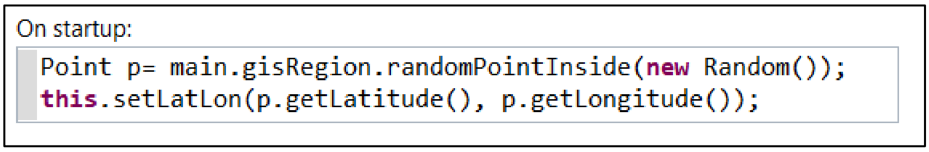


Figure 23: Person agent infection through bite

4.1.3.6 Mosquito layer

AnyLogic agent-based library allows initializing a population of agents using various probability distributions. Besides, it also enables to define custom distribution that fits according to the user's data. We have created a population of Mosquito agent. To place the Mosquito agents randomly over Geographical Information System, a Random distribution of mosquitoes is used. Furthermore, mosquito's agent description and behavior is discussed in the section below.



On startup:

```
Point p= main.gisRegion.randomPointInside(new Random());
this.setLatLon(p.getLatitude(), p.getLongitude());
```

Figure 24: Random distribution of Mosquito agent over GIS

4.1.3.6.1 Mosquito Agent

Mosquito agent's state chart possesses the same states as of Person agent, in addition with Egg, Larva, Pupa, Male adult and Female adult states. There are two states for Adult mosquito i-e Male and Female. Since Male Aedes Aegypti does not make a bite so, Female Aedes Aegypti (Female adult state) contains the biting mechanism.

4.1.3.6.2 Mosquito Agent's Behavior

Infection can take place via two-way bite, i-e either an Infectious mosquito bites an Infectious Person and takes virus into its saliva, gets Infected and pass infection so on; or an already Infectious mosquito (through vertical transmission or Infectious egg laid by Infectious mosquito) bites an uninfected Person. In our work we have covered both two-way biting mechanisms.

There are two separate state charts that run in parallel showing the current state of the agent. The "Mosquito state chart" shows the current state in which the agent lies. The state chart can start with any of the states (Egg, Larva, Pupa or Adult in addition with Idle and Oviposition). Starting with the Egg state, the agent (Mosquito) remains in this state for 2-3 days. Here the agent's appearance (line color) is tan in color. From egg, the agent moves on to the Larva state and becomes yellow green. After spending at minimum4 days agent moves to the state of Pupa with dodger blue color, where it resides for 2 days and move to the Adult stage. The male Aedes aegypti neither makes a bite nor transmits infection. Based on the available data our model caters the behavior of Female Aedes Aegypti only. From each state i-e Egg, Larva, Pupa, Adult the mosquito agent can go to the final state of Dead.

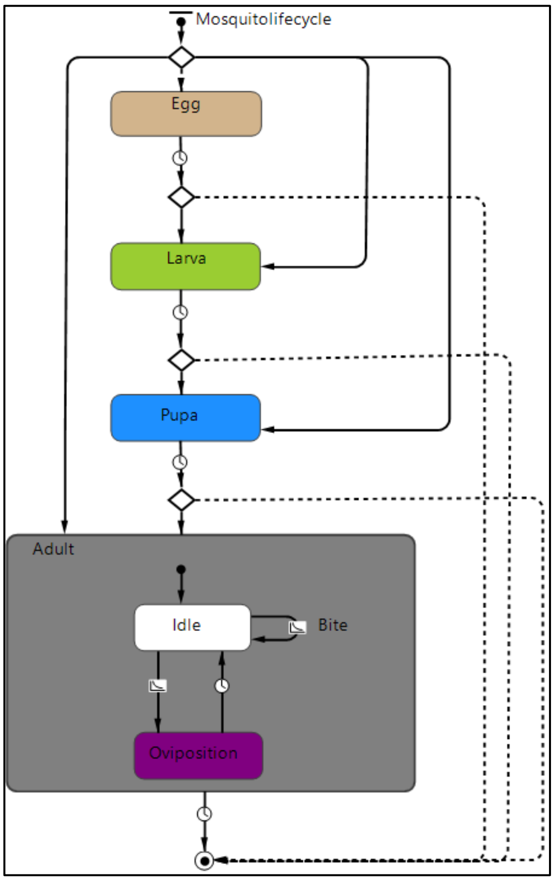


Figure 25: Mosquito Agent State chart

In Adult (Female Aedes Aegypti) state there are further two sub states that portrays the behavior of the agent i-e the agent will either be in Idle state and make a bite or it will be in Oviposition state while laying eggs. The agent will move from Idle state to Oviposition based on the recruitment rate of 0.14 [79]. Female Aedes Aegypti can lay up to five clutches of eggs during her lifetime with 100-200 eggs per batch [80]. Our proposed model has taken oviposition rate on an average as 2 per 14 considering mosquito’s average lifetime as 14 days [79], the rate of oviposition o becomes

$$o = n/l$$

Where n= number of clutches an Aedes can lay and l is the lifetime of Aedes, which becomes 0.14 and will go back to the Idle state after 1 day. During Idle state the agent can make a bite (based on assumption that Aedes mosquito had her fill of blood after each bite) and makes a bite again after 2 days.

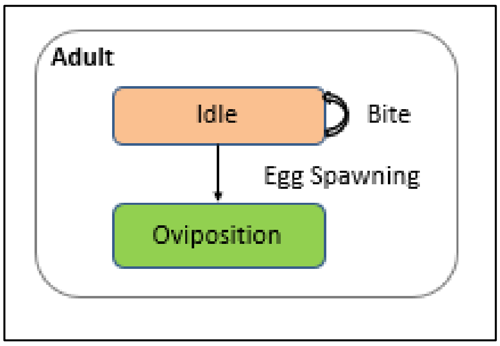


Figure 26: Mosquito Agent behavior

Besides another state chart start runs in parallel with the state chart that caters the mosquito’s state (Egg, Larva, Pupa, Adult in addition with Idle and Oviposition) that shows whether the agent is in Susceptible, Latent or Infectious state which shows the transmission of infection. The agent (depending on the state) can be either in Susceptible state or in Infectious state depending on “Infection”. If agent is Susceptible then it moves from Susceptible state, and becomes yellow otherwise it moves directly to the Infectious state and becomes red. In case of Susceptible state, the agent moves to Latent state by changing its appearance from yellow to navy and completes its incubation/latency period of 10 days (on an average). Afterwards that the agent moves to infectious state and becomes red in color from navy.

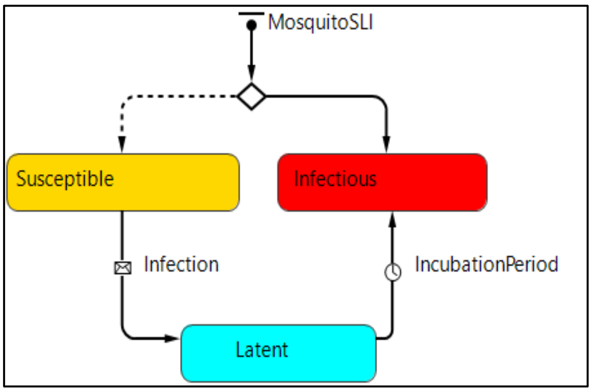
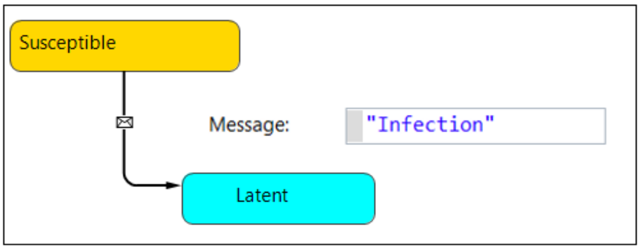


Figure 27: Mosquito Agent SLI state chart

As soon as the mosquito agent receives message “Infection” from Person, it becomes Infectious.

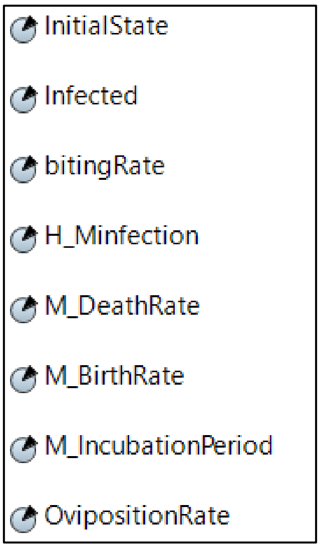


Message: "Infection"

Figure 28: Mosquito agent infection through infectious human bite

4.1.3.7 Mosquito Agent Parameters

The parameters used in Mosquito agent are shown in figure



InitialState
Infected
bitingRate
H_Minfection
M_DeathRate
M_BirthRate
M_IncubationPeriod
OvipositionRate

Figure 29: Mosquito Agent Parameters

The number of times mosquito will bite human is defined by biting rate, which is also temperature dependent. We have applied a mathematical formula used by Jing for biting rate.

$$biting\ rate = (0.03 * T + .66)/7$$

Here T is temperature.

Transmission probability of infection from Human to Mosquito is assumed to be 0.018.

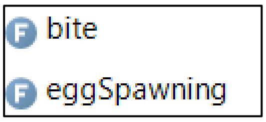
Since female Aedes Aegypti lifetime range from 8-42 days, the baseline of Mosquito is taken as14 days on an average.

Mosquito recruitment rate or birth rate is taken as 0.30, which can also be referred as increase in population.

The average duration of incubation period for Mosquito is taken as 10 days with a range lying between 7-14 days.

4.1.3.8 Mosquito Agent Functions

Mosquito agent has two functions i-e bite and egg spawning. These functions show the behavior of a Mosquito agent. The explanation of both functions is given in this section below.



- F bite
- F eggSpawning

Figure 30: Mosquito agent functions

4.1.3.8.1 Bite

Assumption has been made that female Aedes had her fill of blood after each meal [81] and makes a bite after 2 days.

Mosquito smells human's scent from 10-50 meters [82] within this range a mosquito can bite a human. Our simulation framework has taken this range as 36 meters on an average, which means that bite takes place if a person agent lies in a range of 36 meters.

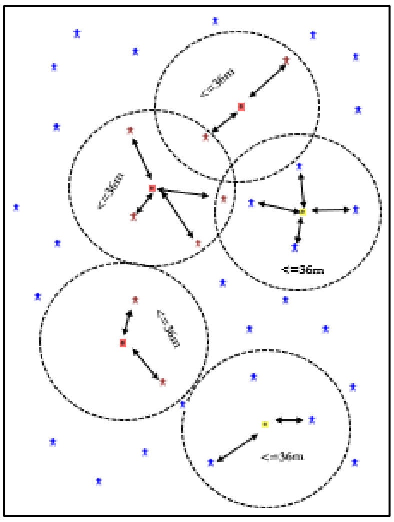


Figure 31: Human vector bite mechanism

Figure 29 shows the susceptible humans in blue and range of mosquito i-e 36m. Red circles show infected mosquitos which bite person agents that lie in its range and red agents show infected humans. Yellow circle shows susceptible mosquito which, if bites, does not infect the human and human agents that lie in its range remain susceptible.

Pseudo code of "when bite takes place" is given in Table 6.

```
Procedure: Bite Criteria
Input: Population of Persons and Mosquitoes
Output: {List of connected Person agents}

for k = 0 to Persons population Size
  for j = 0 to Mosquitoes population Size
    distance ← get Distance(Persons[i],Mosquitos[j])
    if (distance<=36)
            ⊳ Person agents lying within the range of 36m of mosquito agent
      Make connection of person agents[i] ← with mosquito agent[j]
    end if
  end for
end for
Return { List of connected Person Agents }
```

Table 6: Biting Criteria

As mentioned in section 2.1, dengue transmission takes place in two ways i-e from infectious vector to an uninfected person and secondly from infectious person to uninfected vector. Pseudocodes for both ways are mentioned below.

```
Procedure: Biting Scenario A
Input: Persons list

for k = 0 to Person List
  if (Mosquito state = Infectious)
        ⊳ Infectious mosquito bites Uninfected human
    Person agent[i] ← send ("Infection", Person List)
        ⊳ send message to Random Connected agent
  end if
end for
```

Table 7: Transmission from Infectious vector to uninfected person

As bite can take place in two ways, the pseudocodes for both bites i-e the infection transmission from infectious vector to uninfected person is shown in Table 7 and infectious person to uninfected vector through bite is shown in Table 8 below.

Procedure: Biting Scenario B

Input: Mosquitos list

```
for k = 0 to Mosquito List
⊳ Mosquito Connected to Infected Person in range of 36m
    if (Person state = Infectious&& Mosquito state != Infectious)
        ⊳ Uninfected mosquito bites infectious human
      Mosquito agent[i] ← send ("Infection")
    end if
end for
```

Table 8: Transmisson from Infectios person to Uninfected vector

4.1.3.8.2 Egg spawning

Egg hatching takes place in two of the following ways i-e Rapid egg hatch and Delayed egg hatch. In Rapid egg hatch, eggs hatch within two days provides with favorable conditions whereas in Delayed egg hatch eggs may take days or several months to get hatch, depending on favorable conditions. Our model has considered Rapid Egg hatch.

The probability that egg will be male or female is 0.5, which means that 50% of eggs will become male (adult) and other half become Female (adult) [83]. The susceptible mosquitoes lay susceptible eggs and infectious mosquitoes lay infected eggs; the pseudocode given in Figure 34 explains how eggs are added to the mosquito population.

Procedure: Egg Spawning

```
for each Egg
⊳ new egg agent by Mosquito agent
    if (Mosquito state == Infectious)
        ⊳ Uninfected mosquito bites infectious human
      Mosquito agent[i] ← add Infectious Mosquito
    Else
      Mosquito agent[i] ← add Uninfected Mosquito
    end if
end for
```

Table 9: Egg spawning Pseudocode

In our framework we have taken the female population of eggs with assumption that 1 egg is spawned each time. Since female mosquito lay eggs that are 50% male and 50% female, for our proposed model we have considered only female eggs, for simplicity.

4.1.3.9 Main

Main is the environment in which agents interact and contain the properties shared among them. The number of agents (including Person and Mosquito population) are embedded over a GIS map.

AnyLogic enables to use a GIS map to build models in physical space. We used GIS map of Swat city, on which agents (Person, Mosquito) are placed randomly.

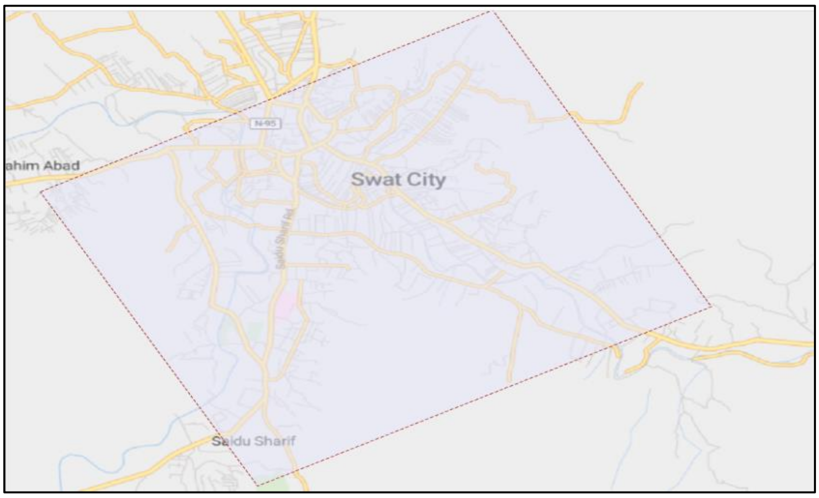


Figure 32: GIS map of Swat city in AnyLogic

Chapter 5

Simulation and Results

In this section, we demonstrate the functionality of our proposed framework.

As mentioned earlier the model is simulated in AnyLogic University Edition for person agent population of 5000 and mosquito agent population of 1000, from 24/07/2013 to 01/12/ 2013, showing the agents behavior over GIS and graphs of the agents on 64-bit Operating System, Intel® Core™ i7-8700 CPU @3.20 GHz, RAM 16.0 GB.

Due to different geo locations, every country has its own climatic conditions (different trends for temperature, humidity, rainfall etc.) that vary in multiple ways from other countries. Similarly, epidemiological disease trends also vary from country to country depending upon multiple parameters and exogenous factors.

If we compare Pakistan’s weather trends with that of Philippines, it is found that there is a large difference in the environments of both countries. So, we can clearly state that there will also be difference in the trends of any epidemiological disease, we compare. Considering Dengue Fever (as a case study for epidemiological study), there lies a huge difference in both countries’ trends, since Philippines is an Island its temperature and rainfall trends differ from Pakistan, so we get different results for both countries.

5.1 Simulation Results

In epidemic modelling Vector and Human population behavior is modelled using Agent-based Approach. The behavior of Human and Vector as an agent is described in this section.

5.1.1 Mosquito Agent

In our proposed framework, population dynamics of vector (mosquitoes) is studied because real data collection for mosquitoes is tedious. It is far difficult to find mosquito traps and their population, and it is incomprehensible to know their exact count and density. Since we can't plot each mosquito due to absence of mosquito's data, therefore we have used simulation approach by using referenced estimates for mosquito agent. Mosquito's population is growing and declining with a consistent rate, maintaining the equilibrium. This equilibrium of mosquito's lifecycle (Egg-Larva-Pupa-Adult) is shown in graph below.

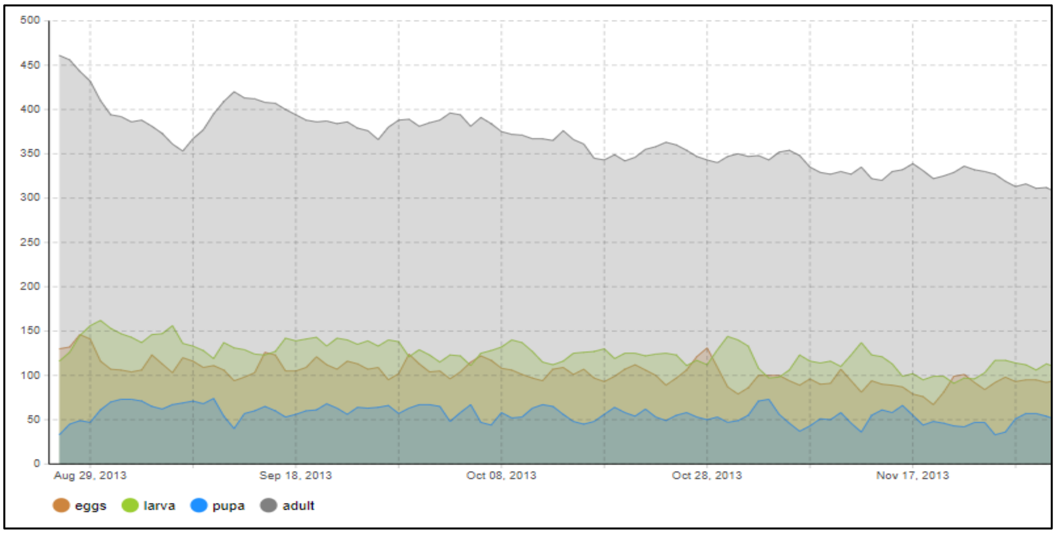


Figure 33: Population growth of Egg, Larva, Pupa Adult

Figure 38 shows a time plot for mosquito's lifecycle growth with horizontal time axis directed to the right and growth of number of agents on vertical axis. The brown color shows the proportion of eggs, the green shows the number of larvae, blue shows the growing pupa and the grey shows the growth of number of adults.

Our simulation started with the initial population of 98.75% eggs, number of larvae is 0.41%, pupa is 0.07% and adults are 0.77%, depending on survival probabilities the egg, larva, pupa and adults grow. The probability from egg-larva is 0.6 and from larva-pupa is 0.9, taken from [29] [84] while the probability from pupa-adult is assumed which is 0.9 likewise. There were fluctuations in the beginning, but the graph becomes stable with the time.

The behavior of Mosquito agent is shown in Figure 39 using SLI(Susceptible-Latent-Infectious) time plot showing epidemic states with respect to time on horizontal time axis and number of agents on vertical axis. We assumed that this epidemiological cycle of vector deals with the Adult population only. The susceptible eggs convert into susceptible adults while the infected ones into infectious adults. There is increase in susceptible population as the agent(mosquito) enters the susceptible state. If mosquito agent is susceptible (yellow in color), and it bites a dengue infected human, then it becomes latent (navy in color) and remain in this state for 10 days, after which the mosquito becomes infected (red in color). Secondly if the mosquito is already infected (either from infected egg or has bitten infectious human), it enters the infectious state, thereby increasing the population of the infectious state.

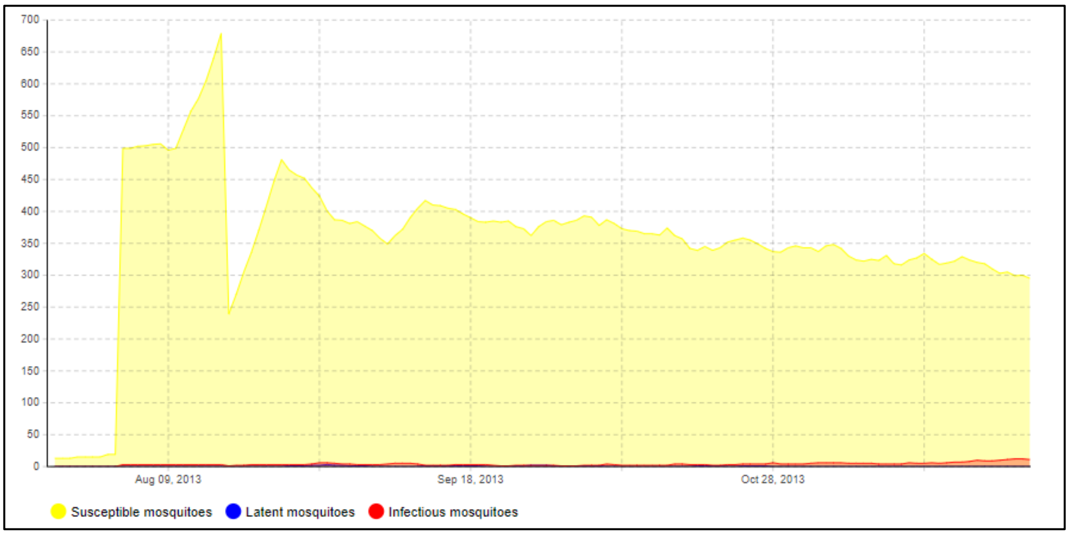


Figure 34: Epidemic states of Mosquito agent

Here the yellow curve shows the number of susceptible mosquitoes, the blue one shows the latent mosquitoes while the red one shows the infectious ones. Since we have large number of susceptible mosquitoes and the number of latent and infectious mosquitoes is less in comparison that’s why the latent and infectious curves cannot be distinguished clearly. The drop in the yellow curve shows that either mosquitoes have started becoming latent or infectious, which decreases the susceptible population and increases the corresponding latent or infectious population.

5.1.2 Person Agent

The person agent's behavior is studied through its Epidemic states of SEIR(Susceptible-Exposed-Infectious-Recovered). Since we have taken 5000 person agents so there comes a huge difference of susceptible curve with the exposed, infectious and recovered curves, that's why we have ignored to plot the population of susceptible person agents. Initially the person agent population is susceptible, as soon as it is bitten by infectious mosquito it becomes Exposed(orange in color), after completing its incubation period of 4-7 days in exposed state it either becomes Infectious(red in color) or susceptible again depending on the infectivity. From Infectious state after completing 4-12 days it either becomes Recovered (lime in color) or die (brown in color). The time plot with the epidemic states along with the time are shown on x-axis and number of agents on y-axis in Figure 40.

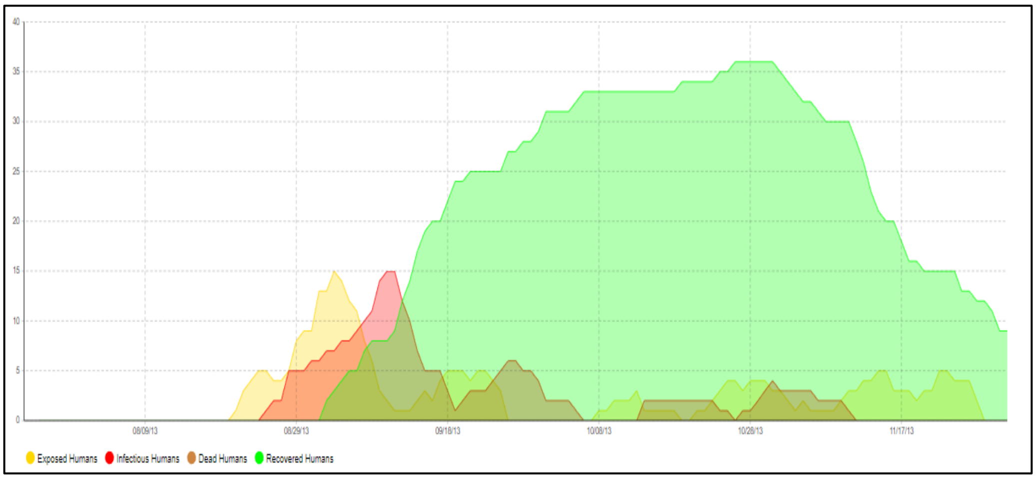


Figure 35: Epidemic states of Person agent

The orange curve shows the increase in exposed persons as they are bitten by infectious mosquito. There is decrease in exposed curve as person starts becoming infectious; with an increase in the infectious curve. The infectious curve decreases as the agents starts recovering. The recovered curve shows high inclination because the person remains in the recovered state for 60 days (Immunity) and becomes susceptible again (Immunity Lost).

5.1.3 Spatiotemporal visualiztion

In this thesis we have combined Agent-based modeling with spatiotemporal visualization by envisioning the behavior of agents and spread of disease over GIS map of Swat city shown in Figure 41.

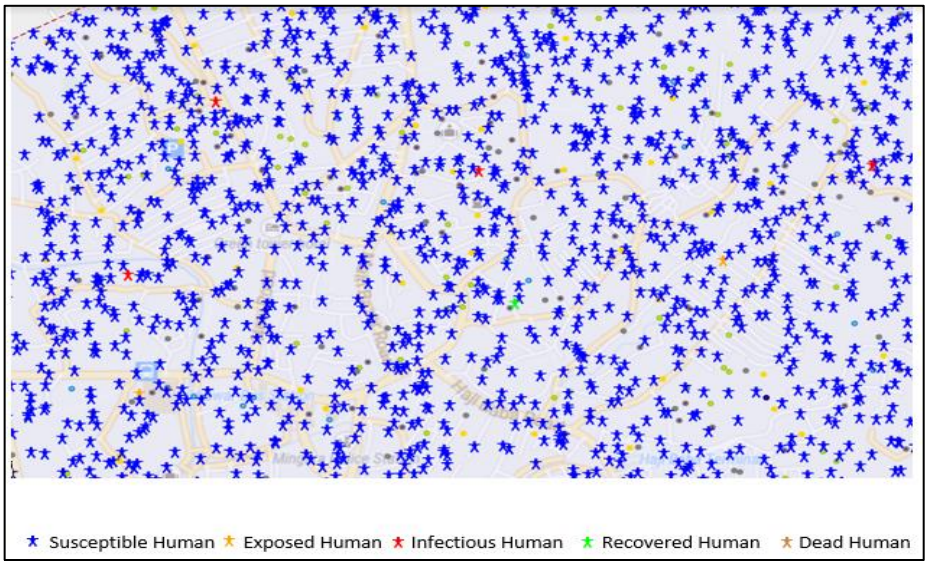


Figure 36:Spatial Distribution of agents over GIS

Here the blue agents show the susceptible population, the red ones show the infectious, the orange agents are exposed, and the green and brown are recovered and dead respectively.

Similar behavior is observed for the Mosquito agent. The mosquito agent changes its appearance as it changes its state. The circle represents the mosquito agent, the circle is tan in color when the mosquito agent is in Egg state, green when its in Larva state, blue in pupa state and grey in adult state. Furthermore, the yellow color shows that the mosquito agent is Susceptible, the blue shows that its latent and red represents the infectious state of mosquito.

Simulation is executed to depict the behavior of agents and spread of Dengue Fever.

Chapter 6

Model Evaluation

In this section, we explain functional and integration testing. We also discuss that how our model has been tested using these testing techniques.

Model validation is required to assure the reliability and applicability of model. Validation evaluate that how well a model replicated the real-world scenario. It is performed by comparing the simulation results with the actual observations.

6.1 Simulated results validation

The simulated results obtained are compared with the actual results (dengue cases) of Swat district.

The actual results of confirmed cases are obtained from the dengue outbreak occurred in Swat in 2013 and are compared with our simulated results obtained. The actual results include the laboratory confirmed dengue cases from August 2013 to November 2013. The trend shows a highest peak surged in September followed by October, and low cases in August (as compared to September and October), followed by November with least cases. The original monthly graph of actual Dengue fever cases in Swat is shown in Figure 39.

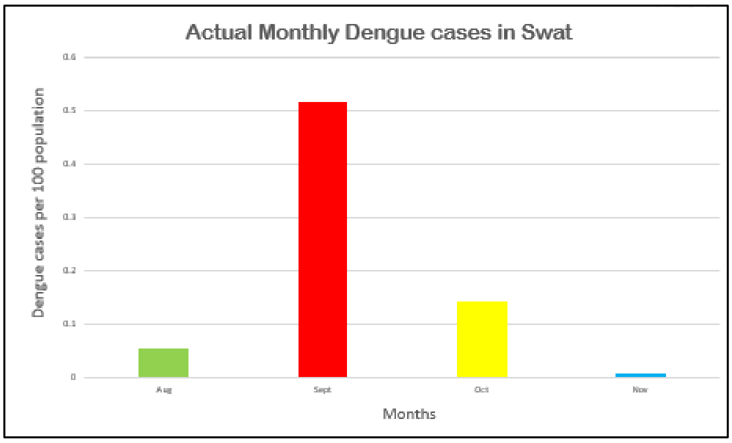


Figure 37: Actual Monthly Dengue casses

The obtained results after the execution of simulation are shown in Figure 40.

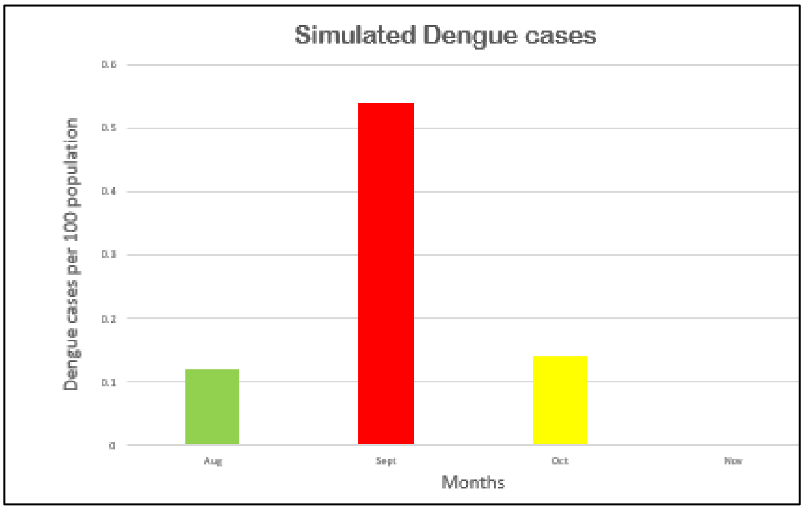


Figure 38: Simulated Dengue cases

The graphs show months on x-axis and Dengue cases per 100 population on y-axis. In order to compare the data results of actual and simulated dengue cases, we have taken prevalence of both data sets.

$$prevalence = (No. of\ Dengue\ case \div Total\ population) \times 100$$

The actual cases of Swat were 9036 out of Total population of 1257602 while the simulated cases obtained were 40 out of Total agents' population of 5000.

For comparison a graph containing both cases is shown in Figure 41.

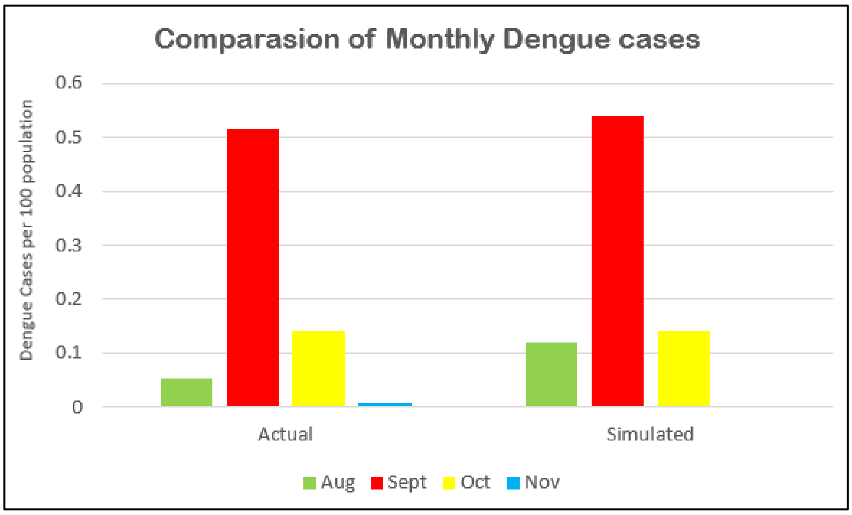


Figure 39: Comparasion of Monthly Dengue cases

A similar trend can be observed between both actual and simulated results with some differences. In August we have got a monthly prevalence of 0.0536, with 0.5160, 0.142 and 0.0074 for September, October and November respectively for actual results. While for simulated results we have got 0.12 for August, 0.54, 0.14 and 0, for September, October, and November.

There is an eloquent increase in the number of reported Dengue cases in September and the simulated results show the same peak with a slight difference. The results show that the Dengue transmission is temperature dependent (assumed the most favorable conditions to the Aedes Aegypti mosquitoes for growth). Among multiple parameters, the most significant factors that play a vital role in Dengue transmission are the biting rate and probability of infection transmission from vector to human. With the increase in temperature, the biting rate of Aedes Aegypti increases that give rise to the Dengue cases [44] as mentioned. From the graphs it can be inferred that our simulation results matches the actual reported cases occurred in Swat region.

Secondly, we have also compared the results based on 15 days and plotted the epidemic curves for both. Figure 42 shows the histogram of reported Dengue cases with blue bars and simulated Dengue cases with yellow bars. It can be observed that the overall trend is almost similar through the four months of August- November. The x-axis shows 15-days per bin (for reported and simulated) and the y-axis shows the prevalence of Dengue case as mentioned above.

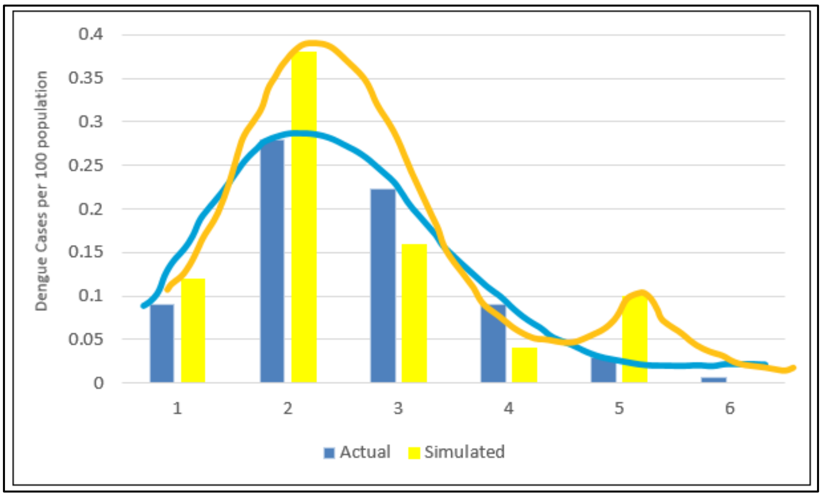


Figure 40: Histogram of Dengue cases per 15-days

It can be noted that the simulation results peak at the same time, (as that of reported results), but with the different peak sizes.

There is a slight difference in curve because we have taken a difference of 15 days, which means that the cases that occurred in a particular month might fall in the next or previous bin because of difference as compared to the next one.

Chapter 7

Conclusion and Future Work

This chapter provides the discussion, conclusion and future work of the thesis.

7.1 Conclusion

In our thesis we have been able to perform practical applied research and propose a forecasting framework that provides visualization and forecasting capabilities and flexibility to the modelers to add further features. It is an open-ended framework to study any type of epidemiology. In our thesis we have taken Dengue as a case study of Swat region in Pakistan. Agent-based modeling approach is used for GIS visualization is used that assists stakeholders (Clinicians, Microbiologists and Public Health) to study epidemiology of a region to make predictions. Modeling and simulation of dengue vector population dynamics, and the disease transmissibility will contribute in the accurate forecasting and prevention of dengue outbreaks over a defined space and time. Our goal is to provide a simulation tool that helps the public health sector to develop action plans in places with a high incidence of A. aegypti and dengue virus infection, to prevent new epidemic outbreaks. With the help of such a simulation model, powerful insights into the vector lifecycle can be investigated. The simulation framework can be utilized for the prediction of rate of spread of dengue infection, which will, in turn, help to forecast dengue outbreaks and support in taking specific preemptive measures against Dengue Fever. Such simulations can help to improve understanding of the spread of diseases and to take better measures for the prevention and control of an epidemic.

7.2 Future Work

Since our proposed framework is useful in terms of flexibility, as it is open-ended and allows adding new features and multiple agent behaviors to make predictions.

In future, we plan to improve our proposed framework further by adding the mobility layer (incorporating movement), in which mobile humans and mosquitoes will interact with each other. We aim to expand our simulation framework to a detailed environment by scaling it in terms of bigger population and large area adding more exogenous parameters like rainfall and humidity. Furthermore, it can also be extended to address the complexity of all serotypes.

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