SIMULATION OF DENGUE OUTBREAK IN THAILAND

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The dengue virus has become widespread worldwide in recent decades. It has no specific treatment and affects more than 40% of the entire population in the world. In Thailand, dengue has been a health concern for more than half a century. The highest number of cases in one year was 174,285 in 1987, leading to 1,007 deaths. In the present day, dengue is distributed throughout the entire country. Therefore, dengue has become a major challenge for public health in terms of both prevention and control of outbreaks. Different methodologies and ways of dealing with dengue outbreaks have been put forward by researchers. Computational models and simulations play an important role, as they have the ability to help researchers and officers in public health gain a greater understanding of the virus's epidemic activities.

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CHAPTER 1

INTRODUCTION

In recent decades, agent-based modeling (ABM), which is the observing of agents' behaviors [1], has attracted the attention of researchers and has been used as a system to study the correspondence of action between populations, objects, areas, and periods of time. Autonomous units in ABM, referred to as agents or individuals, which can interact with each other and produce several results in experiments, have been utilized for software design and software simulation in many research areas, e.g. biology, business, and the social sciences, among others. As one demonstration of the potential of the system dynamic modeling of ABM systems, public health has profited from agent-based design and simulation of aspects of population health such as health care capacity and delivery, emergency and extended care for patients, substance abuse epidemiology, and disease epidemiology. For studying disease epidemiology, ABM systems have been utilized to explore how vectors carry pathogens and spread them to hosts, especially with mosquito-borne diseases, such as malaria, dengue, and chikungunya as mosquito-borne diseases are among those of the highest concern.

Although ABM systems have been utilized in public health for several years, there are still some issues that must be resolved, for example, working with country-sized data for both human and mosquito populations, integrating large-scale movement of populations, and making allowances in the model for members of both populations to meet with others on a more than once-daily basis. To solve this problem, modified Agent-based modeling (mABM), which is a new research framework, has been introduced.

mABM is a hybrid method which can be classified into two groups depending on its main methodologies: (1) computational models, which deploy interaction between agents and the environment; and (2) mathematical models, which solve the problem with reference to very large populations. mABM allows various mathematical equations to be used in the model, such as the calculation of the survival rate of mosquitos or the number of transmissions from adult female mosquitos to their offspring.

The mABM system in this study was introduced to simulate a rapid-growth mosquito-borne disease. The computational models and mathematical models among mABM systems can be described as follows:

1. Computational models consist of two major types of models, which are ABM systems and local stochastic contact modeling (LSCM).
2. Mathematical models are comprised of numerous of methods, including (1) the extrinsic incubation period model (EIP) for mosquitos becoming infectious; (2) the vertical transmission model (VT) for the passing of a virus from female mosquitos to their offspring; and (3) the gonotrophic cycle model for new offspring production.

mABM can simulate a large-scale agent population and complex processes of interaction between agents and the environment for mosquito-borne diseases. In addition, the mABM in this study has controlled and maintained the mosquito population effectively in order to keep those numbers close to those reported by Thai public health.

1.1 Mosquito-Borne Diseases and Dengue

Mosquito-borne diseases are of high concern for public health because at least 700,000 people are killed annually by major mosquito-borne diseases, such as dengue, malaria, yellow fever, and others. Whereas malaria is the deadliest disease, dengue is rapidly becoming widespread worldwide. Over 40% of the world population, or 2.5 billion people, live in areas of high exposure to dengue, and dengue virus infection is a major concern in several countries. The number of dengue cases is between 50 and 100 million each year worldwide [2][3].

Dengue is a viral infection found primarily in tropical and sub-tropical locations worldwide. Being bitten by female mosquitos can lead to disease for host organisms. The primary mosquitos to transmit dengue virus to humans are *Aedes Aegypti*, and *Aedes albopictus* also accounts for some virus transmissions. Four dengue viral serotypes, DEN-1, DEN-2, DEN-3, and DEN-4, are intimately correlated and give rise to dengue symptoms [4]. The infection of dengue can be classified according to three kinds of symptoms: dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). A host will have lifelong immunity against dengue after recovering from the infection, yet cross-immunity to the other strains is only temporary and partial. Having been infected with one of the serotypes, the host will be at high risk for developing severe dengue infection from a different strain [4][5][6].

A virus can spread rapidly when people experience displacement. According to WHO, almost 900 million global travelers are in transit each year [7]. On this scale, these journeys expose people to a wide range of infections, and human mobility is a central factor leading to spatial dynamic outbreak and related incidents. Outbreaks can go viral on a large scale owing to the distance humans travel. For example, an influenza pandemic can speedily spread internationally due to the high traffic of cosmopolitan journeys [8][9].

That dengue can be spread from a dengue endemic area to a non-endemic area is evident. The United Kingdom, for example, confirmed that 15 travelers who returned there from dengue-originating countries (India, South-east Asia, Uganda, and Barbados) [10] had contracted the disease. Similarly, another report investigated 61 returning tourists who had visited Latin America; 57 cases were confirmed for infection even though none of the infections were rated serious enough to meet the WHO hemorrhagic dengue criteria [11]. From 1993 to 2001, a laboratory in Germany tested returning travelers to Berlin, and 71 cases showed positive for dengue contraction.

It was found that 77.5% of the patients had visited South Central and South East Asia and returned showing the symptoms of dengue fever: headache, retro-orbital, myalgia, arthralgia, and morbilliform rush; some patients, indeed, met the WHO criteria for DHF [12].

In preceding decades, epidemics had occurred in only nine countries. Recently, however, more than 100 countries have experienced epidemics of severe dengue, and the disease has become a health problem in most tropical countries including South-East Asian Countries and Thailand, which is the study area for this work and an area with one of the highest rates of dengue cases. In Thailand, the first recognized diagnosis of dengue was reported in the 1950s. Five years later, dengue was infecting patients every year, mostly in Bangkok and Thonburi. Dengue rapidly spread to the whole of Thailand due to its speedy transportation across population-dense areas [13]. In recent years, dengue has evolved into Thailand’s primary national public health concern. In 2012, dengue caused the deaths of 79 Thai people and the infection of more than 74,000 [14]. Dengue has been for many years the most important outbreak disease according to the Bureau of Epidemiology in Thailand [15]

A simulation model is an important tool for identifying the dynamics of dengue outbreaks. It incorporates multiple resources and evidence to make possible the best understanding of the outbreaks. A simulation model allows health researchers to address the problems and assign various parameters, which are directly related to health conditions along with conditions related to timing and the environment.

1.2 The Surveillance System

To monitor outbreaks including mosquito-borne diseases, the public health system needs a surveillance system to facilitate the development of prevention and control plans for these diseases;

therefore, the surveillance system is becoming increasingly important as a tool for handling public health crises. The system can prepare data to support public health strategies, including (1) providing early notification and recognizing public health emergencies, (2) recommending plans of action for public health, and (3) achieving a deeper understanding of the disease conditions and situations.

Researchers can develop sophisticated data-driven strategies to detect and investigate outbreak emergence. They can apply various methods ranging from mathematical to computational models. They can either compile the data and use statistical techniques to predict the outbreaks or simulate the outbreak to achieve a deeper understanding of outbreak processes. Both mathematical and computational models have been used to explore the nature of outbreaks, for example, outbreaks of flu, chronic diseases, mosquito-borne diseases, and others. In the area of mosquito-borne disease, only a small number of computational software applications are presently available for integrating a number of scenarios, taking into consideration contributing factors, such as vector ecology, climate conditions, virus evolution, and human host mobility. Such computational models could bring even more benefit to researchers, health care personnel and public health institutions, and policy makers; however, with a population size in the millions interacting with a micro-object like a mosquito, with no computational tools available, it is difficult to use ABM to simulate this kind of problem, due to the necessity of generating micro-objects in the hundreds of millions, or multiple times of the human population. A new method, such as the one to be developed in this research, is needed to solve this micro-object management problem.

An accurate reproduction of the number of cases from an outbreak in humans requires understanding the spatio-temporality of hosts from a specific location and the relationship between host and vector. Geography and population mobility patterns are utilized for prediction of disease spread. To study the possibility of contagion dynamics arising from population displacement, the model must be able to incorporate agent dynamics and the relationship of people to their environment. To handle recently recognized factors for modeling mosquito-borne disease, a new methodology must meet this requirement.

In short, surveillance systems and control efforts are for the purpose of preventing the spread of dengue in endemic countries. Most systems use only raw data to identify the outbreak areas and do not perform in-depth analysis. To get more advantage from the available raw data, a useful technique for study and prevention outbreak must be established.

1.3 Problem Statements

To meet the above requirements, the mABM system in this study is presented as a novel method to model the interaction among demographics, geographies, and infections by deployment of data from Thailand. To take into account the inter-association between people and mosquitos, the model applies the Local Stochastic Contact Model (LSCM) as a substitute for the relationship between mosquito and human populations. For human mobility, the model allows researchers to enter different types of populations, namely Thai people and immigrant people, to test the effect on a potential outbreak of human mobility across the country’s borders during holidays and regular working times. The new model can perform a more realistic simulation by including weather conditions, which affect mosquitos’ ecology and the development of the viruses. The Modified ABM provides the benefits of a computational tool to the researchers.

One possible way to deal with a large-scale pandemic of dengue is to establish an effective plan for preventing the disease by understanding how it spreads in a large population, i.e., by considering the way people travel, the environments, and the ecology of viruses and vectors.

Many health risks can be reduced by the early issuing of cautions before, during, and after travel. Computational models provide information on health risks in advance to travelers. The aim of this dissertation is to develop and apply a simulation-based method to compute the time as it varies with different circumstances and events by providing essential elements for outbreak conditions that meet the following criteria: (1) the model has the potential to create a simulation for the entire country, (2) the model includes features of human mobility both within the country and without, taking into account the arrival and departure of people across borders, (3) the model includes actual data in the simulation, e.g., the climate of regions and the demographics of the population, and (4) the model takes into account the micro agent, i.e., the mosquito.

The mABM system was designed to simulate disease outbreak throughout the whole country of Thailand, assuming contact between host and vector. To attain the research goals, the research questions are as follows:

(i) How do we improve the realism of the computational simulation by integrating data from different sources?

(ii) How can Agent-based modeling (ABM) be used to represent human behavior in large populations across varying distances?

(iii) How can we represent the mosquito population and its ecology?

(iv) How can regional temperatures be integrated into an outbreak model to capture their effect on dengue outbreak?

(v) How can different modeling methodologies be linked to represent these interactions?

The main focus of this research is to simulate an outbreak through the whole country involving two kinds of objects, humans and mosquitos. The main challenge is to design a model with improved performance when it is working with a very large-scale number of agents. Certain field data and reported data are used in this mABM system to increase its fidelity. However, missing and unreported data are a cause of major concern.

The synthetic population of humans is generated from statistics from the National Statistical Office (NSO) in Thailand. Vector population dynamics are driven by conditions of climate as recorded in local environmental data from the Thailand Meteorologist Department (TMD), and of mosquito ecology; both are required in order to produce a dynamic mosquito model for mosquitos in four stages: egg, larva, pupa, and adult. This scenario simulates for millions of synthetic people in Thailand, and it is thus described as a large-scale model.

1.4 Overview

The motivation to develop a new approach to simulation involving a very large population has been introduced in this chapter. The structure of this dissertation is as follows: Chapter 2 reviews previous related work, providing the background of the study area, the disease background, and methodologies. The methodologies are presented in Chapter 3, corresponding to all research questions. Chapter 4 presents the experimental results corresponding to each assumption and describes each outcome. The validation of the experiment will be compared to the report of dengue cases from the public health of Thailand in order to answer the first and second research questions. Chapter 5 presents a summary of the results and discusses aspects that were not incorporated in the study as well as directions for future work.

CHAPTER 2

LITERATURE REVIEW

This chapter introduces general information on dengue, the study area, related work, and two important methodologies: agent-based modeling and local stochastic contact modeling.

2.1 Dengue

The dengue virus has become widespread worldwide; it has been ranked as the world's most rapidly spreading viral disease. Dengue is a vector borne disease in which infection is spread to humans primarily from the mosquitos Aedes aegypti and Aedes albopictus [2][3]. More than 40% of the entire population in the world, or approximately 2.5 billion people, are at risk of dengue, and dengue virus infection is a major concern in several countries. Each year there are almost 50 million cases of the disease, affecting 250,000 to 500,000 patients, and leading to 20,000 deaths. The disease reaches into primarily tropical and subtropical areas due to growth in urbanization, poor mosquito control, and ineffective treatment in such areas [2]. Two thousand cases of infection were reported in one year occurring in non-endemic areas in western Europe, including the Portuguese Atlantic island of Madeira [16][17]. In 2013, dengue was ranked by the World Health Organization (WHO) as having the fastest rate of outbreak of any disease in the world in the pandemic areas: Asia, the Americas, and Africa [18]. Today, the disease is distributed globally in up to 125 countries, and dengue threatens the world [2]. The endemic areas are shown in Figure 2.1.

Dengue is a viral infection found primarily in tropical and sub-tropical locations worldwide. It is caused by four serotypes of arthropod-borne (arbor) viruses: DEN-1, DEN-2, DEN-3, and DEN-4. Through the bites of contagious female mosquitos, the virus can be transmitted from vector to host. Because of the trans-international mobility of the host population and the worldwide shipping of merchandise, the disease has occurred in worldwide outbreaks and has become a serious public health issue. The disease now seriously threatens populations because of global climate change and urbanization of the tropics.

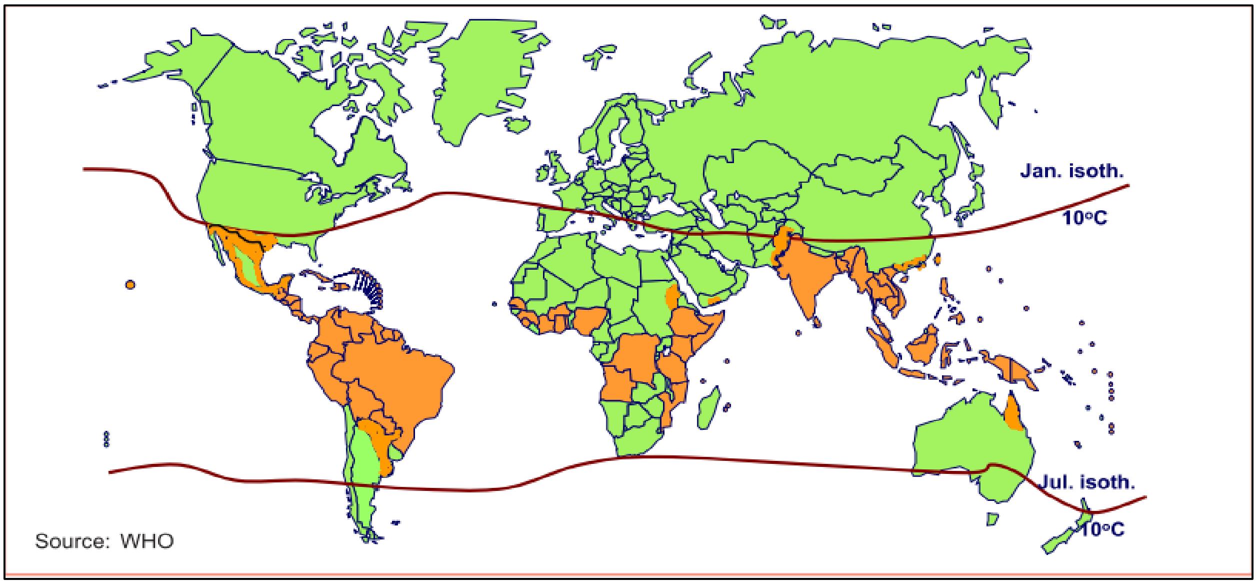


FIGURE 2.1. Tropical areas and countries at risk of dengue outbreak, 2008 [4].

The full spectrum of illness and severity can develop when an individual is infected with one or more of the dengue serotypes. Symptoms can range from a mild fever to pain behind the eyes, severe headache, joint paint, muscle pain, rash, dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). People who suspect they may be infected should be concerned when they have a fever above 40°C or 104°F for 2 or more days and have symptoms including severe headache, pain behind the eyes, nausea, vomiting, muscle and joint pains, swollen glands, or a rash lasting for 2 to 7 days.

To classify DF, DHF, and DSS, the WHO has defined the clinical conditions of each illness according the guidelines shown in Figure 2.2; short descriptions for each illness typed as dengue fever follow:

The illness termed DF may present with at least two of the following symptoms: headache, myalgia, rash, retro-orbital pain, hemorrhagic manifestations, arthralgia, and leukopenia and supportive serology. If patients with these symptoms live in areas with confirmed cases of DF, there is a high likelihood that they are suffering from DF. Unlike DF, the feverish illness termed DHF presents all of the following: fever lasting between 2 and 7 days, bleeding, thrombocytopenia, and the evidence of plasma leaking.

For diagnosis of DSS, symptoms in patients will include all manifestations given above plus all of these four criteria: rapid and weak pulse, blood pressure beneath 20 mm Hg, cold clammy skin, and restlessness.

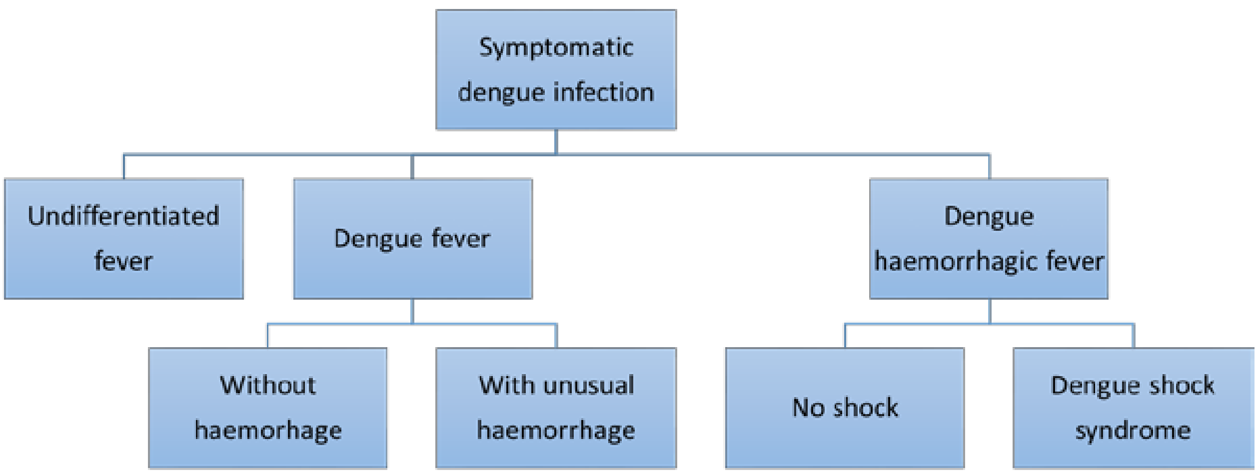


FIGURE 2.2. Classification of case definitions from WHO.

The conditions of DF, DHF, and DSS will appear two to seven days after the virus has been contracted, and the warning signs will be reported by clinical and laboratory workers.

Dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF) are the primary forms of the disease occurring among Thai children [19][20]. The cases of dengue are obviously of concern due to human suffering and economic costs [21][22]. Dengue symptoms are extremely dangerous, and patients must undergo a medical exam in order to avoid serious bleeding or even death.

2.2 Study Area: Thailand

2.2.1 Introduction and Geography of Thailand

The Kingdom of Thailand, normally referred to simply as Thailand, is located in the tropics. A country of Southeast Asia, Thailand is located at the geographic coordinates of 15.00 N, 100.00 E. Thailand's total area is 513,120 square kilometers, which includes 510,890 square kilometers of land and 2,230 cubic kilometers of water. Thailand's administrative divisions are divided into 5 regions: Central, Northeast, Northern, Eastern, and Southern, and 77 provinces; Bangkok is the capital of Thailand. Each region has one or more provinces that function as its hub or center. To illustrate, the Northeast region has 4 major provinces: Nakhon Ratchasima, KhonKaen, Ubon Ratchathani, and Udon Thani; and the Northern region has 3 major provinces: Nakhon Sawan, Phitsanulok, and Chiang Mai. The nations and geographic features bordering Thailand are as follow: Laos and Myanmar, north; Cambodia and Laos, east; Myanmar, west; Malaysia, south; and the Andaman Sea, south [23][24][25].

The residential areas in Thailand are distributed between rural and urban areas. A survey report from the National Statistical Office (NSO) in 2012 showed that 44.2% of people lived in rural areas, and 55.8% lived in urban areas. The average density of population, classified by region, was 125.4 people per square kilometer for the Southern Region, 112.3 for the Northeast Region, 177.7 for the Central Region, 68.7 for the Northern Region, and 5,294.3 for Bangkok [26].

2.2.2 Season in Thailand

According to the Thai Meteorological Department, Thailand has 3 seasons, which are summer, rainy, and winter. The summer period, a hot and dry season, is from mid-February to mid-May. The temperatures during that season can exceed 40º C. The average for the whole country during the summer period is 28.57° C, with 35.8° C for the highest and 21.4° C for the lowest average temperature.

The rainy period is from mid-May to mid-October for most provinces in Thailand, but it continues for a longer time in the southern region, ending there in December. The average temperature for the whole country during the rainy period is 27.75° C, with 32.1° C for the highest and 23.7° C for the lowest average temperature.

The winter period is from mid-October to mid-February, and the average temperature may fall to 16° C or lower. The average temperature for the whole country during the winter period is 25.43° C, with 31.7° C for the highest and 17.1° C for the lowest average temperature [25].

The summary of seasons in Thailand and their temperatures are presented in TABLE 2.1.

TABLE 2.1. Seasons in Thailand with lowest, average, and highest temperature for each season.

Summer	Rainy	Winter
21.40°C | 28.57°C | 35.80°C	23.70°C | 27.75°C | 32.10°C	17.10°C | 25.43°C | 31.70°C
Mid-February – Mid-May	Mid-May – Mid-October	Mid-October-Mid-February

2.2.3 Travel and Transportation in Thailand

For traveling connections among locations in Thailand, Thailand has a variety of choices of transportation: Thai people travel primarily by car, bus, train, and airplane, having at their disposal 108 bus stations [27], 106 major train stations [28], and 34 airports [29]. In 2012, almost 54.8 percent of the population traveled recreationally to other provinces [30].

Not only do Thai people travel cross country, but also non-Thai people from surrounding countries often come into Thailand for different purposes, such as jobs, education, and travel. Thailand shares borders with the neighboring countries of Laos, Myanmar, Cambodia, and Malaysia, so people can travel across the borders between those countries and Thailand. Thailand has 93 border crossing points: 47 stations for Laos, 21 stations for Myanmar, 16 stations for Cambodia, and 9 stations for Malaysia [31]. The number of people who come from neighboring countries is almost 5 million people per year [32].

2.2.4 Dengue in Thailand

With population displacement and suitable temperature, there exist conditions favorable for the rapidity of disease outbreaks. Consequently, people in Thailand face mosquito-borne diseases, such as malaria, chikungunya, and dengue. The first recognized diagnosis of dengue in Thailand was reported in the 1950s, when there were a small number of patients. Five years later, dengue was infecting patients every year, mostly in Bangkok and Thonburi. Dengue rapidly spread to the whole of Thailand due to its speedy transportation across population-dense areas [13]. In recent years, dengue has evolved into Thailand's primary national public health concern. In 2012, dengue caused the deaths of 79 Thai people and the infection of more than 74,000 [14]. For many years, dengue has represented the most significant disease outbreak according to the Bureau of Epidemiology in Thailand [15].

Demographic changes in the population of communities, human travel, lack of control in urbanization, low quality in water management systems, and the increasing use of plastic containers, along with used tires that hold standing water in which mosquitos can breed, are impacting the rates of outbreak of dengue [33][34][35].

In the present day, DHF is a serious issue of high concern for public health in Thailand and is becoming the number one vector-borne disease ahead of malaria, chikungunya, elephantiasis, and other similar diseases. In 2016, the number of confirmed cases reported by Thailand's public health institutions showing the family of symptoms caused by dengue was 63,310, leading to 61 deaths, as compared to only 1,849 cases and no deaths reported for malaria [36].

The goal for Thailand's public health ministry is to reduce the number of confirmed cases by 20% each year compared to the year before. Consequently, the Thailand Vector Borne Disease Bureau has promoted programs to control the vector and to reduce the outbreaks to manageable proportions in under a decade.

The strategies to reduce dengue public health cases are field work aiming to eliminate new mosquito populations and breaking the continuity of human-vector contact. Nevertheless, there are few or no computational models that can be used to simulate the disease. The current research could help public health institutions test and prepare plans and increase understanding of the dengue disease in different conditions.

2.3 Mosquito Life Cycle

Mosquitos can easily be found in tropical or sub-tropical areas including Thailand. There are as many as 3,500 species of mosquitos in the world. Thailand has approximately 400 species of mosquitos. Some species merely cause a nuisance by sucking blood from humans and animals as food, but many other species can transmit dangerous diseases to humans and animals, such as Malaria, Zika, and Dengue.

After a female mosquito has mated and obtained blood, she will have the potential to produce offspring, which go through 4 different stages from egg through adult; all mosquito species will go through these four stages of their life cycle [37][38]:

1) The egg is the first stage of the mosquito. Eggs are laid by a female mosquito on the surface of water, close to water, or on something that can be loaded with water, such as soil or the

base of a plant. The female mosquito needs a small amount of water to lay her eggs; for example, the water in a cup, bowl, used tire, or similar small receptacle is sufficient. The number of eggs per oviposition is generally 100 to 300 eggs, and mosquito eggs can remain alive in dry conditions for up to 8 months. The drought tolerance of mosquito eggs maintains contagion of dengue due to there being mosquito populations in an environment along with dengue virus from vertical transmission.

2) The larva or wriggler emerges from the hatched egg. The larva lives in water and hangs under the water's surface for easy breathing. It molts its skin four times. In the last molt, a larva will develop into a pupa.

3) The pupa or tumble lives in the water and has a comma-like shape. The pupa does not require or obtain any food during its development into an adult mosquito.

4) The adult emerges and climbs out of the pupa shell. It is ready to fly after it has taken a few minutes to dry out its body. The male mosquito requires two days for the full development of its reproductive organs; then he looks for a female for mating. After mating, the female mosquito requires blood in order to develop her eggs; only female mosquitos bite humans and animals. After sucking blood, a female mosquito will find standing water in which to lay her eggs. Aedes aegypti and Aedes albopictus mosquitos readily bite humans, and they tend to live inside or near humans' homes.

The first three stages of development take place in water. The development for each stage depends on temperature and environment conditions. A female mosquito needs to mate at least one time and continues developing eggs after each blood meal.

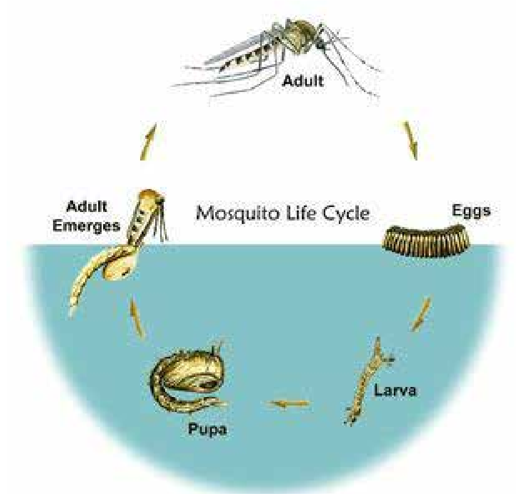


FIGURE 2.3. Mosquito life cycle [37].

2.4 Displacement of Thai People

The displacement of Thai people in Thailand can be classified into 2 patterns: 1) traveling during the holiday season and 2) taking a short trip for a weekend getaway.

2.4.1 Traveling during the Holiday Season

Thailand has three majors holiday seasons: New Year’s Day, the Thai New Year or Songkran, and the Candle Festival. According to a report from the Ministry of Tourism and Sports [39], the data show that January and December see the highest rates of hotel occupancy during the first and fourth quarters and during the whole year. During the second quarter, April, which is the month of the Thai New Year, has the highest rate of hotel occupancy. Another major holiday is the Candle Festival, which is held in July every year, so July has the highest rate of hotel occupancy during the third quarter.

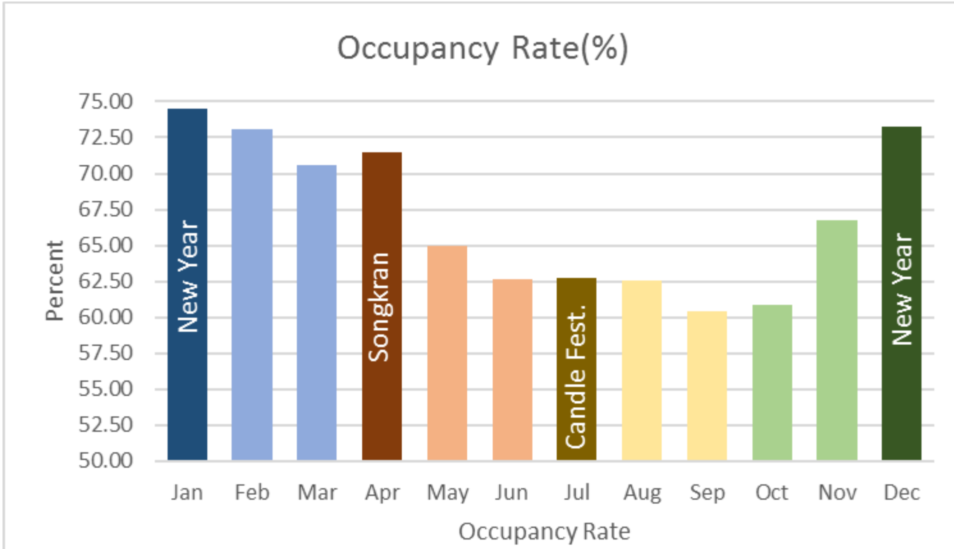


FIGURE 2.4. Highest occupation rate (%) per month for each quarter.

Holiday seasons can result in a population's displacement from its current areas for different purposes, such as its members visiting their family in their hometown, traveling to popular places, and touring temples and religious sites. The celebrations for these major holidays are held for three to four days during one month depending on the region.

2.4.2 Taking a Short Trip for Weekend Getaway

NSO had conducted a survey of Thais aged 15 and above regarding their travel practices and found that the number of travelers was higher than in the previous several years, rising from 54.8% in 2010 to 65.2% in 2014; the data showed that the most frequent type of trip was the one-day trip, at 39.8% of trips overall, and three-day trips came in second, with 19.9% of the sample [39].

2.5 Agent-Based Modeling

Agent-based modeling (ABM) is a computational methodology used to represent various independent variables. ABM applies a system of rule-based dynamic interactions and a time-dependent process to carry out experiments in the virtual environment consisting of interactions among autonomous agents [40][41][42]. ABM provides the necessary tools to simulate complex systems that are difficult to model by other methods [43] and maintains a record of agent behavior over time. In the model, agents interact with other agents and environments, and the model provides a natural characterization of many kinds of individual and physical systems [44]. Because each agent has its own state and behavior rules, the different components can be modeled as entities involved in real-world phenomena. The simulation represents a whole conceptualization of a system or organization rather than a simple calculation for part of each element. The discrete incidents of the simulation are produced by the relationships of the agent components, which have been well-tested using object-oriented programming frameworks on individual behaviors. For purposes of modeling the scope of agents' decision-making, the sets of properties and behavior rules are the main components of complex adaptive systems [42]. While attributes represent characteristics of agents, behavior rules describe how agents act reciprocally with the surroundings or conditions and with other agents in the entire system; the components are thus (1) agents, (2) relationships, and (3) the environment [45].

The agent is the basic element of any ABM system, acting as an entity in the virtual world and making decisions affecting the model's outcome. Most models have several types of agents, and the specific types of agents are identified by their states, their environments, and their interactions with other agents. Although most agents in a system share possible behaviors at a specific time, some agents might have particular characteristics in terms of their actual behaviors. For example, a human agent who performs in the contagion situation can have illness status, which is susceptible, infectious, or recovery.

In the context of biology, agents of some types may be of limited life-span. Particular conditions, such as food, weather, and predators, apply to death and birth rates of agents as nature controls the population [46].

The term relation refers to how agents in the system are defined by rules of interactions and actions, and the set of rules is the second ingredient in the ABM system. Two types of rules are followed by agents: (1) independent and (2) interactive. Generally, agents have interactions with their neighbors following simple independent rules. Although complicated interactions make the model hard to understand and analyze and require a set of parameters for configuration [46], it can address a broad variety of situations, e.g., public health issues.

Agents perform within a virtual environment. The environment has effects on the simulation process. Ways to represent the environment can range from the simplest of empty spaces to a verisimilitude of real-world geometry. The simplest virtual space is the measurement of length between agents, which may be discrete. Most systems use two-dimensional grid layouts to represent virtual space, and agents' location in the same cell space corresponds to their having similar real-world locations. For example, mosquito and human agent can live in the same virtual space and interact with each other. In ABM, interactions among agents in the system can be allowed only among agents that are near each other and in a particular time. The "neighborhood" may be understood as the relation connection among agents and can change over time [46].

For the outbreak of a disease, many simulation models use differential methodologies based on uniform mixing. Agent-based modeling is one type of simulation modeling that has been used for dynamic models of contact patterns between agents and environments in specific locations. Agent-based modeling is the product of the mobility of agents between specific locations. The review of related works below summarizes agent-based modeling and dengue outbreaks as discussed in previous work.

C. Deng, H. Tao, and Z. Ye created a simplified ABM system with basic behaviors. The model consisted of 2 different agents, a host and a vector agent. The vector agent had specific behavior, such as biting, oviposition, and finding hosts. The vector behavior was affected by several conditions, such as the mosquito's ecology, the environment, and human agents. Both types of agents had illness status. For a mosquito, a status could be susceptible, latent, and infectious, whereas a human agent could have one of four statuses, susceptible, infected, infectious, and recovery. The virtual environment of the model was a small world of 30x30 grid size and contained for both agents [47].

C. Isidoro, N. Fachada, and F. Barata focused on the mosquito population. The authors observed the mosquitos' ecology and behaviors and included them as parameters in their model in order to make the simulation more realistic. An important strategy for controlling the mosquito population, Sterile Insect Technique (SIT), was used in the simulation. The model was based on a five-year simulation of the dynamics of the mosquito population. However, some important factors, e.g., wind, temperature, and precipitation were not included in the model, and other inputs for some parameters, including population size and transmission rate, were inaccurate [48].

L. F. O. Jacintho, A. F. M. Batista, and T. L. Ruas developed agent-based modeling using the SWARM platform to simulate dengue outbreaks in two scenarios, the summer season and the winter season. To focus more on mosquitos' behavior, they included the mosquitos' gonotrophic cycle and environment. The temperature played an important role in this model, and it affected mosquito ecology at each stage of mosquito development: egg, larva, pupa, and adult. The authors introduced land use, involving standing water, which would affect mosquitos' behavior, and traps, for their population control, as part of the environment in the model [49].

In S. J. De Almeida et al., researchers provided a computational model for representing the dynamics of a vector population in a small geographical location, for example, a single home or a city block. The researchers defined the multi-agent system (MAS) as including male and female mosquitos, dogs, cats, and humans, taking into account the interaction of each such agent with the environment and with other agents. The dynamics of mosquito mobility was limited by several conditions, such as lack of standing water, fewer blood meals, and treated water sources [50].

2.6 Local Stochastic Contact Modeling

The local stochastic contact model (LSCM) is a computational framework to simulate the outbreak of diseases in a geographic region in order to model contacts among individuals.

In the LSCM, a population P is associated with two attributes: (1) current statuses, which are Susceptible (S), Latent (L), Infectious (I), Recovered/Removed(R), and others, and (2) the corresponding time for which each status lasts. The execution time can be represented by ΔT, which is the discrete time in the epidemic progression. The association with the status can be indicated as disease transitions, L à I, I à R, R à S, and others. The corresponding time values used to model the function in a population depend on the statistics of distribution for a particular disease. The new disease status is assigned after ΔT, when the LSCM scans for each individual in the entire population. For each ΔT, the change of disease status will be recorded for the investigation, and the progression of the epidemic might be different depending on the placement of major cases within the population.

All possible ways to make contacts for the LSCM come from two parts of the population, which are infectious and susceptible, between each ΔT for a population $|P| = N$ is calculated by : $C(t) = \frac{1}{2} \times \sum_k (CR_k \times N_k)$, where Nk is the number of a single object in a specific proportion, and the LSCM can be used for various groups of contact rates.

The simulation of an outbreak using LSCM begins with one or more individuals in a population becoming infected. The potential of disease transmission is generated from contact between individuals, one susceptible (S) and one infectious (I). A random number is used to generate the likelihood of disease transmission for every contact. However, the use of a random number in large populations for some regions which have long-lasting epidemics might become highly costly. To reduce this expense, the concept of disease exposure will be used for every contact coming from susceptible and disease positive. The randomness of transmission will be observed, and each new infected individual will be counted over ΔT. The likelihood of disease transmitting can be calculated by $p(\text{transmission}) = 1 - ((1 - \text{trans})^{\text{exp}})$, where trans and exp indicate the potential of transmission and the count for a single exposure, and the status of the individual will change to Latent(L) [51].

CHAPTER 3

METHODOLOGY

This chapter presents the research framework and provides an in-depth description of a module that is employed to meet the research objectives. Multi-agent simulation of human mobility will be demonstrated from a computational perspective. The contact model will represent interaction between host and vector, and this will serve to represent the large-scale interaction of micro agents in this simulation.

3.1 Computational Framework

A new framework, so-called modified agent-based modeling (mABM), a hybrid platform between mathematical models and computational model, is used to simulate a dengue outbreak in human and mosquito population. This framework is based on the Agent-based modeling (ABM) system on the upper level and the Local Stochastic Contact Model (LSCM) on the lower level. Five databases will be used in the model, including a map database, a synthetic human database, travel statistics from the National Statistical Office (NSO) database, a synthetic mosquito database, and a temperature database. For the map, synthetic human, and synthetic mosquito databases, the data will be prepared though an established process. For the map database, the early processing is to classify types of land uses, which are home, school, and factory. In addition, each area in the map database also contains the human population, the mosquito population and offspring, and essential values for running the simulation. The human database contains human characteristics in order to force each human to follow definite rules. For the mosquito database, the system requires the perfect parameter that can be used to calculate dynamic numbers of mosquitos per person. This process might take multiple time to find the best value, so it is necessary to prepare before running the simulation. The transmission rate, access to bloodmeal, and other factors for this model will be integrated into the system through a parameter file. The system will present the simulation results on graphs and the area of Thailand. The overall system is presented in Figure 3.1 below:

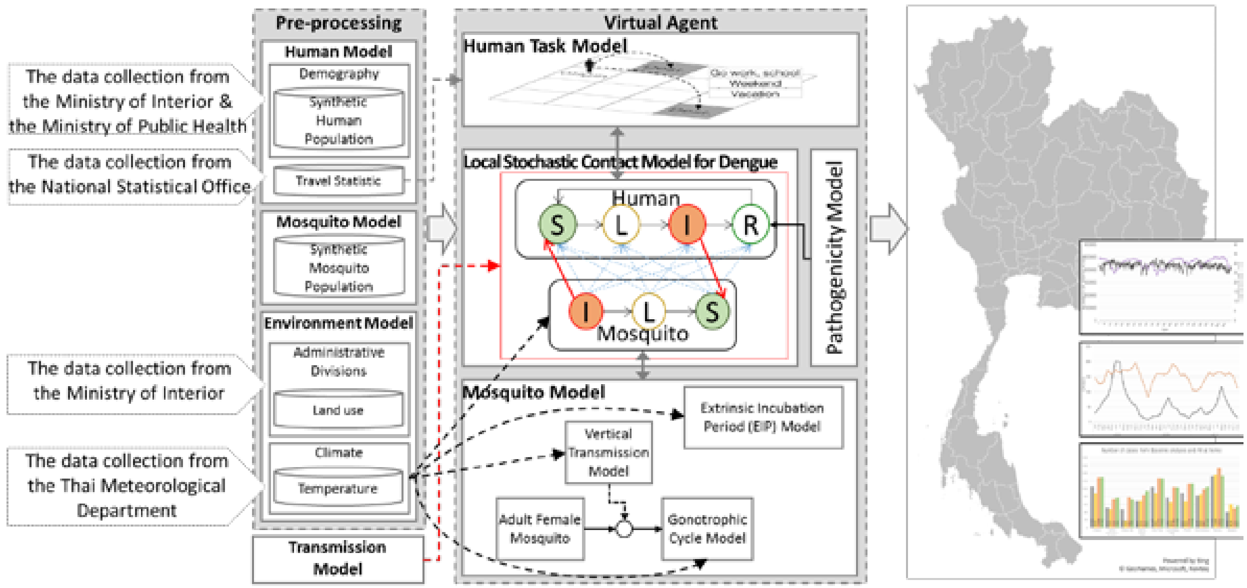


FIGURE 3.1. The modified agent-based modeling for the dengue outbreak simulation in Thailand.

The framework utilizes available field data as much as possible for human agent initialization, model calibration, and model formation. The framework consists of the following 3 main components: 1) the data preparation for the model, 2) the processing model calibration via a virtual agent model, and 3) the presentation. Pre-processing comprises 3 sub-modules: 1) the synthetic human population with daily activity and travel behavior, 2) the synthetic mosquito population with setting numbers for all of the states of the mosquito from egg to adult mosquito, and 3) the virtual spaces, which are made from each province in Thailand, for land use and environment. Most of the types of data will remain constant except the synthetic mosquito population, which is the dynamic number. When the system finishes preprocessing, all data will be set as the initial values for the simulation. The processing model utilizes a virtual agent model to produce the results. The model starts with daily activities of humans moving between defined cells, such as home-school-home cell or home-factory-home cell. A mosquito will have a chance to bite a human in each particular cell. When a mosquito makes contact with a human, the virus will be transmitted between these two agents if one or both are dengue positive.

At the end of each simulated day, the model will change the state for each human agent and the number of mosquitos for all groups will be recalculated to control for the dynamic mosquito population. The model can be operated for the sequence of years. However, the daily operation of this work will be for three consecutive years from 2008 – 2010 based on completion of data collection. When the simulation is finished, the results will be presented in graphs or a map.

As shown in Figure 3.1, the mABM system used data collected from five different sources: the collection data from the Ministry of Interior, the Ministry of Public Health, the national Statistical Office, and the Thai Meteorological department. This extends the range of the computational simulation by making the simulation more realistic, through the inclusion of two conditions: 1) the synthetic population will be created based on field data and distributed to virtual space to include the possibility of outbreak throughout the whole country, and 2) travel activity will be assigned to the human population in order to investigate the spreading of the virus under conditions of displacement. By collecting data from multiple sources, the framework can improve the realism in the computational simulation, and this provides an answer for the first research question.

3.2 The Synthetic Human Population for Thailand

The simulation represents humans as hosts of the dengue virus. A host can carry a virus to many places such as schools, workplaces, and others and can transmit a virus to a vector by random contact with the mosquito population. One of the key features of the simulation is the characterization of the host behavior during the daytime based on the demographic structure of Thailand's population. The synthetic population in this system can be divided into two groups: 1) the Thai population and 2) the immigrant population. Population numbers are drawn from reported data from the National Statistical Office of Thailand for each province and from the Immigration Bureau of Thailand for people who cross borders [52].

The population of Thailand was 65.9 million individuals in 2010 [53]. For administrative purposes, the population is hierarchically grouped by 4 regions, 77 provinces, and 927 districts [54]. Population data on age structure and household size will be used to assign individuals co-located to a household, and the appropriate number of households will be generated to match the actual resident population.

3.2.1 The Synthetic Human Population

The population model assumes that the population remains constant in the system. The non-Thai population is introduced at the beginning of the system, and the total number is not changed in the system. Human are assigned a random age according to the country's age distribution from the NSO in 2010.

The synthetic population for Thailand population is based on reported data from the NSO, 2008[53]. The data are classified for each 5-year age range (e.g. 0-4, 5-9, etc.). The population is divided into 4 main age groups, i.e. before school, school age, working, and retirement. This model focuses on age range and disregards gender. The four main groups of population of this study are shown in Figure 3.2. The NSO's report on population (the population component only) will often be referred to hereafter as the "Thai census."

Each individual has a home residence and features three additional patterns relating to work days, weekends, and vacations. A person has a fixed pattern for those three categories, which is obtained from the preprocessing method. For each category, the pattern relates only to the daytime because it is assumed that the vector does not bite during the nighttime [2]. The daytime pattern is divided into two portions, i.e., business hours and evening times. Individuals are assigned to locations for specific time slots. For example, people of school age spend most of their daytime hours in school and during the evening are at home. This assumption was used for employed people also, i.e., employees worked by day and were at home in the evening.

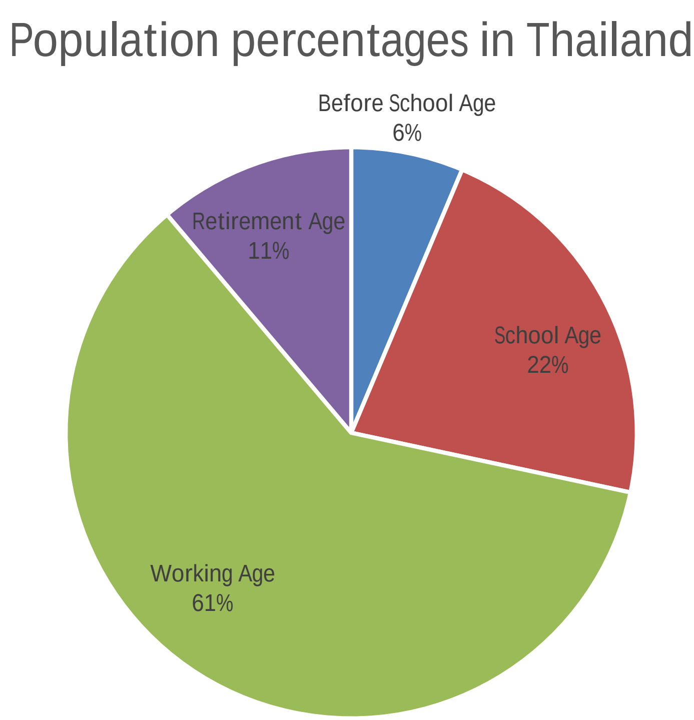


FIGURE 3.2. Population percentages in Thailand for age/occupation categories.

```
Algorithm 1. SYNTHETIC POPULATION
    Number of Cell ¬  Province Area in km^2
    for Each Group Age
      Cell ID ¬  + ( Number of Population in Each Group Age / Number of Cell)
    end for
    for Each Individual
      for I = 0 To I < Number of Population for Each Group Age in Living Cell
        Living Cell for Population ¬  Current Cell ID
        if (Number of Population == Number of Population in Living Cell)
          next Cell ID
        end if
        if (Group Age in School Age)
          Population Working Day ¬  School Cell ID
        end if
        if (Group Age in Working Age)
          if (Working Age Population in Percent of Industry Worker)
            Population Working Day ¬  School Cell ID
          else
            Population Working Day ¬  Random Cell
          end if
        end if
      end for
    end for
```

TABLE 3.1. Synthetic Population Parameters

Parameter	Explanation
Area	Area for each province in km^2
P	Size of Population

3.2.2 Synthetic Immigration Population

The synthetic immigration population is based on reported data from the Immigration Bureau of Thailand from 2008[55]. Non-Thai nationals can come to Thailand directly arriving in 27 provinces at checkpoints throughout the country. However, this work focused only on checkpoints located on borders shared between Thailand and neighboring countries; the number of provinces surrounding the shared borders totaled 25 provinces. The total number of immigrant people from the Bureau report was 9,513,201, which averages to 25,993 persons per day who traveled in and out of Thailand to work, to shop, and to visit friends, and who did so daily (especially workers). The information for each checkpoint province is shown in Table 3.1. This simulation does not consider the provinces from neighboring countries; it applies only to provinces in Thailand.

TABLE 3.2. Number of travel instances for each province per year and day.

Province	**Number of migrations per year**	**Average number of migrations per day**
Chanthaburi	113,510	310
Chiang Mai	368,620	1,007
Chiang Rai	260,803	713
Chonburi	44,303	121
Krabi	158,422	433
Loei	16,810	46
Mukdahan	209,437	572
Nakhon Phanom	71,362	195
Nan	1,966	5
Narathiwat	199,903	546
Nong Khai	1,291,269	3,528
Phuket	2,961,386	8,091
Ranong	104,560	286
Rayong	84,434	231
Sa Kaeo	556,541	1,521
Samut Prakan	836	2
Satun	78,886	216
Sisaket	2,515	7
Songkhla	2,164,778	5,915

(table continues)

Province	Number of migrations per year	Average number of migrations per day
Surat Thani	292,968	800
Surin	12,218	33
Tak	13,186	36
Trat	58,410	160
Ubon Ratchathani	126,954	347
Yala	319,124	872

3.2.3 Age Distribution and Behavior

Demographic, school, and workplace data will be applied for classification of the population into categories such as student, worker, or unemployed person, and individuals will be classified on an age basis. A synthetic population will be created for the whole country, which covers 513,120 km^2; the population density was obtained from the Thailand census [56]. Houses, schools, and workplaces will be specified within each district to match the population density in Thailand. Data will include the ages and genders of the entire population of Thailand in 2008. In Thailand, children 5 to 21 years old, a total of 1.7 million children, go to school. Adults from 22 to 60 years old, a total of 19.7 million people, go to work. The simulation rules for the non-school population are based on Thai culture; the activities of individuals who do not go to school can be described as below:

1. Females aged 15 and older in a household with children 5 years and younger stay home all day.
2. Individuals aged 22 to 60 will be assigned to work outside the home.
3. Everyone who is not assigned to work or attends school stays home all day.

There are no differences of types of jobs, unemployment rates, or school grade levels. The age distribution is shown in Figure 3.3.

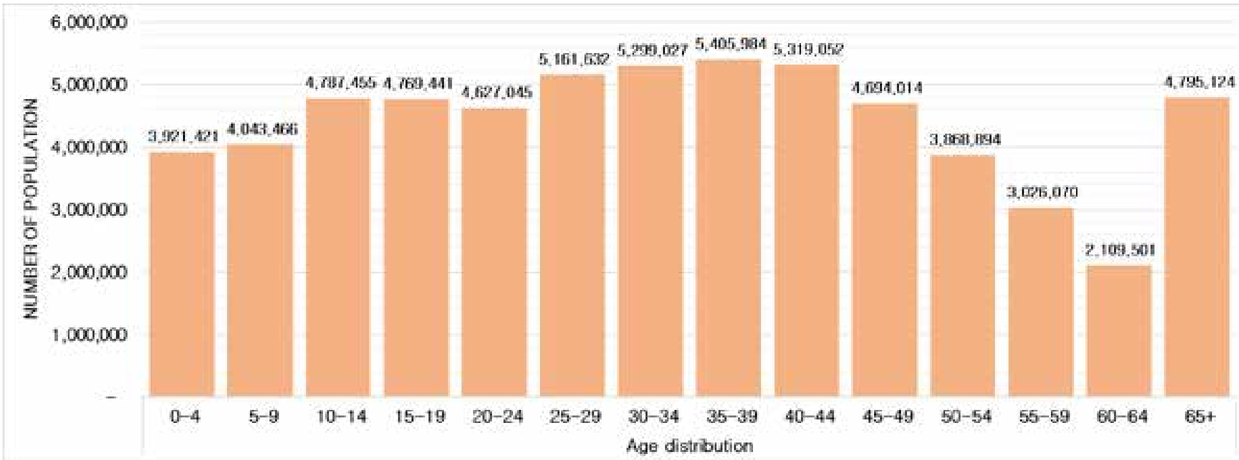


FIGURE 3.3. Population in Thailand by age range.

3.2.4 Attributes for Each Person

Each person in the model is made up of these properties:

1. Age: Age is used to define the behavior for each person.
2. Living Cell: This cell is set for all residents. Daily activity will be started and completed in the living cell. One cell can contain many people since the cell size is equal to 1 km^2.
3. Activity Cell: All residents will be assigned daily activity specifying the place or cell to which they migrate such as school and work cells. The density for each cell of the same type is equal, so some people will get the same number of activity cells.
4. Health Status: For each person the current status of the SLIR model is represented: S-susceptible, L-latent, I-infectious, and R-recovered. When an individual has recovered from a specific strain, the immunity for the individual will last indefinitely, but they will not be immune to other strains and will revert to susceptible to infection from another virus type.

3.2.5 Allocation of the Population in Virtual Space

Thailand has a total area of 513,120 square kilometers (km^2) and has 510,890 km^2 of land. To create virtual space, the total area of Thailand was divided into small cells of 1 km^2 and was assigned to 3 types of cells: residential, school, and industrial, as shown in Figure 7.0. Residential cells can consist of household and work places, e.g. small shops, restaurants, or local businesses.

Each cell type will have an equal population with age range distribution based on data from the NSO; the summary process can be seen in Figure 3.5. Cell information will be assigned as part of the individual attributes. Agents inside the model will have equal time to travel between two places. However, they are assumed to never travel across province boundaries in the regular day movement.

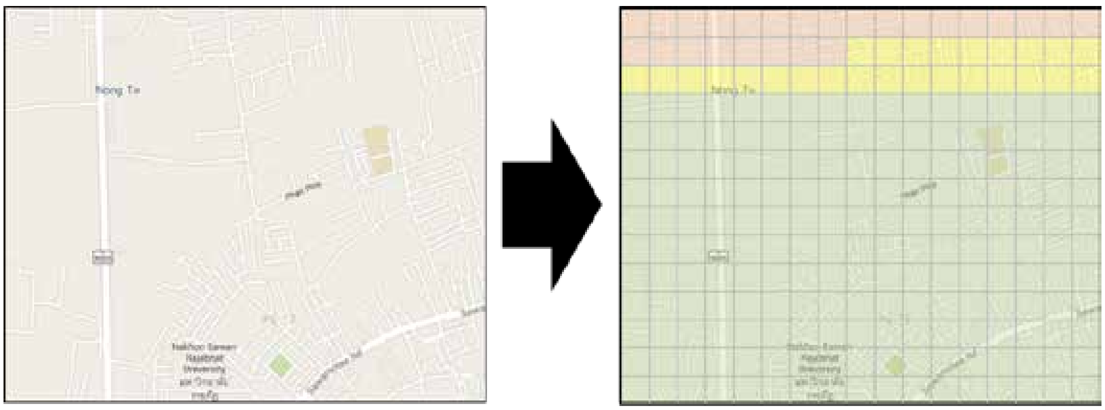


FIGURE 3.4. The conversion from land to virtual space.

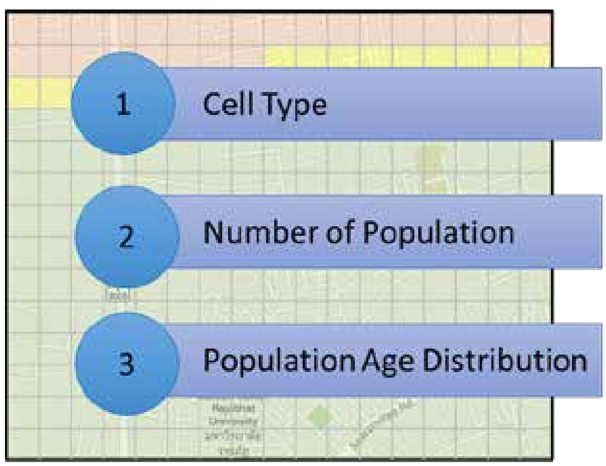


FIGURE 3.5. The process to create a cell.

3.3 Virtual Space

To distribute population in a particular province, the virtual square kilometer will be used. All provinces will be made to consist of virtual cells; each cell may be one of two types of cells: living and non-living areas.

3.3.1 Living Areas

Living areas represent people who live within particular cells. Each cell is mixed and has various people of all ages. The number of residential can be calculated by: 1) finding the number of living cells by subtracting the non-living cells from all cells, 2) dividing the population in particular province by the number of the living cells.

3.3.2 Non-Living Areas

Non-living areas can be classified into 2 groups: school places and large industrial workplaces. The Non-living cell size is equal to the Living cell size, which is 1 km^2. Each place will have a number of people, approximately 1,000 per square kilometer. Any of the population of school age will be drawn to school areas. The number of school cells is $S\frac{P_{sc}}{1000}$, where S is the number of schools, and P_{sc} is the school age population in a province. Those of the population employed by industry will be drawn to plant locations. The number of plant cells is $I\frac{P_{id}}{1000}$, where I is the number of industrial plants, and P_{id} is the number of workers employed in such industrial facilities.

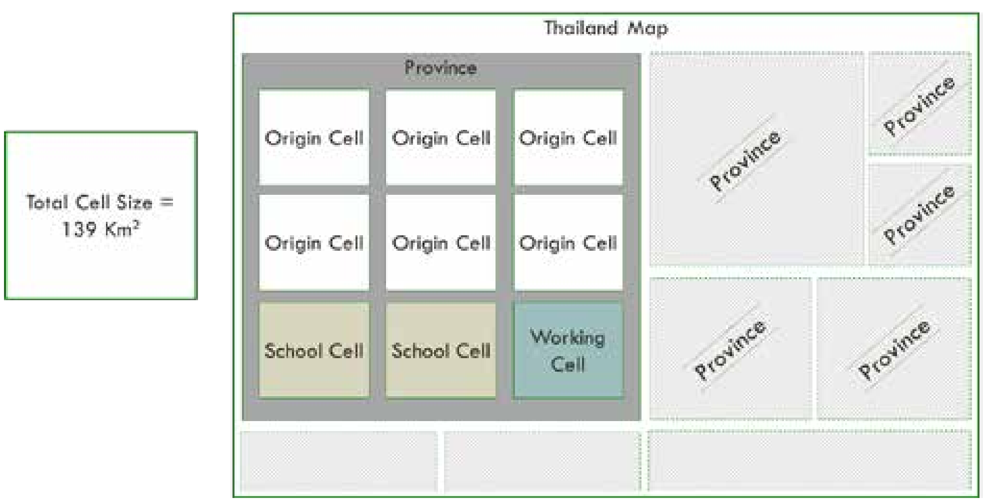


FIGURE 3.6. The virtual areas for simulation. The cell size is 1 km2, and the classification of living area, school area, and industrial area is shown.

3.4 Human Movement

The real world has many movement patterns that are more complex than those in the model: daily human movement in this model will consist of only two types, namely, weekday and weekend movement. The daily movement pattern implemented in this model can be seen in Figure 3.7.

The first pattern of human movement is the routine route for weekday activity. The action of traveling for an individual will always be directly between two specific locations, the living cell and the activity cell. Another pattern of human movement is weekend route. Individuals can move to any cell in their province or stay at their home cell.

For both patterns, the movement will be in the daytime, but individuals will be at their home cell in the morning and evening. Moreover, people can travel only along short routes inside their province. Long distance travel will occur during the holiday in Thailand.

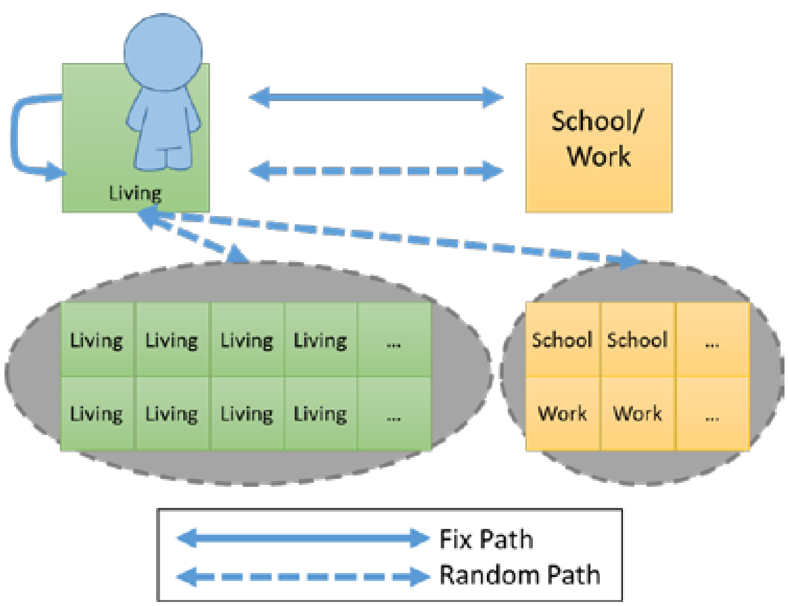


FIGURE 3.7. Schematic daily movement for individuals based on cell types.

Figure 3.7 shows two different types of movement. The first is the workday movement. The home cell and the activity cell are assigned to the individual. These two cells can be the same based on the rule for each individual in the population. Another type of movement involves random distance, in which the individual can freely move to another cell.

As a result of the definitions of the rules for each human population portion, the activities for each group of humans will affect disease outbreaks. The modeling technique applies to each host in the system and can be used to observe the disease outbreak in relation to human behaviors. In short, a synthetic human population with particular attributes can be related to a simulated disease outbreak for individuals throughout the whole country, facilitating the exploration of these dependencies as part of this research.

3.5 The Mosquito Dynamic Population Model (MDP)

This section will illustrate how the synthetic mosquito population is reproduced. The process comprises several models, including the mosquito life cycle, vertical transmission, and dynamic population controlling models. The mosquito model aims to maintain the ratio of mosquitos to humans based on previous research [57].

3.5.1 The Synthetic Mosquito Population

To perform the simulation, the synthetic mosquito population must be produced along the simulation running time. However, a model should have a starting number for the first simulated running day. The number of mosquitos comes from the mosquito larval survey from Thailand's public health service. In the survey, they use several methods to monitor the mosquito population. The health service investigates the population of immature mosquitos by employing a house index, a container index, and the Breteau index [58][59].

The House Index (HI) is the percentage of houses examined that found larvae or pupae in containers:

$$(1)\quad HI = \frac{Number\ of\ Houses\ with\ infected\ mosquitos}{Number\ of\ Houses\ inspected} \times 100$$

The Container Index (CI) is the percentage of water-holding containers in which larvae or pupae were found:

$$(2)\quad CI = \frac{Number\ of\ positive\ containers}{Number\ of\ containers\ inspected} \times 100$$

The Breteau Index (BI) is the number of containers with larvae or pupae per 100 houses inspected:

$$(3)\quad BI = \frac{Number\ of\ positive\ containers}{Number\ of\ houses\ inspected} \times 100$$

The mosquito population is based on field collection data from the Thailand Vector Borne Disease Bureau for the years 2011 – 2012 [14]. This report represented three types of pupae indices: the house index (HI), the container index (CI), and the Breteau index (BI). Each index came from different areas: economic areas, high density of population areas, and living areas. The economic areas are urban areas. The high-density population areas are the areas which have a population of approximately 100,000 people. The living areas are the areas for houses. The sample province data from Nakhon Ratchasima province are shown in TABLE 3.2

TABLE 3.3. Reported number of pupae in Nakhon Ratchasima province for HI, CI, and BI.

		Economic Areas			**High Density Population Areas**			**Living Areas**		
Year	Month	HI	CI	BI	HI	CI	BI	HI	CI	BI
2012	Nov.	-	-	-	-	-	-	10	3.63	11
2012	Nov.	13	3.35	13	-	-	-	-	-	-
2012	Nov.	-	-	-	4	1.11	4	-	-	-
2012	Jul.	-	-	-	-	-	-	5	1.17	5
2012	Jul.	8	1.98	8	-	-	-	-	-	-
2012	Jul.	-	-	-	8	1.86	8	-	-	-

(table continues)

		Economic Areas			High Density Population Areas			Living Areas		
Year	Month	HI	CI	BI	HI	CI	BI	HI	CI	BI
2012	Mar.	-	-	-	-	-	-	16	6.32	18
2012	Mar.	12	5.06	13	-	-	-	-	-	-
2012	Mar.	-	-	-	23	5.02	26	-	-	-
2012	Mar.	-	-	-	21	13.08	54	-	-	-
2012	Mar.	-	-	-	-	-	-	18	2.84	21
2012	Mar.	13	7.27	16	-	-	-	-	-	-
2012	Mar.	19	6.01	20	-	-	-	-	-	-
2012	Mar.	-	-	-	30	13.21	42	-	-	-
2012	Mar.	-	-	-	-	-	-	21	7.36	22

According to research from Basso et al., HI, CI, and BI do not represent the number of adult mosquitos because the different container size might hold varying numbers of larvae or pupae, and thus the indices might not represent an accurate number for a particular study area or for a person [60]. For a more precise number of mosquitos per person in Thailand, this work will take the number of mosquito per person from the research of Barbazan et al., which indicates that the person who lives in an urban area will correspond to approximately 0.8 Ae. Aegypti, and there will be 2.3 Ae. Aegypti per person outside the city [57]. However, this model does not classify a type of cell in terms of urban or rural areas. The method for calculating the initialization value for mosquitos in a cell is

$$(4)\quad Init_{Mosqutio\_incell} = average(0.8, 2.3) \times \#people\_in\_cell$$

The estimated initialization mosquitos per cell will be set as a target for the number of mosquitos per cell in preprocessing in order to find final value to use in simulation. The estimated initial number of female mosquitos for each portion from sample provinces in the model can be seen below:

TABLE 3.4. An estimated initial number of female mosquitos from sample provinces.

Province	Number of Population in Cell	Number of Mosquito per cell
Bangkok	4,724	7,558
Chainat	146	234
Nakhon Sawan	121	194
Uthai Thani	56	90
Kamphaeng Phet	93	149
Phichit	134	214

TABLE 3.3 illustrates the estimated number of mosquitos for 1 cell in each sample province. The number of mosquitos for cities, rural areas, living areas, and places of work are the same as in the initial stage of this model.

3.5.2 The Gonotrophic Cycle Model

The model consists of four stages: egg, larva, pupa, and adult. The cycle starts from female mosquitos feeding from mammal blood to obtain protein to produce eggs. This model ignores males because only female mosquitos can transmit the disease and lay the eggs. Each stage from mosquito life cycle has different maturation and mortality rates for survivors into the next stage, depending on temperature. Temperature is an important variable to consider and affects both a mosquito's longevity and the survival rate of its offspring. The effect of temperature on production of offspring can be seen in Figure 3.8. The cycle is started by a viremic female mosquito laying eggs and transmitting the virus via vertical transmission (VT). The number of eggs, survival rates, maturation rates, and mosquito life-spans are temperature dependent; polynomial approximation is used to develop the model. The egg maturation rate model is calculated from the collection of data by Luana Cristina Farnesi et al. [61], and other models are produced from the data provided by Eduardo B Beserra et al., who collected their data from different regions in Brazil [62]. The survival of mosquitos requires a temperature range between 22°C and 34°C. The maturation requires a temperature range from 18°C to 34°C. The development of eggs can take place from 16°C to 35°C. In other temperature conditions, the models will return a value of zero.

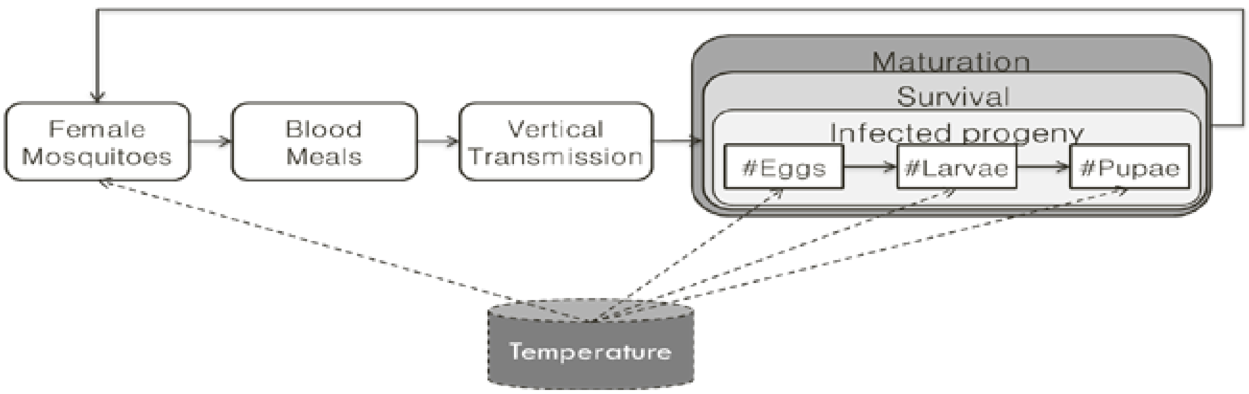


FIGURE 3.8. The gonotrophic cycle.

Each stage, as part of a dynamic population, is affected by birth rate and death rate. Each stage experiences a change in its number of members owing to both a) increased count due to population ingress up from the previous stage and b) decreased count due to less than 100% survivor rate and egress to the next stage. These processes account for the dynamics of each stage over time. Although mosquitos might need more than one blood meal to produce eggs, one blood meal is used in this model for an adult female mosquito to complete the egg-laying process.

To simulate the vector-borne disease dynamics, during a dengue disease simulation, the model used the actual daily temperature data of the Thailand Meteorological Department from 2007 to 2011. Temperature affects all the different stages in a mosquito’s life cycle. For example, the maturation rate for Aedes aegypti develops faster when the temperatures range between 26°C and 35°C. The size of vector population was simulated and recalculated for every time step as the basis for the next maturation phase. The results of the system represent the proportion for that phase of the vector population, i.e., the abundance of eggs, larvae, and pupae, as well as mature vectors. The rates of the biological processes (the specification of the maturation, survival, and mature-vector life span) were determined by curve-fitting laboratory data [61]. The laboratory observations and rate of maturation (M) of eggs (E), larvae (L), and pupae (P) are presented in Figure 3.9 below.

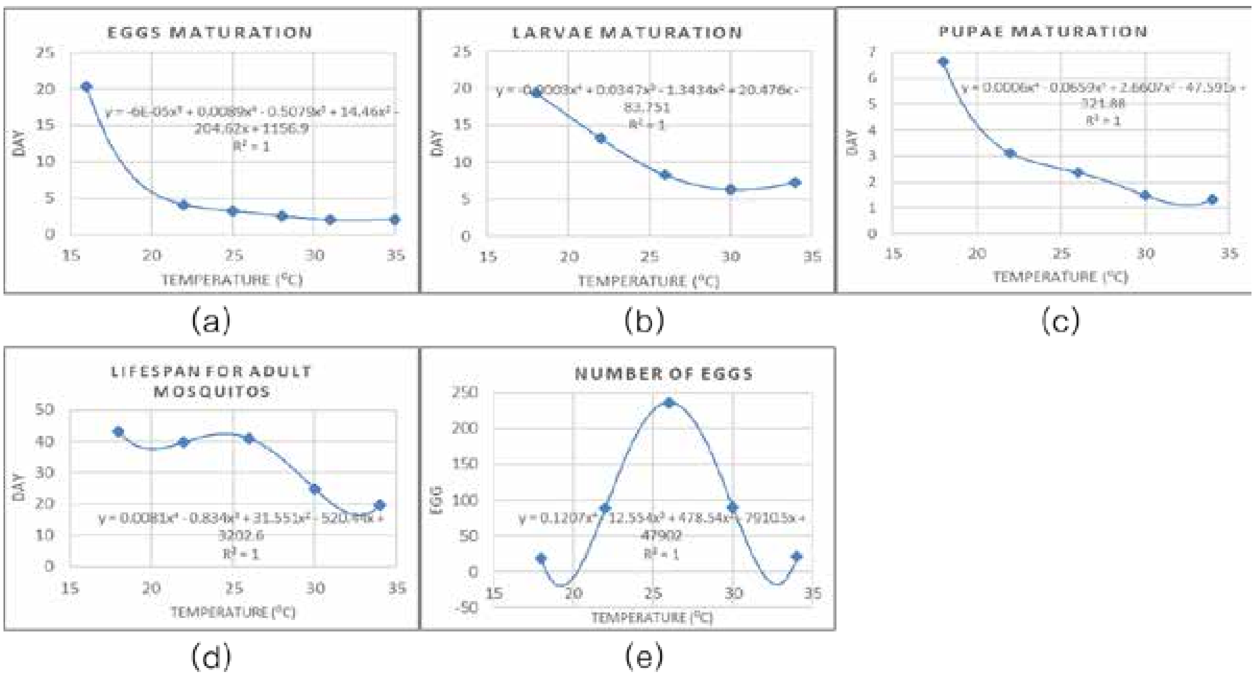


FIGURE 3.9. The rate of maturation for (a) eggs, (b) larvae, and (c) pupae. The lifespan of mosquitos (d). The number of eggs when temperature varies (e).

Figure 3.90 illustrates the maturation rate for eggs, larvae, and pupae; the lifespan; and the number of eggs when the temperature varies, which can be shown below in the following equations [63]:

(5) $\mu_E = -0.00006116 \times T^5 + 0.00885 \times T^4 - 0.5079 \times T^3 + 14.46 \times T^2 - 204.6 \times T + 1156.9$

(6) $\mu_L = -0.0003125 \times T^4 + 0.03474 \times T^3 - 1.343 \times T^2 + 20.48 \times T - 83.75$

(7) $\mu_P = 0.0006087 \times T^4 - 0.06594 \times T^3 + 2.661 \times T^2 - 47.591 \times T + 321.88$

(8) $\mu_A = 0.008096 \times T^4 - 0.834 \times T^3 + 31.551 \times T^2 - 520.4 \times T + 3202.6$

(9) $Eggs = 0.1207 \times T^4 - 12.554 \times T^3 + 478.54 \times T^2 - 7910.5 \times T + 47902$

TABLE 3.5. Variables for calculating the temperature-dependent efficiency

Parameter	**Explanation**
T	Temperature in ^{0}C
eggs	Number of eggs related to temperature
µ	Maturation rate for each stage

3.5.3 The Mosquito Dispersal Model

The mosquito dispersal model is a part of the dynamic population model. This model takes a number of mosquitos for each person in the range between 0.8 and 2.3 depending on the region. Based on the given factors, the system is developed following these differential equations for the mosquito dispersal model [64]:

(10) $\frac{dE}{dt} = eggs(T) \times \rho_{A_0} A_0 - (\mu_E + \rho_E)E$

(11) $\frac{dL}{dt} = \rho_E E - (\mu_{L1} + \mu_{L2} L + \rho_L)L$

(12) $\frac{dP}{dt} = \rho_L L - (\mu_P + \rho_P)P$

(13) $\frac{dA}{dt} = 0.5\rho_P P - (\mu_A + \rho_A)A$

TABLE 3.6. Stage variable definitions.

Parameter	Explanation
T	Temperature (°C)
eggs	Number of eggs related to temperature
m	Mortality rate
r	Maturation rate for each stage
A	Adult Mosquitos
E	Egg stage
L	Larva stage
P	Pupa stage

This MDP model does not include temperature for viability because the mathematical model gives a small viability rate for all stages. However, the MDP model adapts values for viability from [64], which are shown below:

TABLE 3.7. Values of viability as parameters of the model.

Parameters	Explanation	Range
ρ_E	egg viability rate	0 – 1
ρ_{L1}	larvae viability rate	
ρ_{L2}	larvae viability rate	
ρ_P	pupae viability rate	
ρ_M	viability rate of mosquitoes	

The result of the thermal model when the maturation rate and parameter values from the literature are applied is shown below. To calculate a value for every stage of mosquito development, an example starts from a fake initialization value: 1) eggs – 300; 2) larvae – 150; 3) pupae – 100; and 4) female vectors – 1,000. The next step is to calculate and calibrate the population for mosquitos and offspring until these values meet with the estimated initialization value for the simulation. The MDP model uses a constant temperature of 27.7 ºC for 200 days; then it uses the reported temperature to simulate an outbreak. The assigned value for v_{L2} is used in order to control the mosquito population to an average number, from that reported for the pupa population by the Thailand Vector Borne Disease Bureau. The model in this research adjusts the size of the population for all stages in the range of the reported number by 1) increasing the number when the initial population is lower than the reported number and by 2) reducing the number when the initial population is larger than the reported number. As shown in Fig. 3, the initial 200-time steps is the process that precedes the adjusting of the population to where it reaches uniformity in the number of vectors and maintains this number across simulation years.

When the model applies real temperature and changes the L_2 value associated with the report of the number of pupae in the Bangkok area, which is 0.0022 without vertical transmission, the adult population responds to the fluctuation in the temperatures as shown in the following graph.

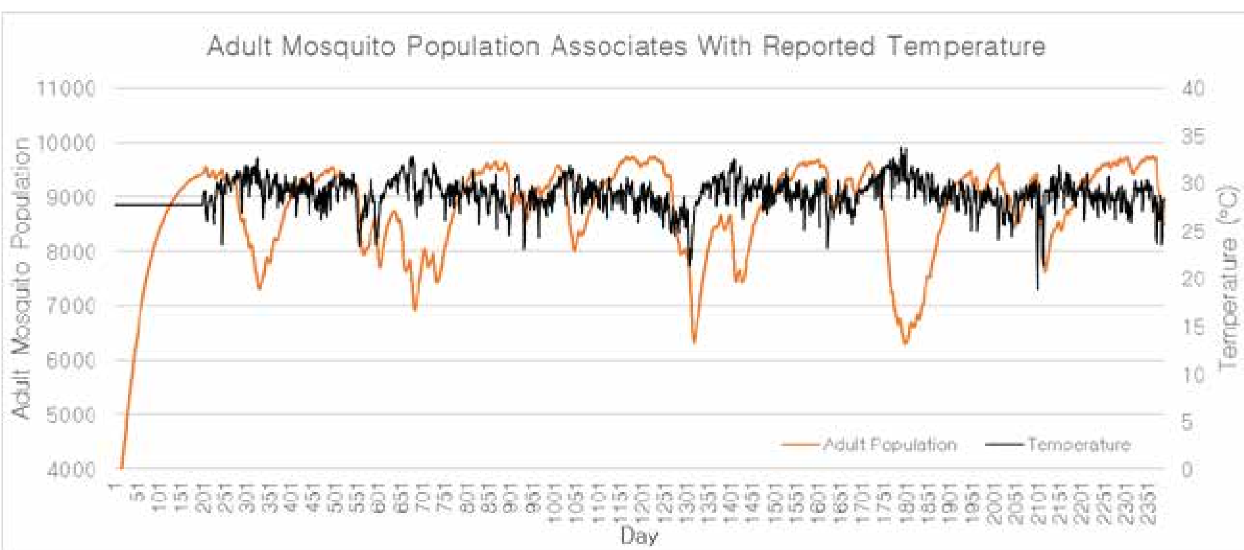


FIGURE 3.10. Population resulting from reported temperature from the Bangkok area.

The population for each stage must be divided into 3 groups, which are those in the susceptible, latent, and infectious periods.

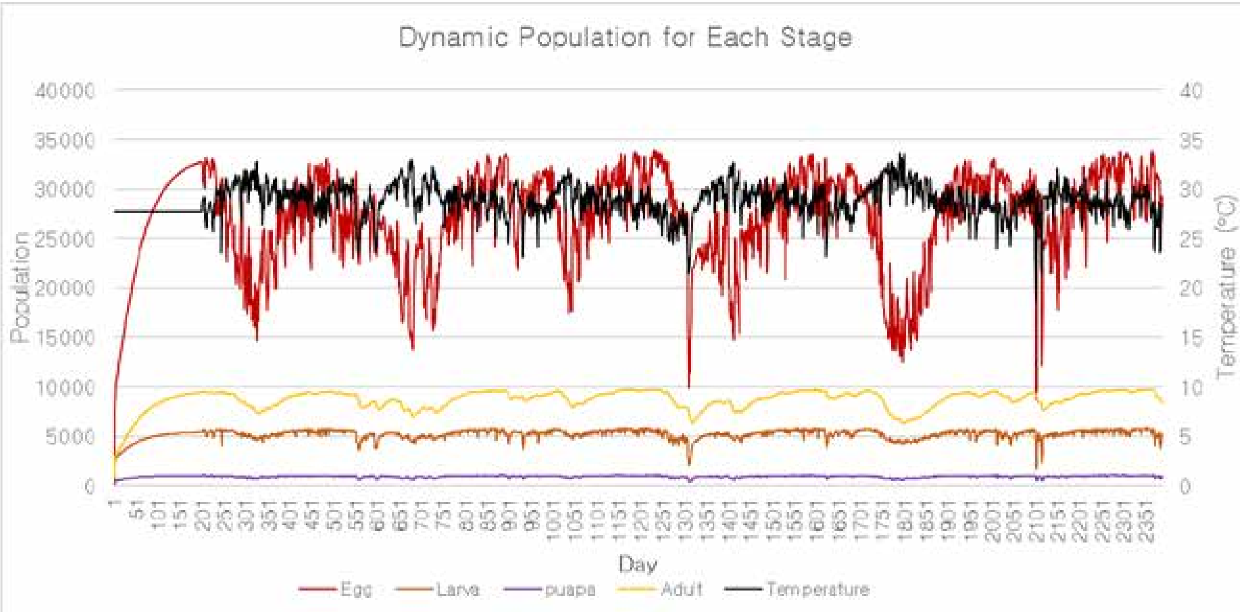


FIGURE 3.11. The dynamic population for each stage as a function of reported temperature.

3.5.4 Vertical Transmission (VT)

The dengue virus can be passed from viremic female mosquitos to offspring, and the inherited mosquitos become the virus positive. The investigation of 7 generations detected that dengue virus can pass down from the parent through offspring, a mechanism termed transovarial transmission (TOT) or vertical transmission (VT). VT from viremic female mosquitos reduces the number of healthy eggs for the next generation, and the range of this effect is between 30.0% and 68.1% [34]. The objective of the VT model is to calculate the survival rate of adult mosquitos from infected eggs. In this work, the value derives from a field study of DEN-3 virus as seen in TABLE 3.7. [34].

To determine the survival rate for the next generation, three pieces of information are required for the calculation: (1) the portion of adult mosquitos that are infected, (2) the number that constitutes the survival rate for eggs, and (3) the ratio between male and female offspring.

For the portion of infected adult mosquitos and the survival rate for eggs, the information from Table 3.7 was utilized. First, it was determined for each generation what percentage had been infected (5) or failed to reach the next stage of maturation (8). The raw data from Table 3.7 were used, and the fraction of adult mosquito survival rate for each generation from the first to the seventh was calculated. For the percentage of infected adult mosquitos, data from the Examined and Positive columns were used, and data from the columns Eggs Hatched and Adults Emerged were used for calculation of the percentage of egg failure.

Because of the variety of samples, the percentage was normalized by the division of the maximum number from each group of infected adult mosquitos by the number of egg failures as shown below for (16) and (19).

Next, the average numbers for the two groups (17) and (20) were calculated by division of the sum of the groups by 6 because some data were absent from generation 7.

For this work, a 1:1 sex ratio will be used even when temperature varies (21). The sex ratio between male and female adult mosquitos is 0.5 for each generation; however, the report shows some significance in the effect of temperature on eggs developing into adult mosquitos. Temperatures at 30°C will affect the portion of population represented by males and females, changing it from 1:1 to 4:3 [65].

(14) $\%adults\_infected(gen_n) = \frac{adults\_infected(gen_n)}{adults(gen_n)}$

(15) $\%norm\_adults\_infected(gen_n) = \frac{\%\ adults\_infected(gen_n)}{max\ (\%adults\_infected)}$

(16) $\%adults\_infected_{TOT} = \frac{\sum_{i=1}|\%norm\_adults\_infected(gen_n)|}{n}, n = 6$

$$(17)\quad \%eggs\_failure(gen_n) = \frac{eggs\_failure(gen_n)}{eggs(gen_n)}$$

$$(18)\quad \%norm\_eggs\_failure(gen_n) = 1 - \frac{\%eggs\_failure\ (gen_n)}{max\ (\%eggs\_failure)}$$

$$(19)\quad \%eggs_{survival} = 1 - \frac{\sum_{i=1}\left|\%norm_{eggs_{failure(gen_n)}}\right|}{n}, n = 6$$

$$(20)\quad female_{eggs} = \frac{1}{2}$$

$$(21)\quad VT(t) = \%adults\_infected_{TOT} \times \%eggs\_survival \times female_{eggs}$$

The next generation of offspring is represented by VT (13); VT is the product of the percentage of infected adult mosquitos, the survival rate of eggs, and the ratio of females in the new population.

TABLE 3.8. Adult mosquito survival rate from vertical transmission.

Generation	Examined	Positive	% Infected	% Infected Normalized	Eggs Hatched	Adults Emerged	% Failure	% Failure Normalized
1	50	26	52.00	80.20	386	156	57.61	84.55
2	142	79	55.63	85.82	615	431	29.92	43.91
3	431	240	55.68	85.8	108	37	65.74	95.48
4	37	24	64.86	100	204	65	68.14	100.00
5	65	20	30.77	47.40	47	26	44.68	65.57
6	26	6	23.08	35.6	448	180	59.82	87.80
7	180	38	21.11	32.5	N/A	N/A	N/A	N/A
Average				63.50			$failure_p$ = $survival_p$=	79.72 20.28

VT affects the mosquito population as viremic female mosquitos pass the virus to their offspring. The survival rate for the new generation of adult mosquitos is 20.28 percent. The result is shown in the following graph:

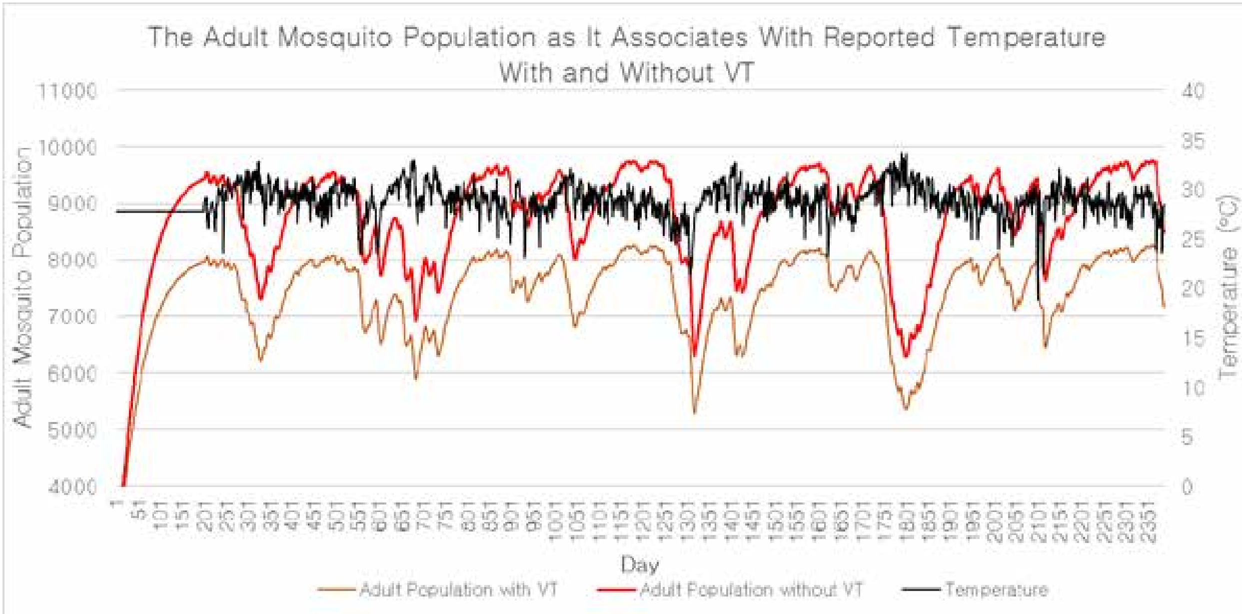


FIGURE 3.12. The population compared with and without VT.

MDP is comprised of several mathematical models related to mosquito population and behaviors, such as the calculation of mosquito survival rate, the population control, passing of the virus to their offspring, and virus development inside mosquitos' body. In conclusion, MDP can be used for representing the mosquito population and their ecology and demonstrates the integration of regional temperature into the framework to capture the effect of dengue outbreak. These two issues make it possible to answer for research questions three and four.

3.5.5 Extrinsic Incubation Period (EIP)

The EIP is the portion of time required for mosquitos to grow the dengue virus inside their bodies so it is ready for transmission to a host. The production time will start from the taking of a dengue positive blood meal from hosts, at which point a mosquito is infected. The development time for the virus inside the mosquito body is temperature-dependent. According to Douglas M et al., the virus development measurements were conducted for Aedes aegypti with several parameters after mosquitos had sucked of blood from viremic rhesus lab monkeys. The experiments were examined with constant temperatures, intervening times, and mosquito organs, including head, abdomen, and salivary glands [66]. The relation between temperature and days required for the virus to develop is shown in Table 3.8. The temperatures on the potentiality of the mosquito to pass on the dengue virus were between 24°C and 35°C; viruses could not be produced outside of this temperature range [66]. To determine the latency period for mosquitos in the temperature range between 24°C and 31°C, this model will apply least-square approximation, which is represented by the eip(T) function. For the range of temperatures from 32°C to 35°C, it will take approximately seven days to complete the EIP. The model can be specified as an f(t) function:

TABLE 3.9. Relationship between temperature and days for the virus to proceed to the salivary gland of the mosquito

Temperature (°C)	**Days**
24	25
26	18
27	13
30	12
32-35	7
eip(T) =	-0.068T4 + 7.5597T3 – 313.44T2 + 5746.7T – 39281.0

(22)

$$f(t) \begin{cases} 0 & , if\ T(t) < 24 \\ \frac{1}{eip(t)} & , if\ 24 \le T(t) < 32 \\ \frac{1}{7} & , if\ 32 \le T(t) \le 35 \\ 0 & , if T(t) > 35 \end{cases}$$

When the temperature range is suitable for virus development, mosquitos are ready to distribute viruses to humans. Clearly, the temperature is one of the main factors driving change of virus transmission from mosquitos to humans and making the outbreak occur.

3.6 Pathogenicity of the Dengue Model

Dengue fever and related symptoms are caused by one of the dengue virus serotypes, DEN-1, DEN-2, DEN-3, and DEN-4. Recovery from infection by one serotype of the dengue virus provides lifelong immunity to that particular serotype but only short-term protection against the other 3 serotypes. However, there is a high chance of repeated infection developing into dengue hemorrhagic fever (DHF). Some evidence shows that temporary immunity may be as low as 2 to 3 months [67].

To facilitate an understanding of the simulation process, TABLE 3.9 summarizes the rules of pathogenicity of dengue.

TABLE 3.10. Summary of the rules of pathogenicity of dengue.

Rule 1:	This rule establishes how the pathogenicity of dengue operates through the simulation
	if an individual gets a first bite,
	    the individual will have lifelong immunity to dengue virus
	else if the individual gets a second bite with a different type of dengue virus
	    if individual does not get bitten during the period of temporal immunity
	        the individual will get sick

3.7 Traveling Rules for Thai People

For the purpose of developing the model's rules for Thai people traveling, data will be collected from the survey report of the NSO for the period from 2008 to 2013 [68]. The frequency of traveling and the number of days for each trip are factors for peoples' displacement. According to this report, the data can be classified as follows:

- The percentage of travelers for each country, region, and province
- The number of times per year travel occurs
- The proportion of day trips and overnight trips

First, the rules will define the number of travelers each year: the number from the survey report of the NSO is approximately 50% of the Thai population.

(23) $Traveler_{Thai} = 0.5 \times Population_{Thai}$

Thai travelers consist of the travelers for each province, and each particular province will have a different portion of the travelers.

(24) $Traveler_{province} = Percentage_{traveler\_province} \times Population_{province}$

The total number of $\text{Traveler}_{\text{Thai}}$ is the cumulative number of travelers from the 77 provinces.

(25) $Traveler_{Thai} = \sum_{i=1}^{n} Traveler_{province\_i}, n = 77$

The travelers from each province will be distributed among all of the provinces in Thailand depending on the proportion of visiting travelers to the destination provinces [69].

(26) $Traveler_{destination} = Percentage_{destination} \times Traveler_{province}$

The number of $\text{Traveler}_{\text{province}}$ (for each province) are distributed to other 76 provinces or destinations depending on report from NSO [69].

(27) $Traveler_{province} = \sum_{i=1}^{n} Traveler_{destination\_i}, n = 76$

The average number of times to travel for Thai people is 4 times a year, with only 1 out of 4 being a one-day trip, the other 3 being overnight stays.

3.8 Rules for People Arriving by Crossing a Thai Border

The rules for the model for people who cross the border will be based on data collected from the Immigration Bureau of Thailand [55]. Unlike the rules for domestic traveling, rules for people who come across the border will follow these assumptions:

- The definition will allow only for one-day trips.

- Only people who live in a province which has a crossing point can cross the border.
- Only short distance trips will be simulated.

3.9 The Local Stochastic Contact Model for Dengue (LSCM-DEN)

LSCM-DEN is designed to simulate contagion between human and vector populations. The proportion of humans is represented by (19) and (20) for the mosquito population.

(28) $|H| = |S_H| + |L_H| + |I_H| + |R_H|$

(29) $|M| = |S_M| + |L_M| + |I_M|$

|H| is the human population, which consists of four states: S, L, I, and R, whereas |M| is the mosquito population, which has only three states: S, L, and I.

The nature of the relationship between the human and the mosquito is that the human gets bitten by the mosquito with a rate of b, the so-called biting rate. The total number of occurrences can be represented by a naïve-contact interaction model in this form:

(30) $Naive_{bite} = \beta|M||H|$

The disease transmission to a population group can be represented by (S_M, I_H) and (I_M,S_H), as shown in Figure 3.13 below.

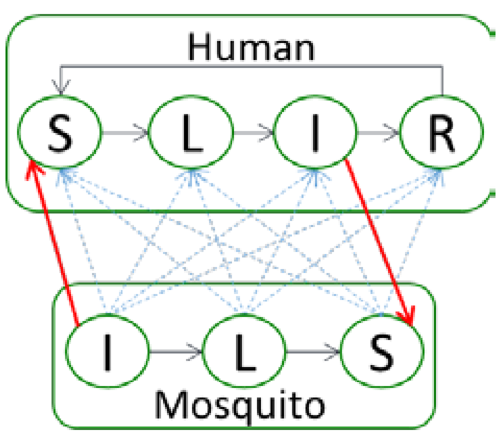


FIGURE 3.13. Local stochastic contact model between human and mosquito population.

The interaction between human and mosquito in LSCM-DEN during the simulation can be represented as:

(31) $LSCM - DEN_{int} = \beta(|S_M||H| + |I_M||H|)$

or

(32) $LSCM - DEN_{int} = \beta(|S_M + I_M||H|)$

LSCM-DEN demonstrates the biting time from mosquito proportions, including non-virus positive and virus positive.

CHAPTER 4

SIMULATION OF DENGUE OUTBREAK IN THAILAND

To test the ability of mABM to produce valid results regarding the dengue disease, multiple experiments were performed using baseline analysis and sensitivity analysis. mABM was carried out with field and reported data from several royal Thai organizations as parameters to complete the simulation. Various computational models and mathematic models were applied, of which some were used for the preparation of initiation variables for use when the model was executed.

Before the simulation was run, the following factors were determined:

- The synthetic human population
- Daily and holiday travel routes
- The initial number of mosquitos for each cell in virtual space.

Weather data from the Thai Meteorological Department that affect the mosquito population were applied while the simulation was running.

The main assumptions are described below:

1. The human population is a dynamic population, but the population has the same birth rate and death rate.
2. Members of the human population move between two cells following the rule for individuals, which was already predefined from the preprocessing stage.
3. Human agents can get dengue viruses as many as four times with different serotypes.
4. After an individual has been infected by all serotypes of dengue virus and been cured, the person acquires life-long immunity.
5. The mosquito population is a dynamic population.
6. The number of mosquitos for each province is based on the control variable from the calculation.
7. There are three portions of the mosquito population: susceptible mosquitos, infected mosquitos, and infectious mosquitos.

8. Dengue viruses inside positive mosquitos will remain there until they die.

The model experiments were conducted given the following conditions:

1. Suitable parameters that produced primary results with comparison to report data were used for baseline analysis.
2. Various parameters were assigned as having crucial roles for the sensitivity analysis to determine their impact on the conclusions.

When all the experiments had been completed, interpretation and comparison of the results were described.

All experiments were conducted based on the algorithm shown below:

Algorithm 1. VIRUS TRANSMISSION AND HUMAN DISPLACEMENT

for all simulation running days

if day in vacation time **and** *vacation*

moving people to target province

else

moving people to daily target cell

end if

random M making contact with random H

if (M_i **and** H_s) **and** (immune_type == 0)

change H_s to H_i

end if

if H_i **and** M_S

change M_S to M_i

end if

end for

TABLE 4.1. Virus transmission in the mABM model

Variables	Explanation
immune_type	Type of immunity: 1) lifelong immunity 0) non-lifelong immunity
vacation	Type of traveling distance: 1) including long distance 0) no vacation
M	Mosquitos
M_S	Susceptible Mosquitos
M_i	Infected/Infectious Mosquitos
H	Humans
H_s	Susceptible Humans
H_i	Infectious Humans

Three classifications of sample provinces were selected to run the experiments. The first category, composed of Bangkok and Ranong, presented the highest and lowest rates of dengue cases, respectively. Another group was the region representatives, Chiang Mai for the Northern region, Nakhon Rachasima for the North-Eastern region, and Kanchanaburi for the Western region. The last group was the provinces under ODPC3, Chainat, Nakhon Sawan, Kampaeng Phet, Uthai Thani, and Pichit. A map of Thailand and the illustration areas are shown in FIGURE 4.1.

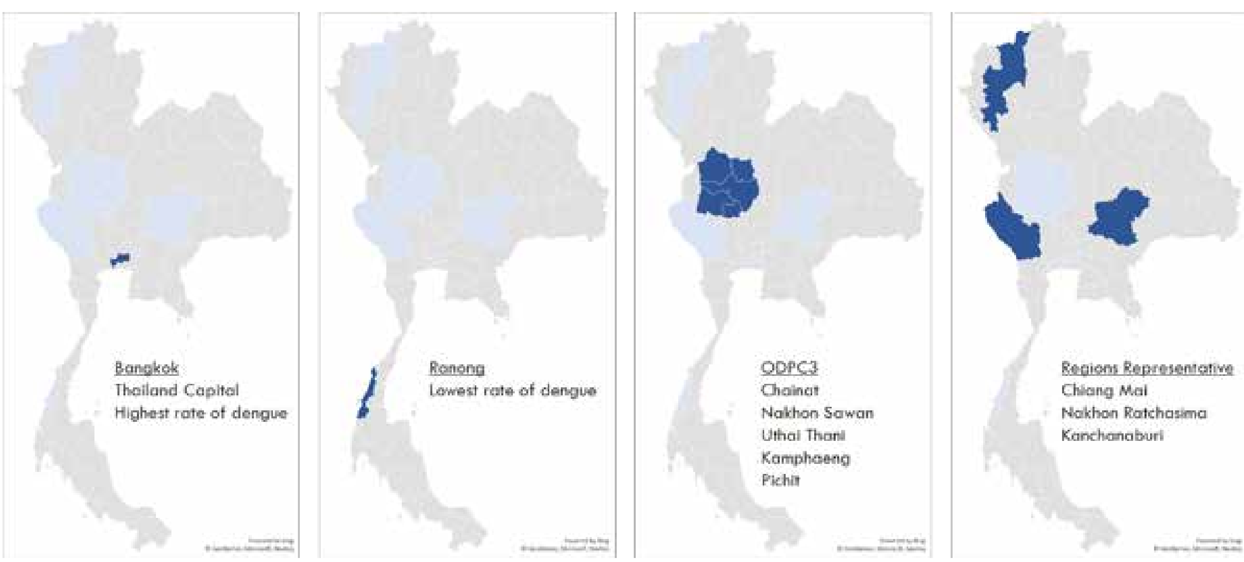


FIGURE 4.1. Map of Thailand and the representative provinces for this simulation.

4.1 Baseline Analysis

The first experiment was designed as a baseline analysis, which had two major purposes: 1) to use the suitable parameters as input for the mosquito model for the dynamic mosquito population, maintaining the number of mosquitos per person in a range adapted from Barbazan et al.'s research, which is between 0.8 and 2.3; and 2) to produce dengue cases in humans, including unreported cases. To reach the goal of baseline analysis, this experiment applied parameters as shown in TABLE 4.2.

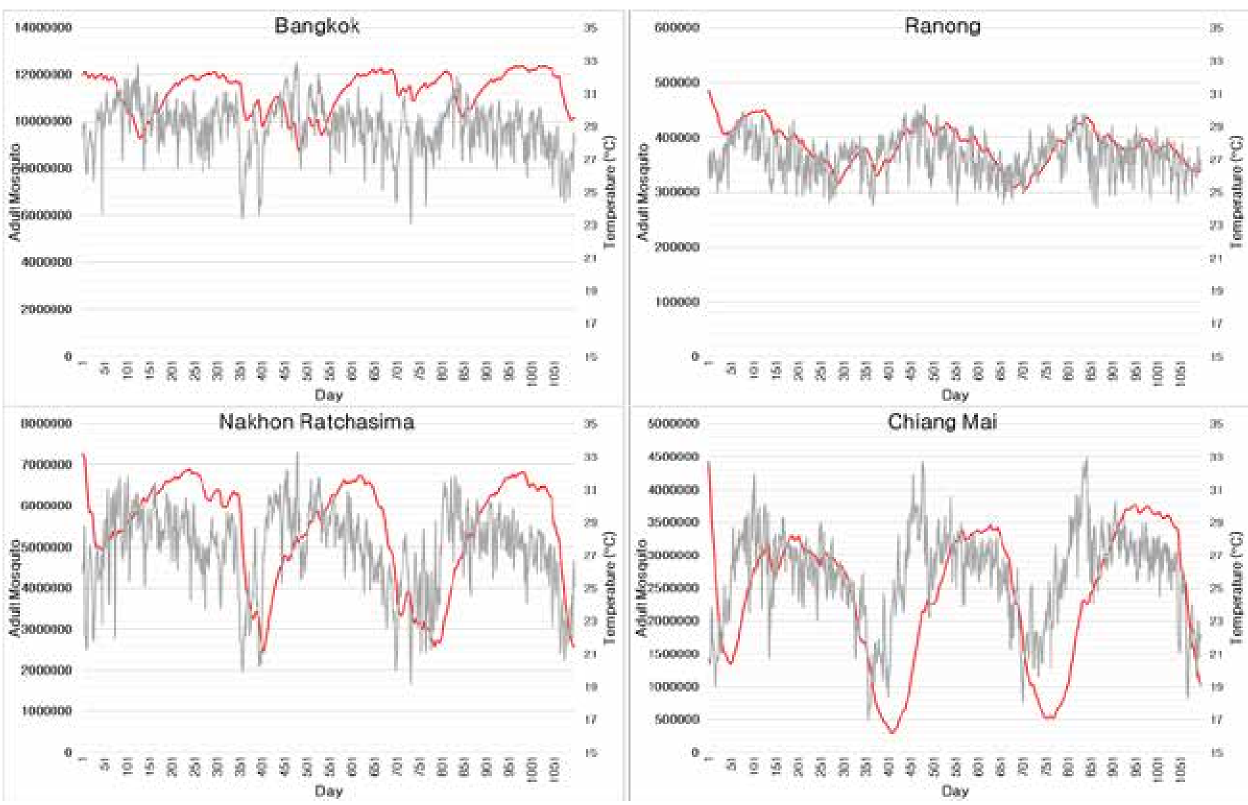
TABLE 4.2. Parameter s for the standard results

Parameter	Value
Displacement	Home, Work place/School
Temperature	Daily Temperature
Dengue virus	DenV-1 (59%), DenV-2 (16%), DenV-3 (14%), DenV-4 (11%)
Time to get bitten	Daytime
Biting time(s)	3
Transmission (H-M)	0.05
Transmission (M-H)	0.05
Percent of mosquito to bite	0.05

With these parameters, human agents have the chance to get bitten by mosquitos 3 times a day, two times in the living cell and another in the daytime activity cell. The dynamic mosquito population includes the effect of the daily temperature in Thailand. The dengue virus will be transferred when both population groups have interaction with each other and one or both are virus positive. For this simulation, when some human agents have recovered from all dengue serotypes, they will become resistant to all kinds of dengue illness. Two specifications from the results of the simulation can be made: the number of adult mosquitos and the proportion of dengue positive humans.

4.1.1 The Number of Adult Mosquitos

The dynamic mosquito population was generated every simulated day by utilizing the Mosquito model and the daily reported temperature from Thailand. The Mosquito model was carried out using Thailand's daily temperature to create a dynamic mosquito population for each simulated day. FIGURE 4.2 illustrates the results of the mosquito population from ten sample provinces. The adult mosquito population of Bangkok has the highest number, whereas Chainat gives the lowest number of all the sample provinces. Chiang Mai shows high fluctuation for adult mosquitos because some daily temperatures are out of the calculation range.



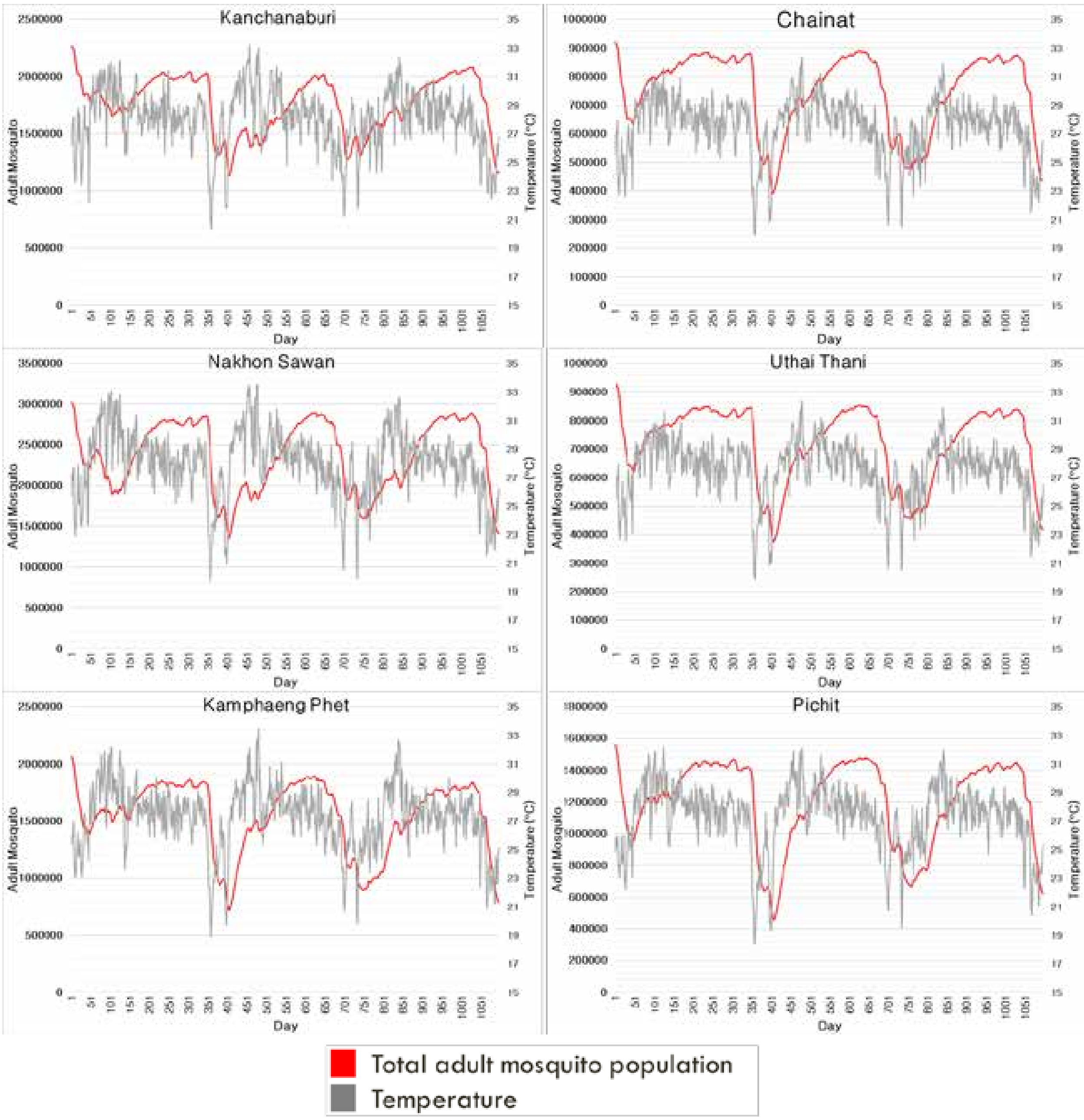


FIGURE 4.2. Total adult mosquito population

The temperature reported daily was taken to find a significant correlation with the number of adult mosquitos, with the results shown in FIGURE 4.3.

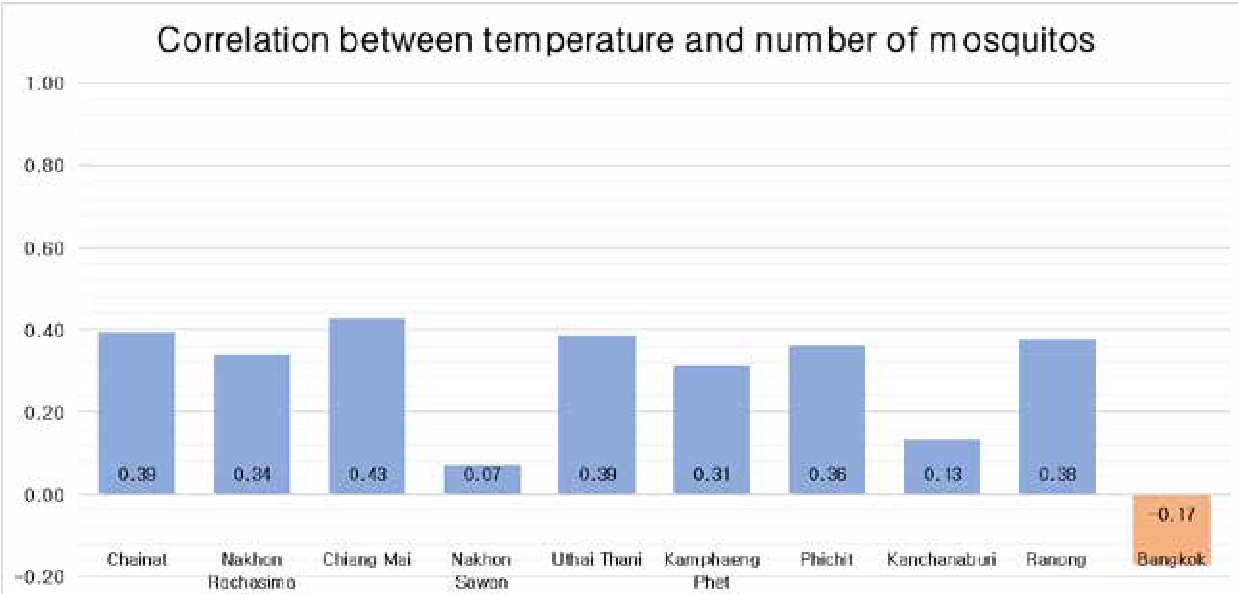


FIGURE 4.3. Correlation between temperature and the number of mosquitos.

FIGURE 4.3 demonstrates the correlation between the daily reported temperature and the number of adult mosquitos. The population from nine of ten provinces was correlated with the temperature; Bangkok was the exception. From among the positive correlations, Chiang Mai represents the highest degree of mutual relationship, whereas Nakhon Sawan returns the lowest correlation between the two variables. The only negative correlation is for Bangkok, so temperature was found to have no correlation in Bangkok.

As a partial validation of the mosquito model, the average number of adult mosquitos for each sample province was compared to data adapted from Barbazan et al., which has the number of mosquitos between 0.8 and 2.3 per person [57]. The average of these two numbers was utilized to calibrate the dynamic mosquito population, and the final capture number was applied as a parameter for the simulation.

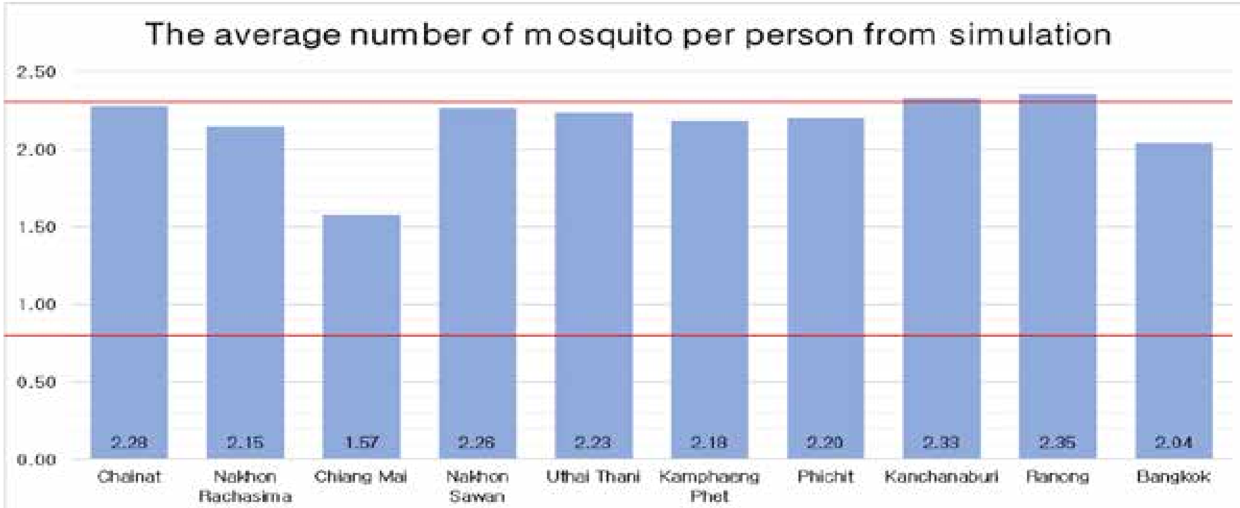


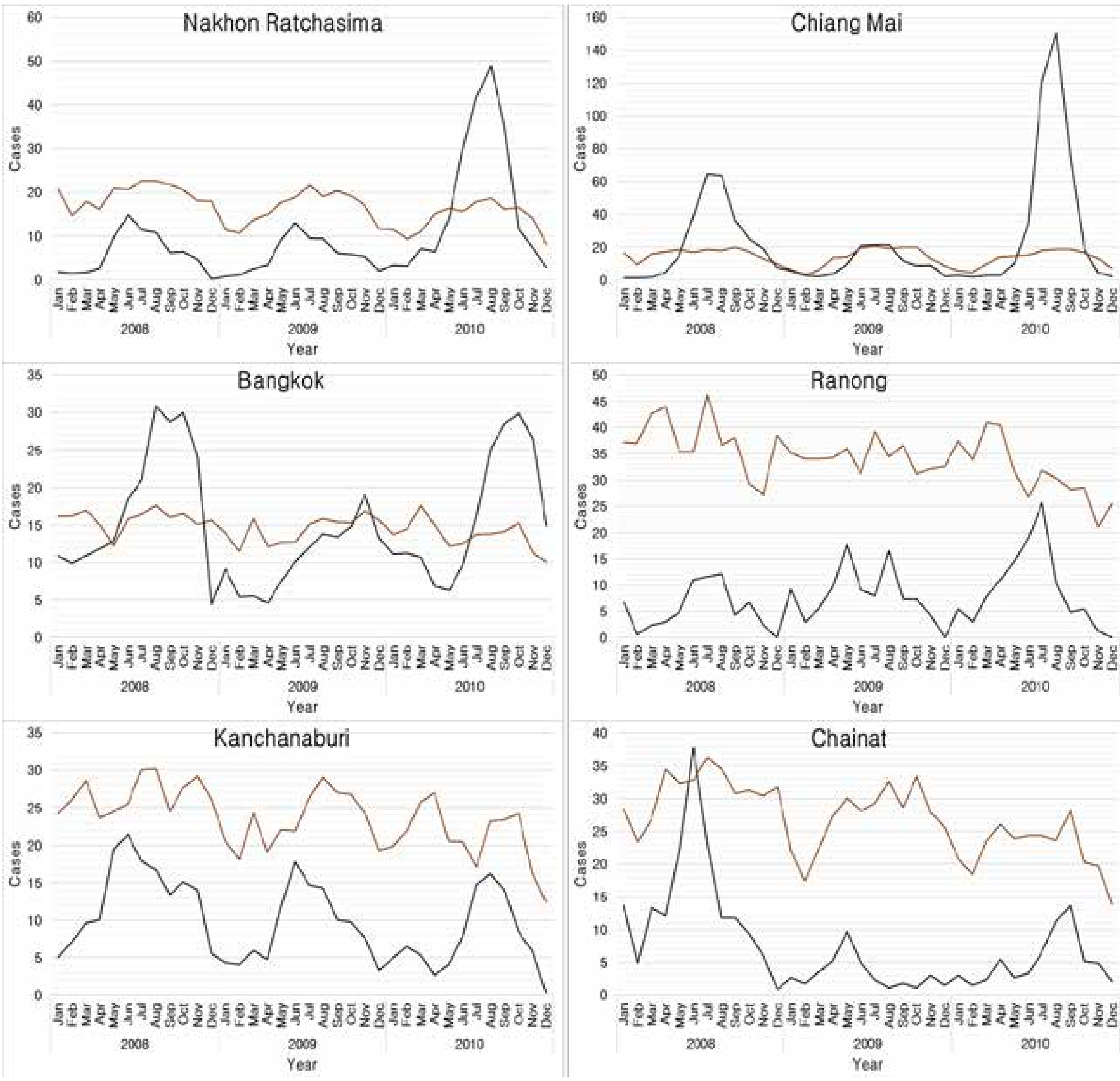
FIGURE 4.4. The average number of mosquito per person from simulation.

After the experiment was run, the average number of adult mosquitos for each province came out to between 1.57 and 2.35 per individual. Most of the sample provinces have values in that range, except Kanchanaburi and Ranong, which returned 2.33 and 2.35 mosquitos per person, respectively. The lowest average number of mosquitos per person was in Chaing Mai, which showed 1.57 mosquitos per person because some daily temperatures were not suitable for reproducing mosquitos and their offspring. The average number of mosquitos per person from this experiment was 2.16. In short, the proposed mosquito model can be efficiently used as a tool to reproduce the dynamic population of mosquitos.

4.1.2 Dengue Positive Humans

Dengue cases, in general, are associated with humans who have the symptomatic infection with any of the four dengue serotypes and have been reported to the Ministry of Public Health of Thailand. However, a patient who experiences no fever and does not meet the case definition criteria for DF may be classified as having an Asymptomatic Infection. Asymptomatic Infection accounts for as many as one-half of all dengue cases, in which patients show no signs or symptoms of the disease. They will not be reported to the Public health, so for these cases, the diagnosis and the number of positive humans will remain unknown [3].

The baseline results for humans were set for a replicate number of dengue cases, including unreported cases, and the data were compared to the number of confirmed cases reported monthly.



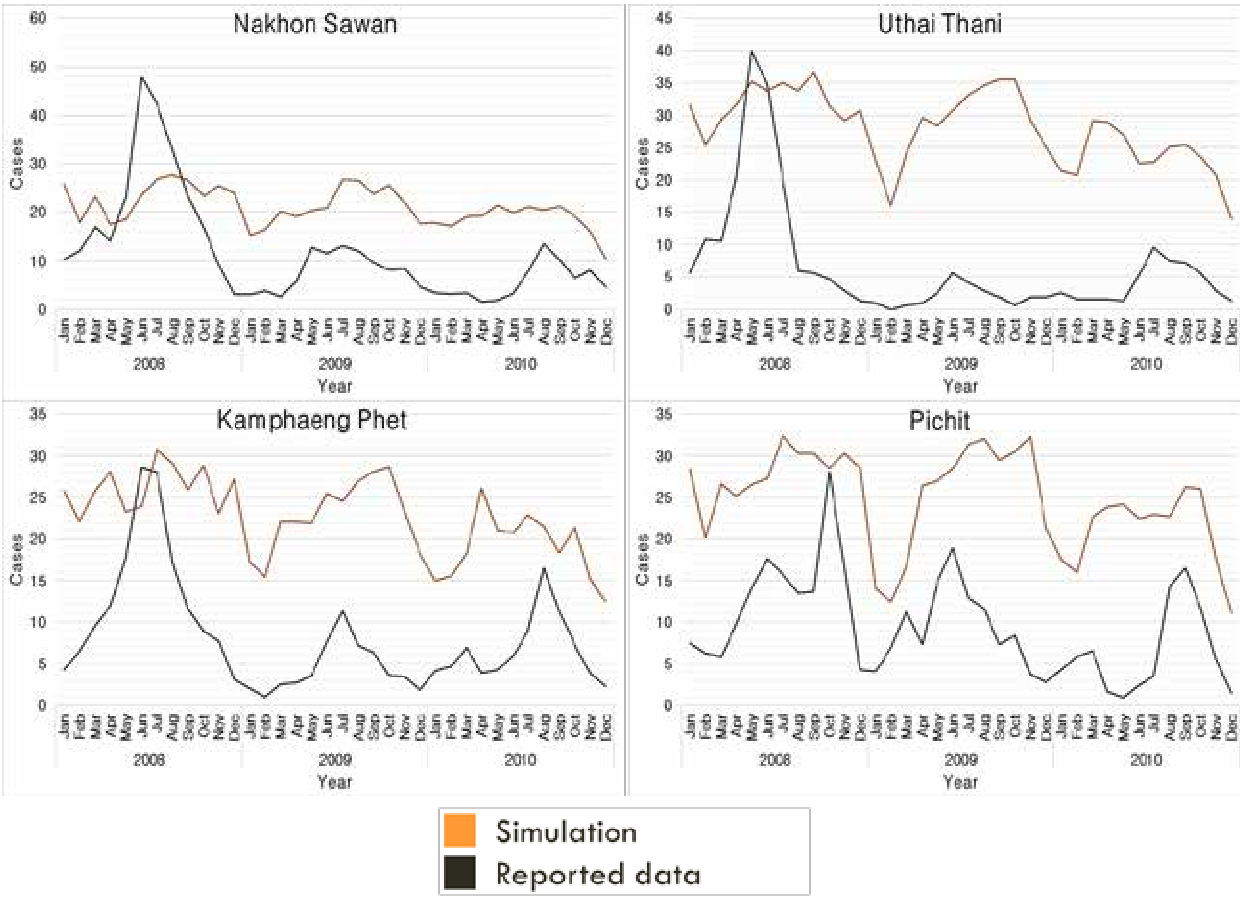


FIGURE 4.5. The number of confirmed cases reported monthly compared to simulation cases.

FIGURE 4.5 illustrates the comparable patterns for simulation data and reported data representing a case incidence rate per 100,000 inhabitants, which are in the same direction. The daily reported temperature and contacts between humans and mosquitos lead to different fluctuations in the results. In general, the number of cases has a high peak during the middle of each year. Suitable temperatures act to increase the rate of cases, whereas cooler temperatures act to reduce the rate of cases.

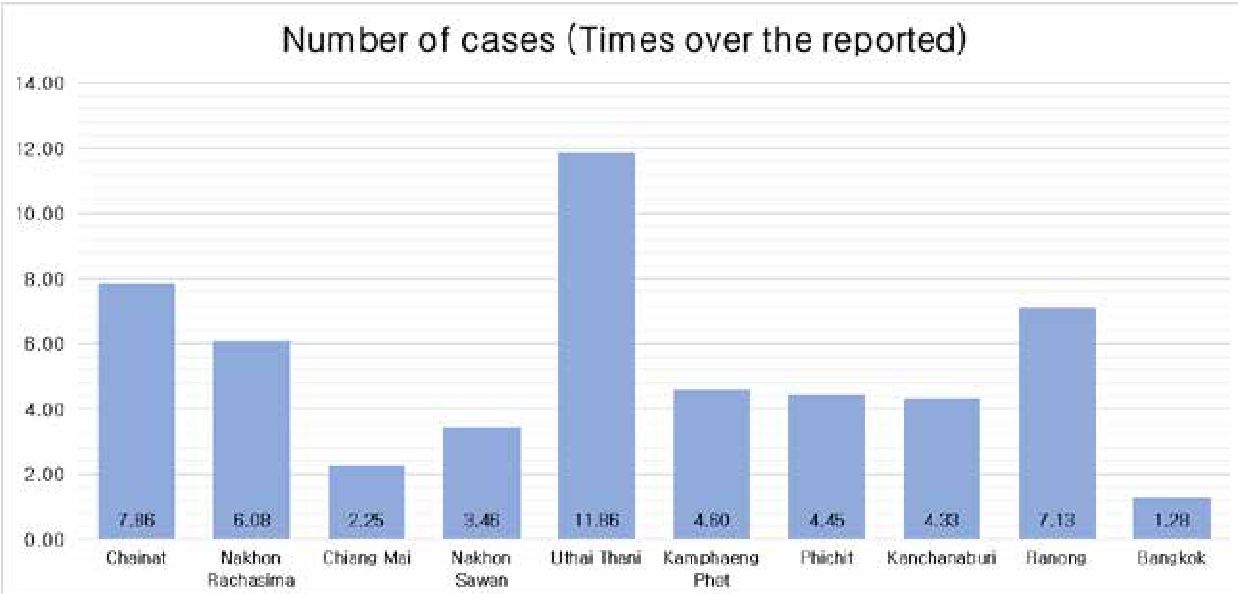
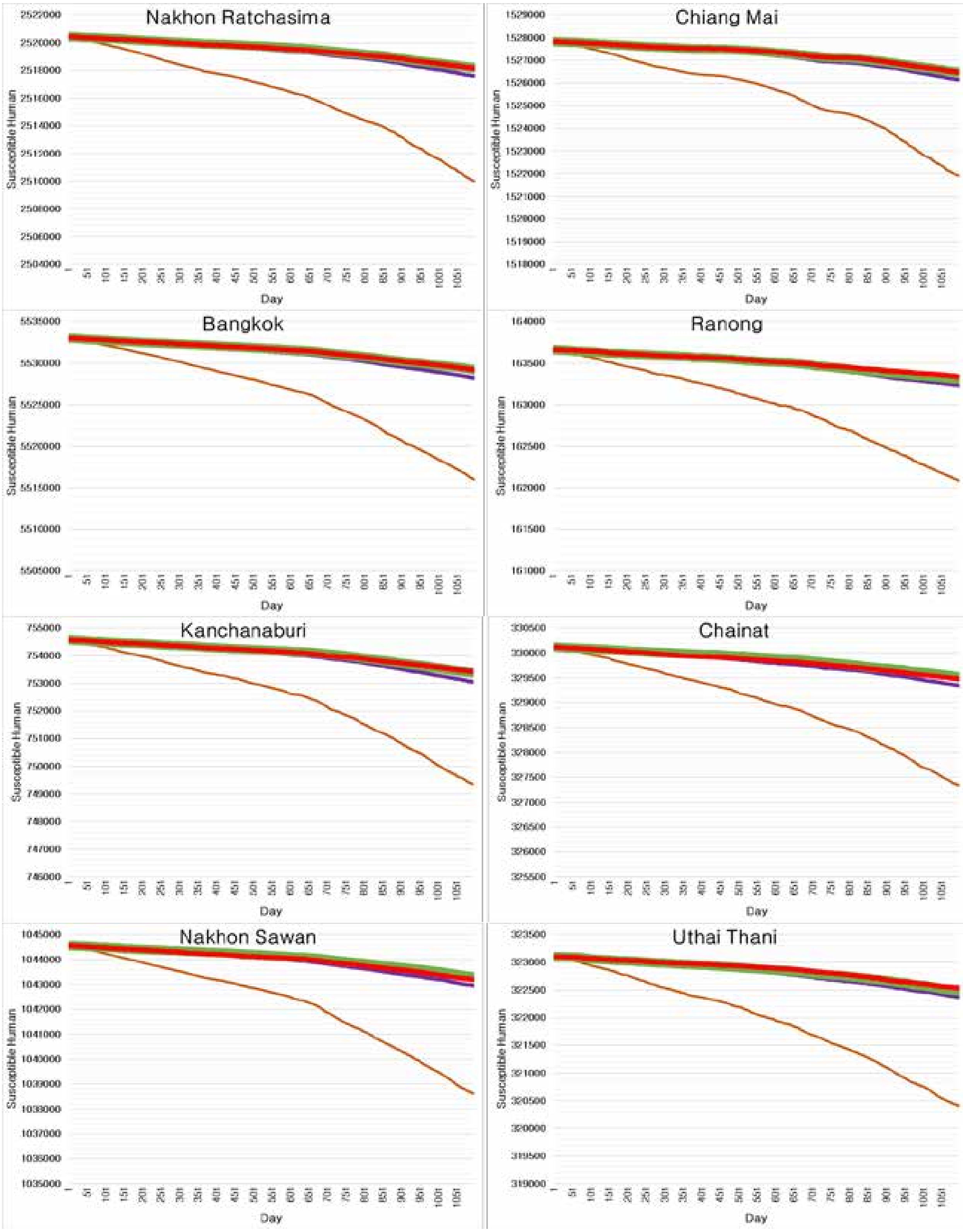


FIGURE 4.6. Number of cases (Times over the reported)

FIGURE 4.6 shows the ratio of positive humans from the simulation and reported cases. Uthai Thani generated the highest ratio of cases, which rose almost to twelve times the number in the report. In other words, the ratio of simulation cases to report case was 12 to 1. The lowest number for the ratio of cases came from Bangkok and Chiang Mai, which showed 1.0 and 2.05 times the number in the report.

The dengue virus serotypes for Thailand show different ratios depending on the region. However, when the data from the MoPH are reviewed, they show a similar pattern for all regions. The common serotype, representing the largest proportion representing over half of all those isolated, was DENV-1, representing 59%. The second was DENV-2, accounting for 16%. The third was DENV-3, followed by DENV-4, at 14% and 11%, respectively [74]. This simulation takes the reported serotype proportions as constant parameters to run the experiment and applies these numbers for all regions. The serotype ratio was used as the possible transmission of dengue virus to humans, and the results from sample provinces are shown in FIGURE 4.7.


Nakhon Ratchasima
Chiang Mai
Bangkok
Ranong
Kanchanaburi
Chainat
Nakhon Sawan
Uthai Thani
Susceptible Human
Day

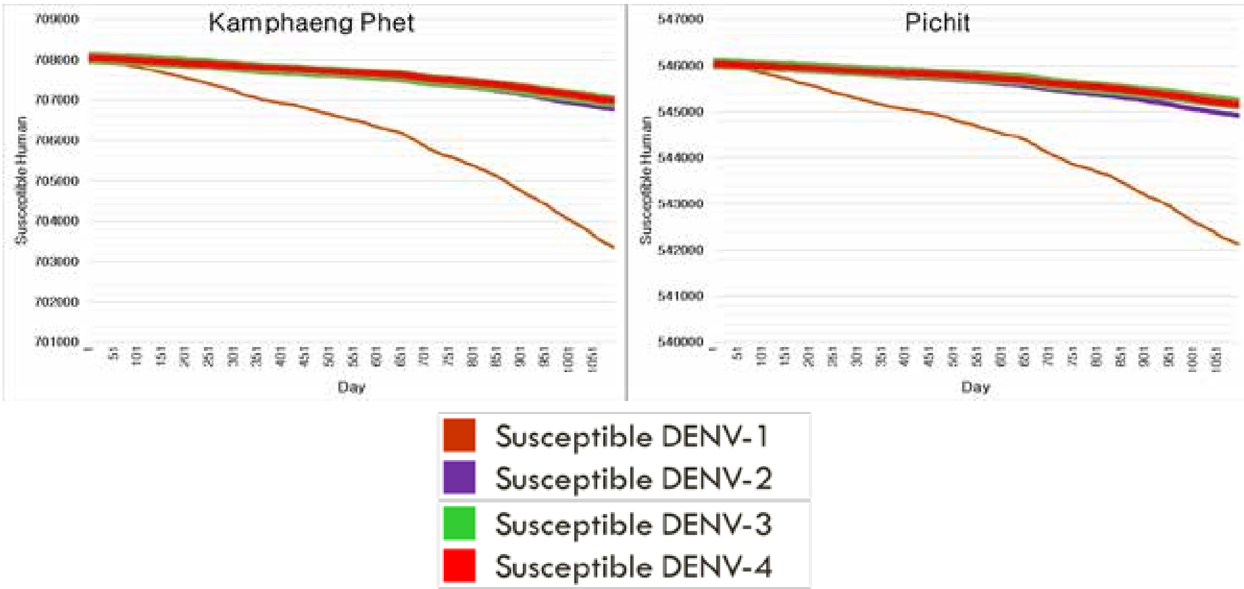
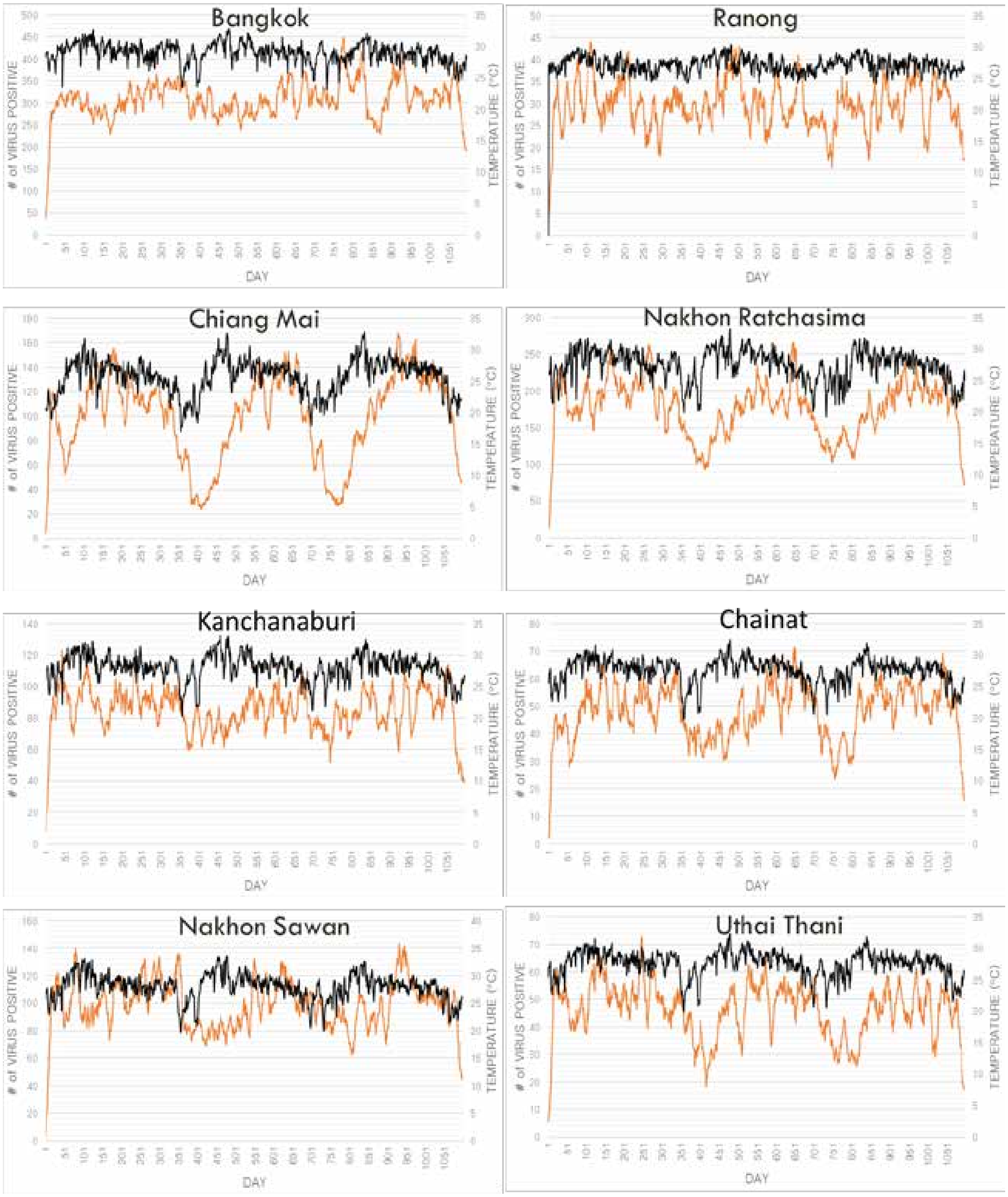


FIGURE 4.7. Susceptible humans for each serotype of dengue virus.

The result represents a similar pattern for all sample provinces, with a decrease in the proportion susceptible to DENV-1, followed by the rest because these DENV-1 serotypes were more common and occurred as a greater proportion than the other three serotypes. DENV-2, DENV-3, and DENV-4 did not much different in proportion, as there was a decreasing number of susceptible humans, produced in nearly the same percentage.

The dengue positive human population is the combination of the infected and infectious human proportions. FIGURE 4.8 illustrates the correlation between the daily reported temperature and dengue positive humans. The occurrence of positive humans should relate to the mosquito population. The gradual increase and decrease in daily reported temperature, in conjunction with mosquitos, virus development, and positive humans, should produce a fluctuation pattern in positive humans. In this experiment, if the temperature on a simulated day is between 24°C to 32°C, which is suitable for the mosquito population and dengue virus development inside mosquitos or the EIP, the number of cases is expected to rise. By contrast, if the temperature on a simulated day goes down, the number of cases is expected to decrease. Given the expectation of these results, the brown line, indicating the positive human proportion, is expected to follow or relate to the temperature line in the same direction.



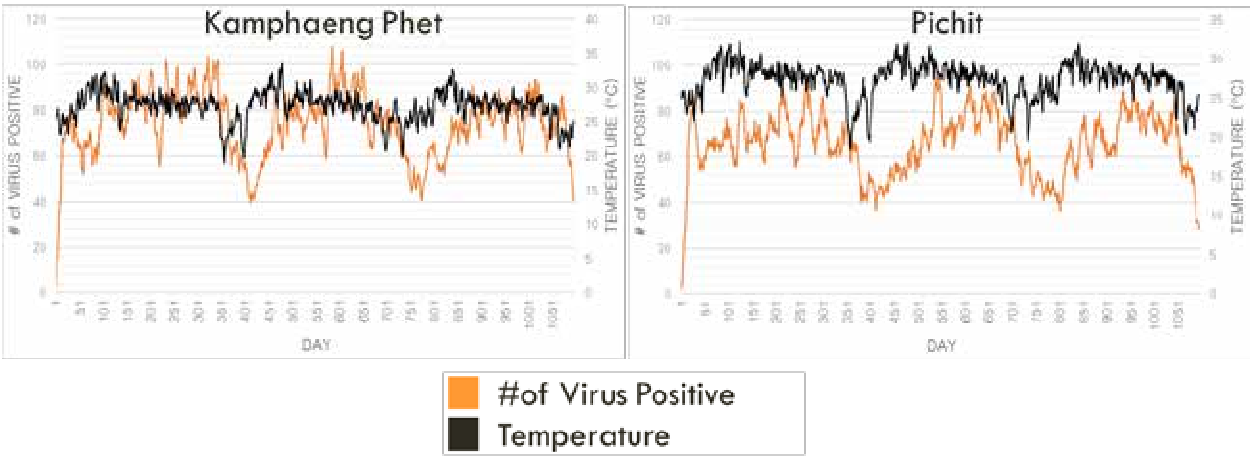


FIGURE 4.8. The number of dengue virus positive humans.

The data show a peak in the number of cases due to the temperature range suitable for mosquitos and virus development. Most peaks occur in the middle of each year, as is clearly seen in the provinces from ODPC3 and Nakhon Ratchasima. However, Chiang Mai shows a sharp decrease in the number of cases at the end of each year because of its cooler temperature.

Temperature plays an important role in this simulation because the occurrence of dengue positive humans is correlated with the abundance of mosquitos. In this review of the relationship for the two variables, the correlation pattern is expected to be in the positive area.

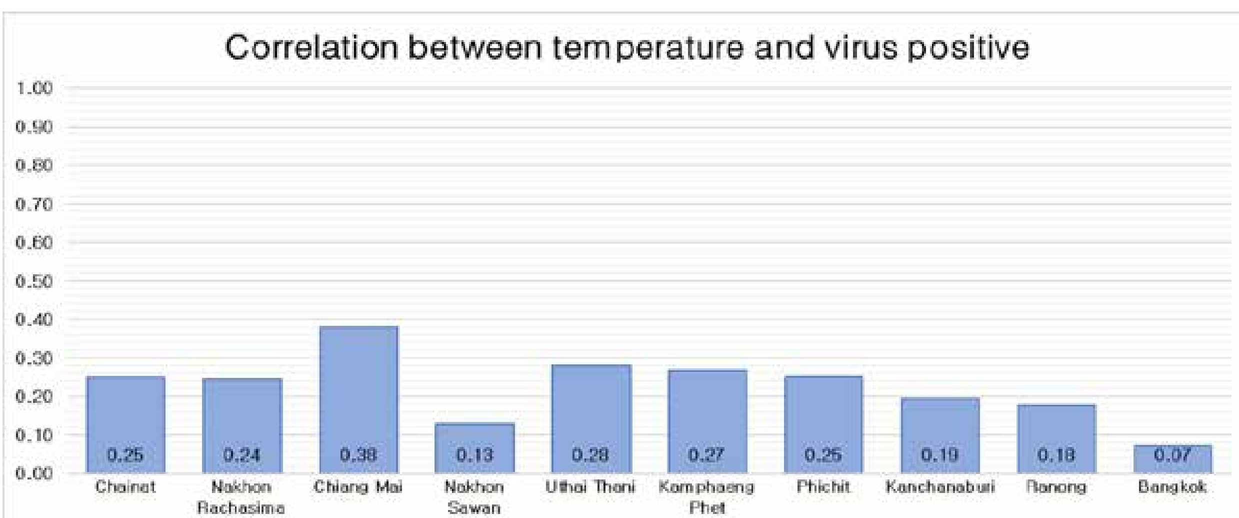


FIGURE 4.9. Correlation between temperature and virus positive.

All provinces are positive for the presence of the relationship between temperature and virus-positive humans. The percentage from Chiang Mai is slightly higher, whereas only Bangkok showed results in the negative area, being more marked in the opposite directional pattern in the graph of temperature and virus-positive humans.

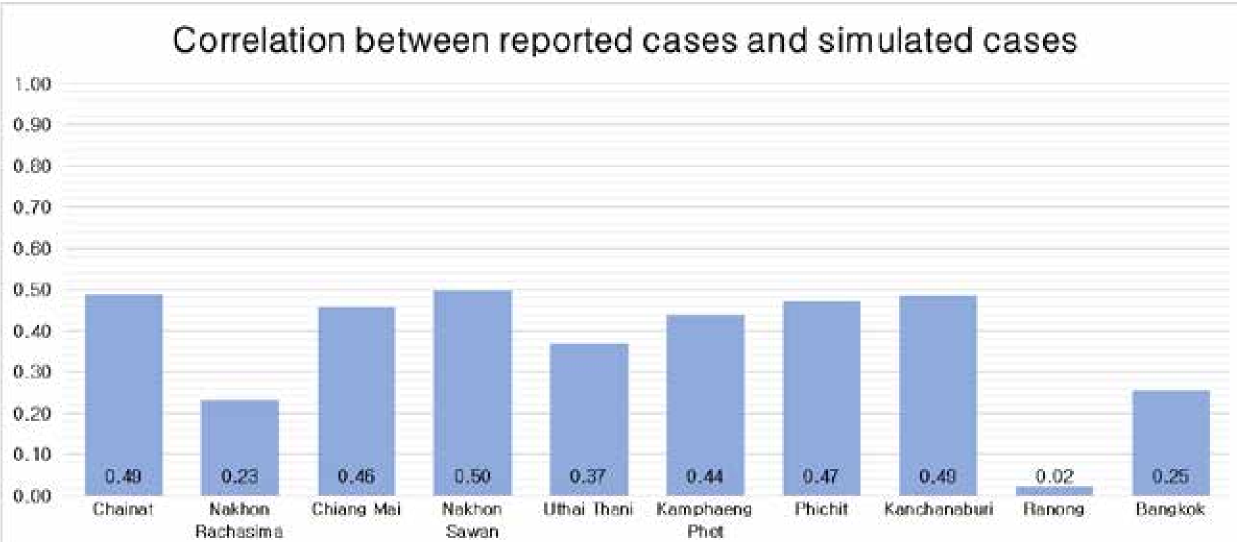


FIGURE 4.10. Correlation between reported cases and simulated cases.

FIGURE 4.10 illustrates the relationship between reported cases and simulated cases. The occurrence of the simulated cases from all provinces was correlated with the reported data. The highest relationship is seen for Nakhon Sawan (0.50), followed by Chainat and Kanchanaburi (0.49), in the correlation statistic. The lowest relationship is seen for Ranong (0.02), followed by Nakhon Rachasima (0.23), suggesting that there are other behavioral or environmental parameters that drive the epidemic. A better understanding of these parameters will allow the integration of additional data to more fully inform the simulation.

The symptomatic characteristic in so-called human prevalence is another means to discover the relationship between the simulation results and the reported cases. One period, which comprises three simulated years, is the specific time frame for measurement of the mutual relationship between the two sets of data. Reported data were calculated by the different numbers of the population, depending on the year of interest. Simulated data were calculated using the constant population number from the first simulated year run.

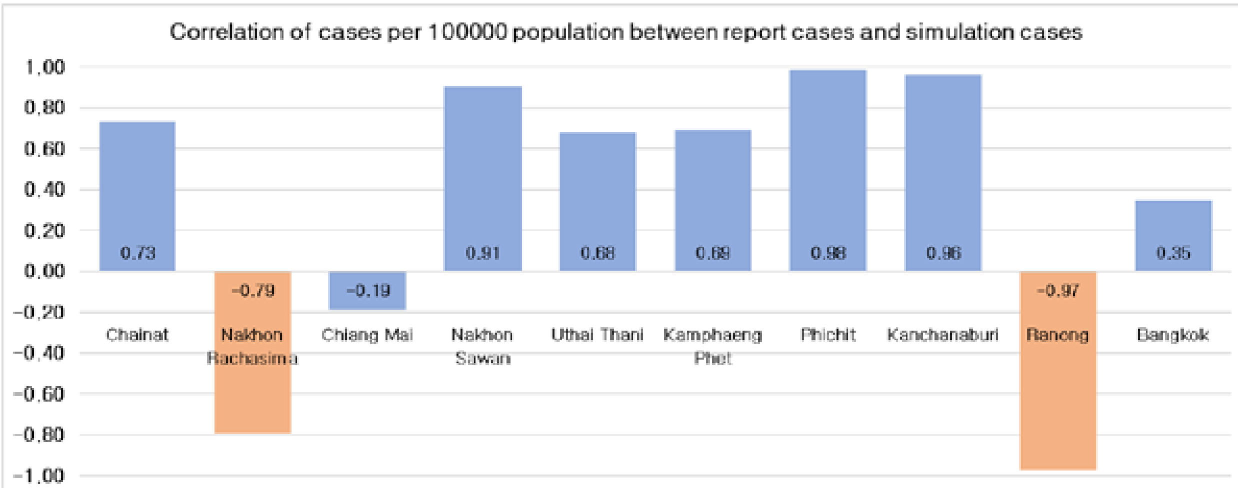


FIGURE 4.11. Correlation of cases per 100,000 population between reported cases and simulated cases.

Three provinces from FIGURE 4.11 show nearly perfect results, with a relationship value close to +1.0. Three provinces return a relationship in the middle range. Only two provinces, Nakhon Rachasima and Ranong, show negative values.

4.2 Sensitivity Analysis Methods with Various Parameters to Test the Response of the System

Sensitivity analysis is designed to improve the performance and reliability of the framework by changing the input parameters. The parameters for sensitivity analysis are categorized as seasonal, staying at home, and holiday. These three categories of focused parameters are described below.

4.2.1 Seasonal

Because temperature plays an important role in this framework, the seasonal factor was used as a parameter to discover the pattern when there are seasonal changes in the climate. The experiment for the seasonal factor was designed to answer the question regarding seasonal temperature differences' effect on virus transmission in the human population. Three different average temperatures from annual seasons, winter, summer, and rainy, were applied as a fixed parameter for each simulated day for the entirety of a particular year, and three average temperatures were recalculated at the beginning of the next year. Therefore, only nine constant temperatures were used for this experiment, with three temperatures assigned for each year. The average temperature for the season in each year can be seen in TABLE 4.3.

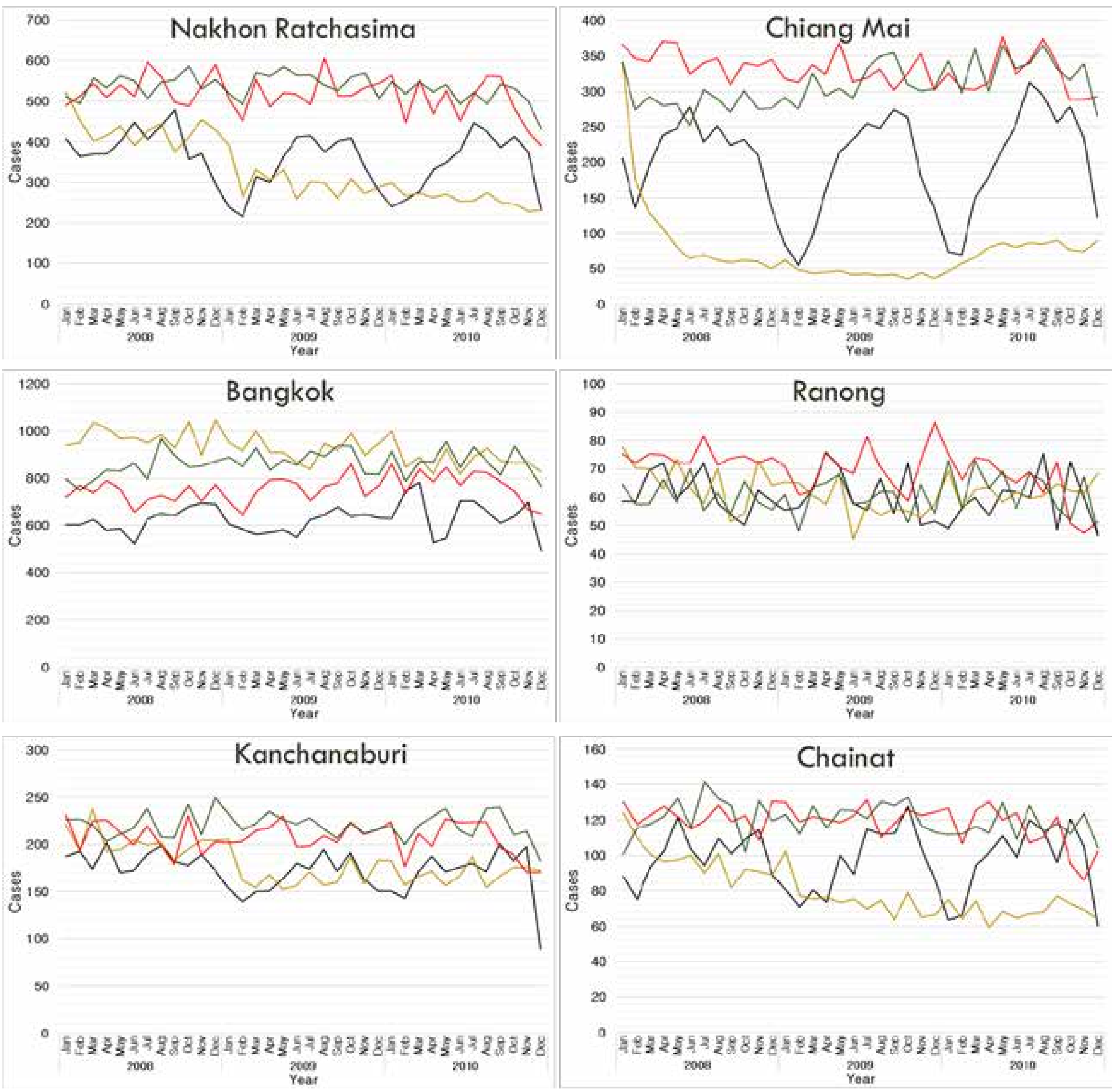
TABLE 4.3. Average temperatures in each season in each year (°C).

	2008			2009			2010		
	Winter	Summer	Rainy	Winter	Summer	Rainy	Winter	Summer	Rainy
Chainat	26.34	29.17	28.15	25.53	28.76	28.56	25.41	28.32	27.97
Nakhon Rachasima	25.94	29.02	28.33	24.98	29.32	28.61	24.58	28.17	28.10
Chiang Mai	22.85	27.61	26.44	22.42	27.24	27.04	23.37	27.92	27.44
Nakhon Sawan	26.50	30.49	28.35	25.86	30.18	28.74	25.58	29.24	28.31
Uthai Thani	26.34	29.17	28.15	25.53	28.76	28.56	25.41	28.32	27.97
Kamphaeng Phet	25.90	29.46	27.70	25.17	29.01	27.99	25.00	28.40	27.60
Phichit	25.63	29.42	27.99	25.05	28.94	28.37	24.92	28.37	27.87
Kanchanaburi	26.84	29.91	28.32	26.13	29.85	28.61	26.20	28.88	28.67
Ranong	26.94	28.35	26.70	26.65	28.13	27.11	26.94	27.76	27.19
Bangkok	28.59	30.41	29.12	28.05	30.09	29.35	27.35	29.52	28.88

TABLE 4.3 shows the average temperatures for each season. The lowest average temperature is in Chiang Mai, followed by Nakhon Ratchasima and Phichit for winter. All three provinces have elevations above that of Bangkok and have cooler temperatures during the winter. Bangkok has the highest temperature on average almost every year, reaching over 30°C one year,

but the highest temperature, 30.49°C, was in Nakhon Sawan in 2008. The average temperature for all data shown in the table is 27.58°C. The best temperature for the mosquito life cycle is 27.7°C.

Each temperature season for a particular province was run separately for the purpose of investigating the effect of temperature in a human population. Results from the three seasons were compared to the baseline experiment after the experiment was finished. The outcome is shown in FIGURE 4.12.



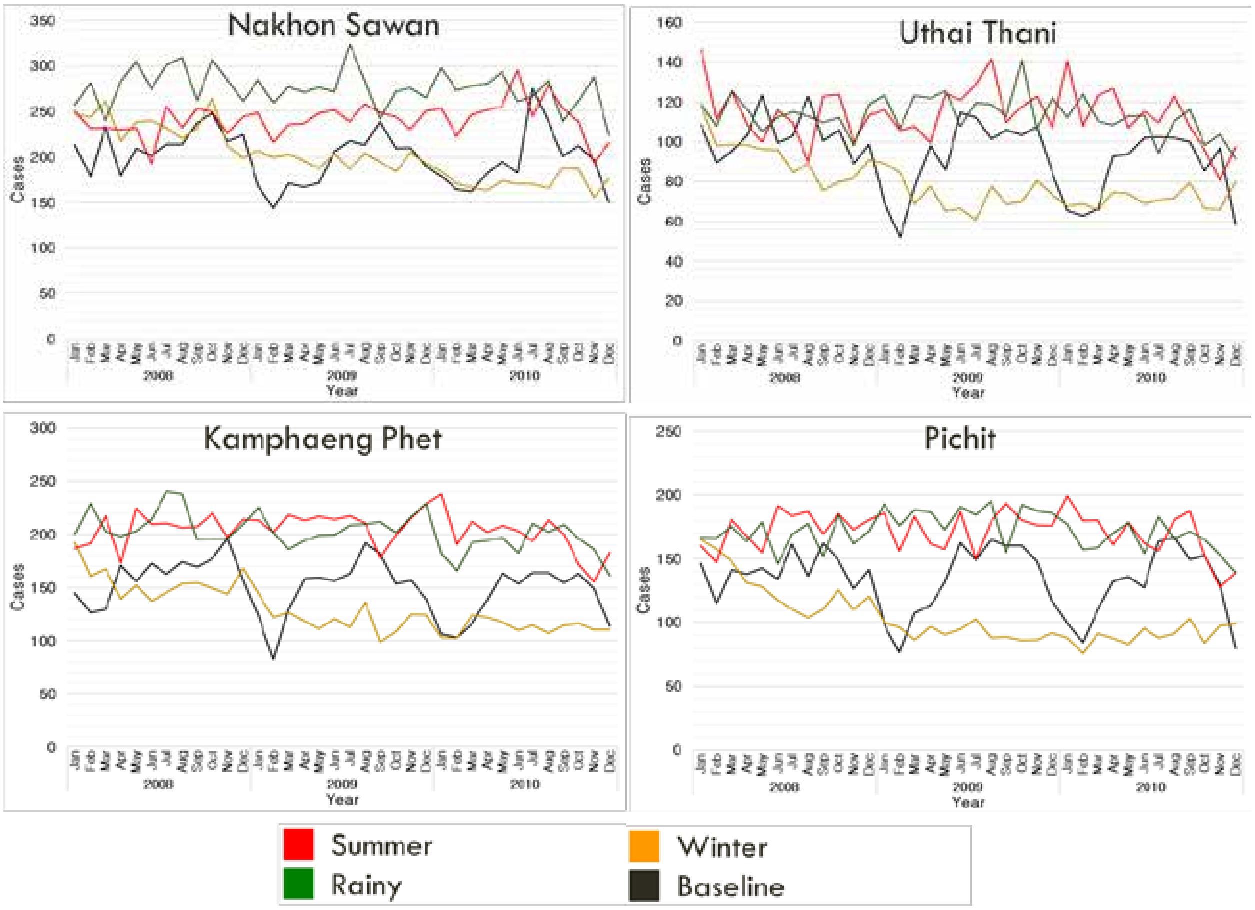


FIGURE 4.12. Sensitivity Analysis for season temperatures.

For the winter temperature, most provinces with elevations higher than that of Bangkok, such as Chiang Mai, Nakhon Ratchasima, and OPDC3, produced lower numbers of positive humans. Yellow lines from these provinces generally indicate results under those of the baseline analysis result, especially in Chiang Main. In contrast, Bangkok showed the highest number of positive humans because the average winter temperature in Bangkok is suitable for mosquito population and dengue virus development.

For summer and rainy season temperatures, the average temperatures were closer and produced similar numbers of positive humans. However, the number of positive humans was slightly higher for the rainy season in Bangkok, Nakhon Sawan, and Kanchanaburi because the average temperature for the rainy season in those places is suitable for mosquito population and dengue virus development. In addition, the highest association between summer temperature and positive humans was found in Ranong.

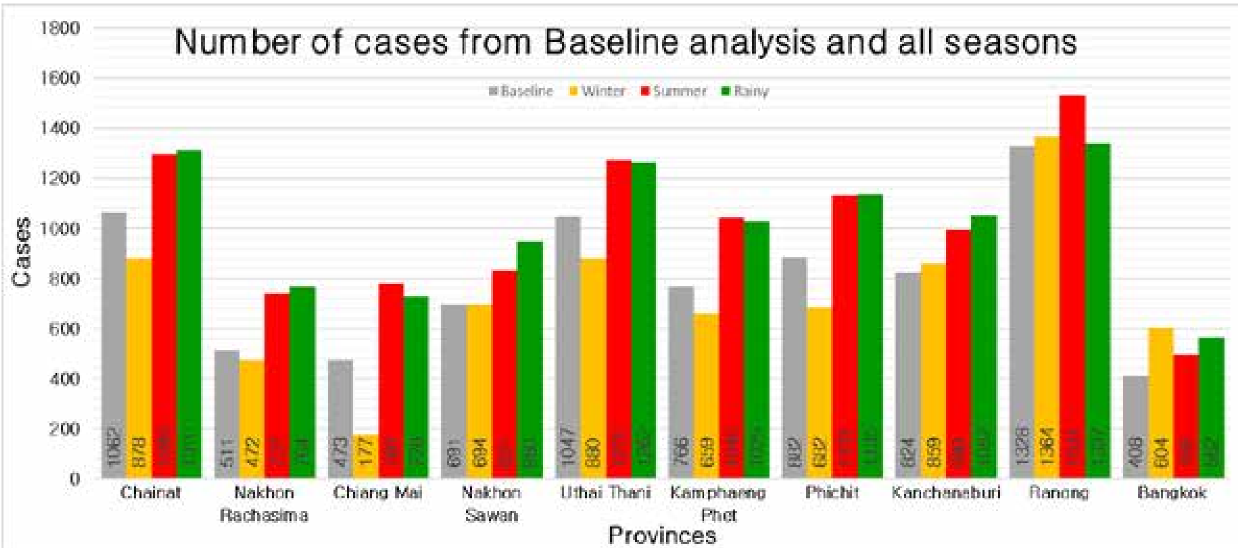
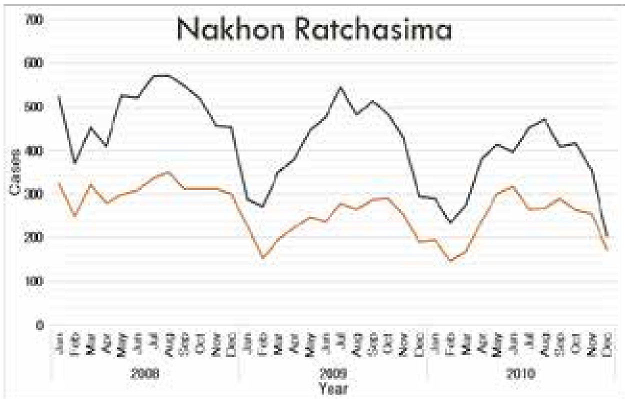


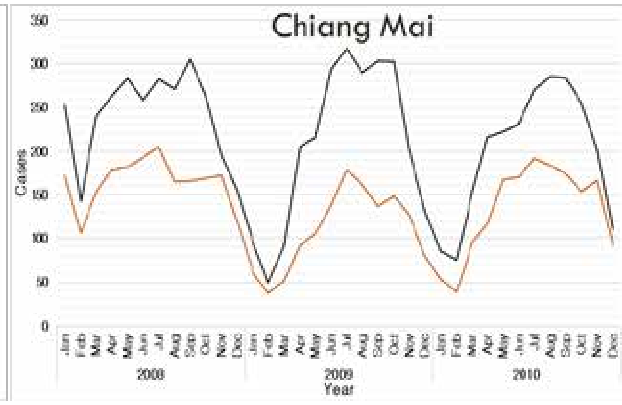
FIGURE 4.13. The number of positive humans from the baseline analysis and all seasons.

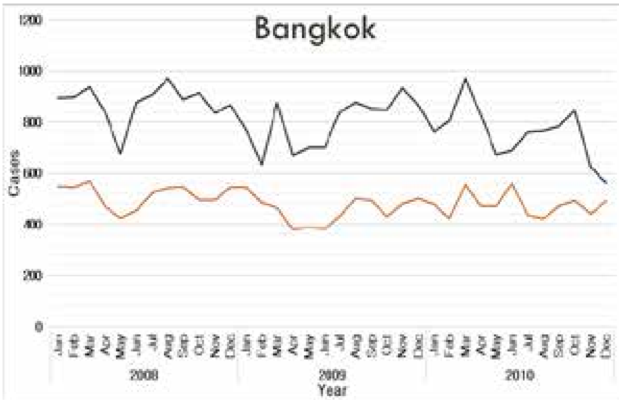
FIGURE 4.13 represents the total number of positive humans for seasonal factor in a particular province. Chiang Mai stands out for producing the lowest number of cases in winter, whereas Ranong shows more cases during the summer.

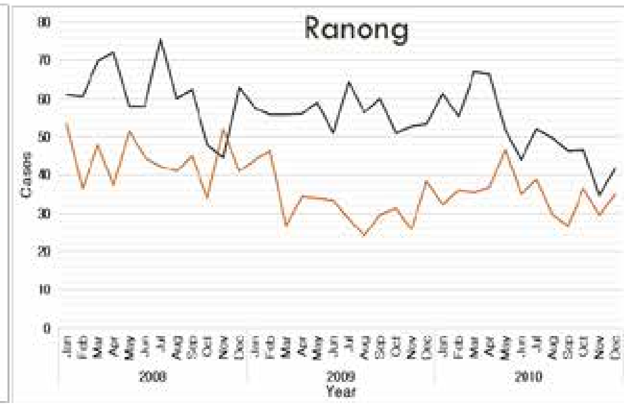
4.2.2 Staying At Home Cell

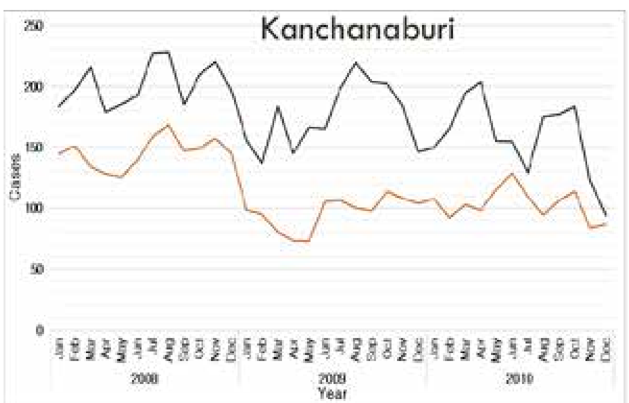
The second experiment for sensitivity analysis involved forcing people to stay at home and avoid the travel routes, e.g., to school or factory. This procedure serves to answer the question of what the effects of staying at home on virus transmission in the human population are. In this experiment, all chances of getting a bite from mosquito occur at home three times. This experiment applied the same parameters as the baseline analysis except for the moving of people to other cells. The results can be seen in FIGURE 4.14.

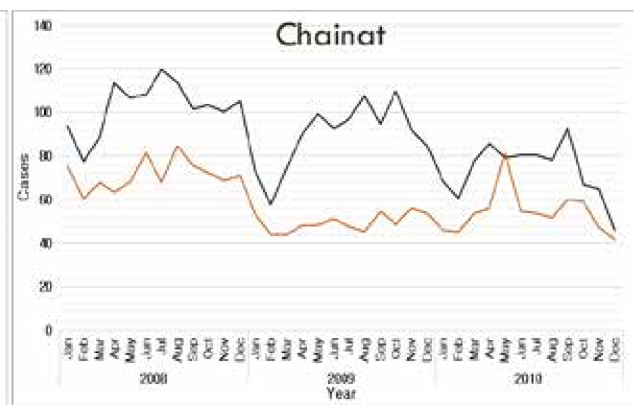

Nakhon Ratchasima
Cases
2008
2009
2010
Year

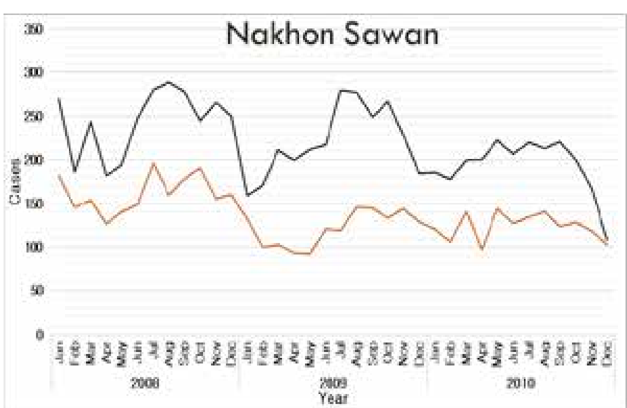

Chiang Mai
Cases
2008
2009
2010
Year

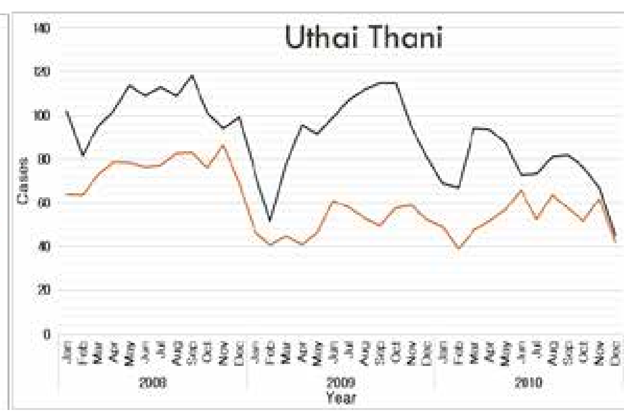

Bangkok
Cases
2008
2009
2010
Year


Ranong
Cases
2008
2009
2010
Year


Kanchanaburi
Cases
2008
2009
2010
Year


Chainat
Cases
2008
2009
2010
Year


Nakhon Sawan
Cases
2008
2009
2010
Year


Uthai Thani
Cases
2008
2009
2010
Year

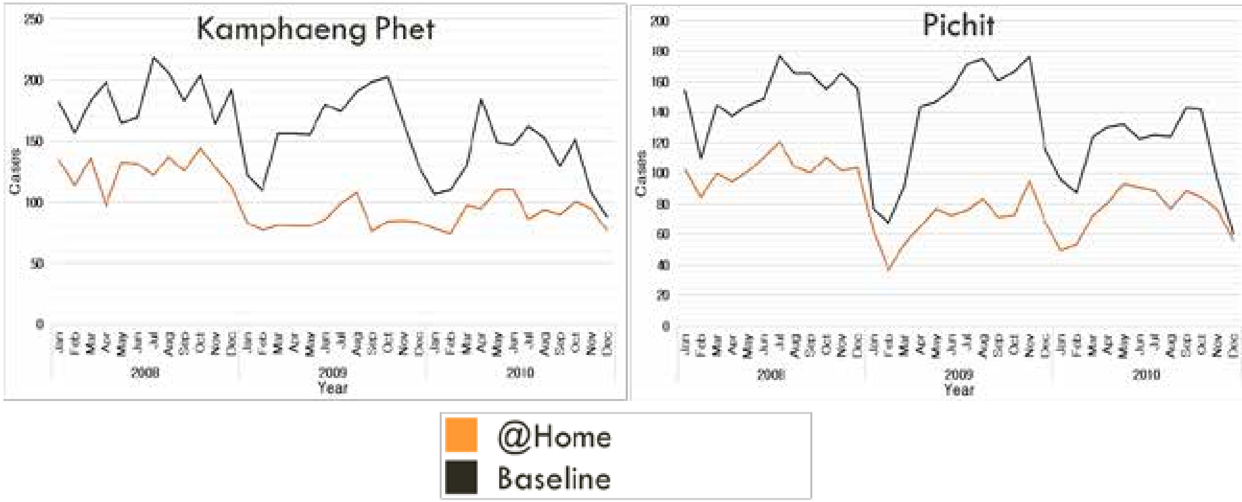


FIGURE 4.14. Sensitivity for staying at home.

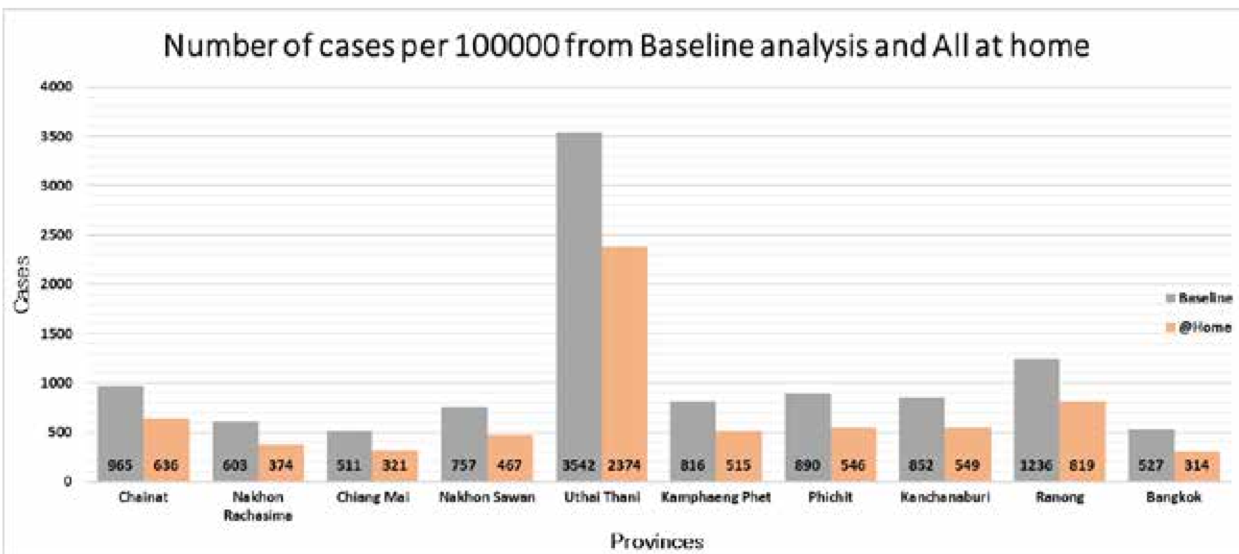
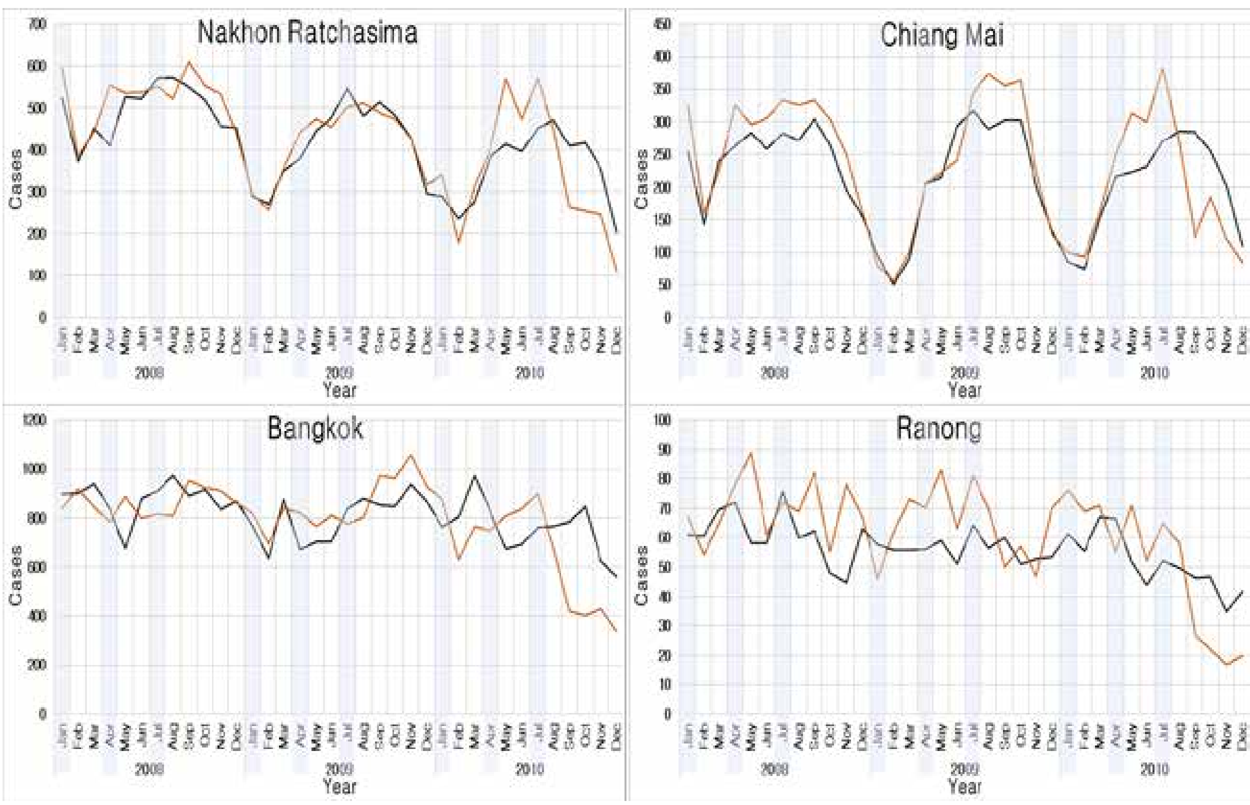


FIGURE 4.15. Number of cases per 100000 from Baseline analysis and All at home.

The graph pattern from Figure 4.15 presents broadly in the same direction when the simulation limits the route for human movement by keeping members of the population at their home cell. The number of cases is lower compared to a baseline analysis because the number of mosquitos in a living cell is less than those in a school cell or factory cell. Although people are not allowed to move to other cells, they are free to move inside a cell and are not limited to staying at home, so this activity produces a number of cases for each region.

4.2.3 Holiday

The next experiment for sensitivity analysis was to allow people to travel for a holiday. This procedure allows individuals to move across the province. The purpose of the demonstration is to answer the question of what the effects of people traveling for holiday on virus transmission in the human population are. For a holiday, the framework gives permission for an agent to travel in places different from their origin three times a year: 1) from the last week of December to the first week of January, 2) in mid-April, and 3) in the second week of May. The results of this experiment are shown in FIGURE 4.16.



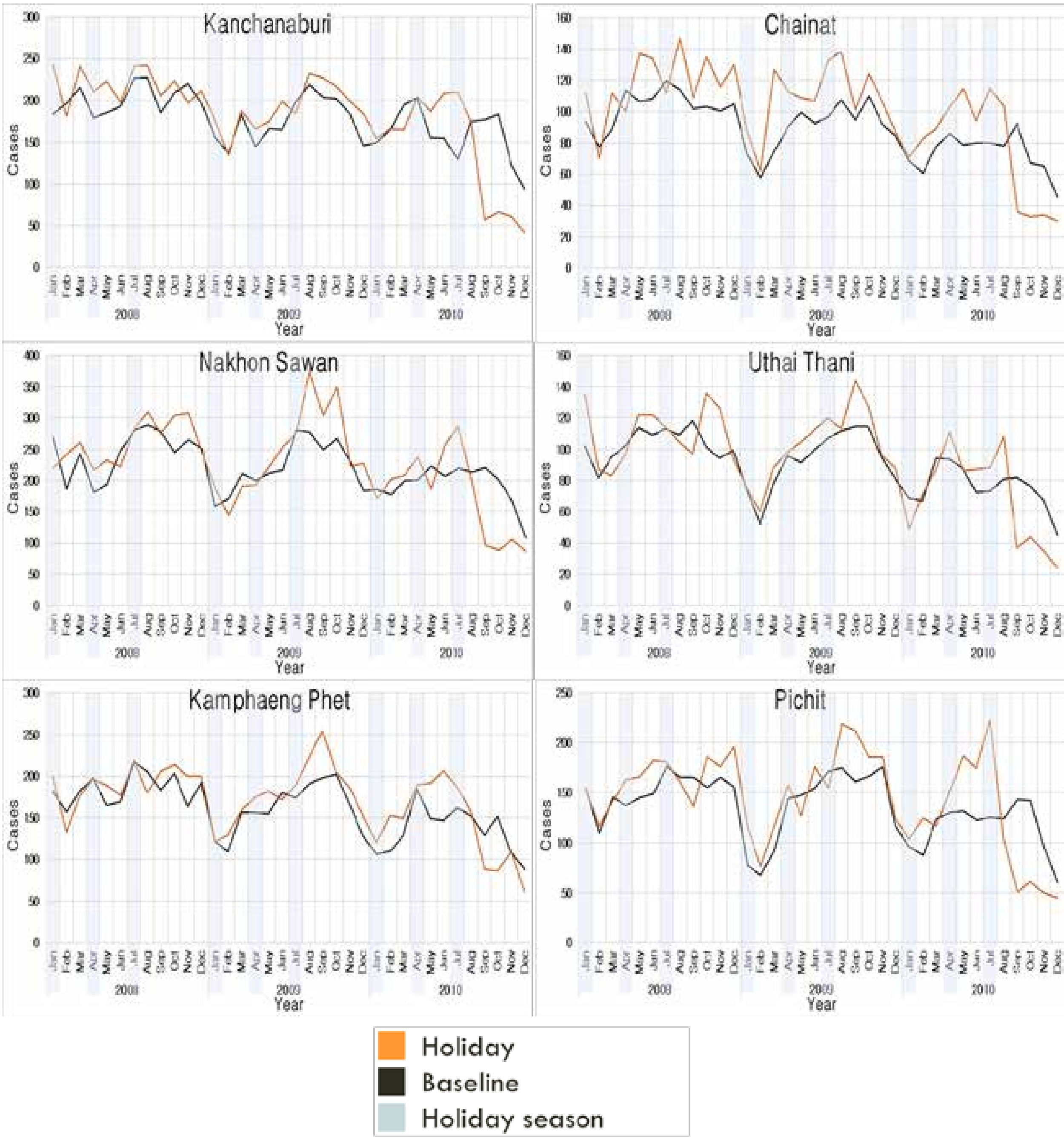


FIGURE 4.16. Sensitivity analysis of people traveling for holiday.

Overall, the graph pattern from FIGURE 4.16 is broadly similar to the baseline analysis for all provinces. However, the results are calculated at the current place for each individual at the end of each holiday. The expected the results would be represented by hiking up the graphs for all observed provinces in the range of holiday seasons. The investigation extends to weeks or to a holiday month. Most provinces show a rise in the number of cases for all simulated years. The results obviously show the highest peak for the Thai New Year and the Candle Festival because the temperature is suitable for growing mosquitos and for virus development.

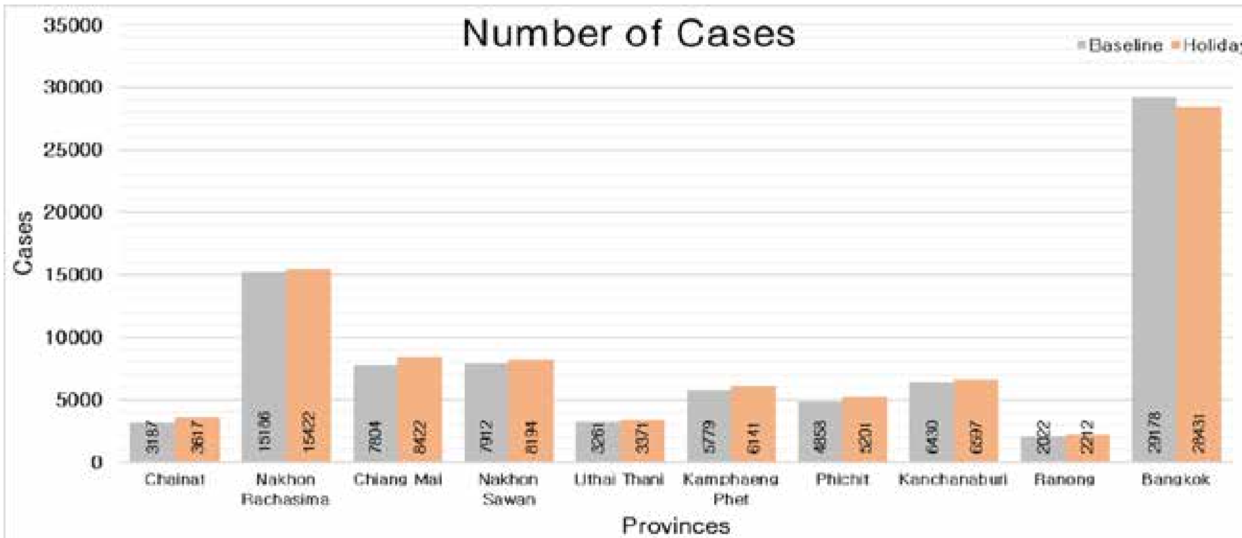


FIGURE 4.17. Number of cases from the Baseline analysis and holiday.

FIGURE 4.17 illustrates the calculation of the incidence proportion of the period of prevalence. Only Bangkok has a lower number of cases compared to the baseline analysis because most people in Bangkok travel to other provinces during the holiday. In short, the transmission of dengue virus can occur during travel periods.

CHAPTER 5

CONCLUSION

The issue of spatial epidemiology is important in understanding epidemic patterns, especially as it concerns the spread of a virus through populated areas. The incidence and spreading out of disease outbreaks in particular populations must be examined with a combination of geographic and demographic analysis, and a dynamic framework should be developed for a deeper intuitive understanding of outbreaks. This research project designed and built an mABM framework that has the ability to simulate a nationwide disease outbreak; this study simulated a dengue endemic for the area of Thailand, and the spread of this endemic, as accelerated per the diverse activities that take humans from place to place during their daily travels, was investigated.

The simulation of dengue outbreaks using mABM was implemented to study and analyze the simulation outbreak outcomes. The results from human mobility, mosquito life cycle, and characteristics of the disease spread are presented given a constant human population mixing with a dynamic mosquito population. Results were compared to data obtained from the Thailand Vector Borne Disease Bureau for the selected year. This research carried out experiments to discover the effect of specific parameters in producing several outputs by changing the rate of transmission, blood meals, and initial number of mosquitos, in order to analyze the outbreak in the provinces studied.

Sensitivity analyses were conducted to find the robustness of an assessment based on one or more parameter changes in biting frequency for adult mosquitos, limited traveling for the human population, fixing of the serotype of the dengue virus, or differences in seasonal temperatures. The results of the sensitivity analyses were dependent on questionable assumptions which resulted from the parameter settings. Clinical trial design and analysis depend primarily on assumptions, which lead to research conclusions. Consistency between baseline analysis and sensitivity analysis results is helpful for establishing the conclusions of the system or answering the clinical questions.

5.1 Analysis of the Framework

To improve the performance of the simulation, several techniques were applied, including tuning the compiler, reducing the time to access the disk, and using parallel processing. One important technique used in this system was data preprocessing. Data preprocessing was used for three main components of the system: (1) humans, (2) mosquitos, and (3) geography. Data preprocessing helps a system to reduce the processing steps by cutting some repeated actions from the simulation. For example, before the system generated the results for the patients in the human population, it needed to know the number of mosquitos in the particular area. Pre-running with a constant temperature in degrees Celsius was used to generate a synthetic mosquito population and to carry out calibration for 200 days. This would have been time consuming if the program had been run without prior preparation of the data.

Accessing of the I/O was another parameter of system performance. This system reduced the number of times required for accessing the I/O to two. In the first connection to the disk, the system read all the data into the memory when it was started. If it had to update a value, it only updated it in the memory. In the other connection to the disk, when the system completed the simulation, it wrote all the results to files on disk. All output data were written into a single file to reduce the cost of contacting the I/O. Even though in the framework the database symbol is shown, the system itself used a plain text file as the data file in order to increase system performance by avoiding accessing the database. Consequently, the system became more efficient with relation to processing time.

5.2 Contribution

The contribution of this dissertation has been to demonstrate a newly designed framework incorporating elements of a mathematical model and a computational model, mABM. mABM improves the realism in the computational simulation by integrating data from different sources. The representation of human behavior involves a large population across variant distances. The mosquito dynamic population model (MDP) can represent the mosquito population and its ecology along with regional temperature integration to capture their effect on dengue outbreak. The Local Stochastic Contact Model for dengue (LSCM-DEN) and the Extrinsic Incubation Period (EIP) are the other modeling methodologies that were integrated to represent the interactions between human and vector populations.

To simulate contact between the human and mosquito populations, this framework utilizes parallel programming to create multi-threads for several modules, such as the interaction between human and mosquito populations and the updating of human status related to SLIR stages. As a result of replacing loop statements with parallel statements, and of using most of the CPUs from the Fatman machine, results were obtained faster than the serial loop would have produced them; further, the program was easier to design than it would have been using the regular thread in the previous version of the software. This helped the developer to work more easily with large quantities of data.

In order to more quickly regenerate the mosquito population and offspring, the novel method of the MDP model takes a control for dynamic mosquito population. The MDP model integrated the actual temperature for each region into the model to calculate the maturation rate for mosquito and offspring populations. The mosquito dispersal model is used for controlling the dynamic number of mosquitos in the range of the reference work by Barbazan et al.

In addition, the effectiveness of the mABM system is supported as it reproduced the number of cases reported by the MoPH. With suitable parameters, such as the control of the mosquito population, biting rate, and transmission rate, the graph shape shows a result similar to that of the reported data. Furthermore, each parameter can be set for a particular region in order to obtain the best results without having a negative effect on the results for other regions.

Another benefit of this research, is that it can be used to study other vector-borne diseases of concern to public health, such as malaria and chikungunya. Thailand Public Health has a major mission to reduce the number of dengue cases at least 20% each year compared to the year before. The mABM framework had been shown to staff members from ODPC3, and officers from ODPC3 were interested in mABM and expressed an interest in using it as a tool to study dengue.

5.3 Limitations

This simulation consisted of several data sets and parameters, so the ensuring the accuracy of results became a significant challenge of this work. Data were obtained from various organizations in Thailand’s government such as the census, weather forecasting, public health, and others; some data were available on the Internet, while others involved cost for their use. Even the data that originated from official Thailand organizations were incomplete. For example, there was no reported temperature for some provinces from the Thai Meteorological Department. When data were used, a system had to be employed to select the temperature from surrounding provinces. Another example is the number of mosquito pupae. This number was reported for few provinces, and there were missing data for some important cities, e.g., Bangkok, Chiang Mai, Nakhon Sawan, and others which had a high percentage of dengue outbreak. The average number for each region was used in provinces without reported numbers, and the average number for the whole country was used for Bangkok.

The simulation involved two kinds of parameters: constant parameters for the whole system and control parameters for the particular sub-system. The most used control parameter was for the mosquito population. Because there was no report of the actual number of mosquitos per person or household, the estimated number of mosquitos in virtual space came from the research results of the average number of mosquitos per person by Barbazan et al. [57].

The processing time of the simulation was another issue of concern. Some elements in the simulation contained a large number of objects including the number of cell size, the human population, and the the mosquito population. For example, the processing time for the contact activity between the human and mosquito population depended on the meeting times for both populations. Either increasing or decreasing the population can affect the processing time in the simulation. To increase performance and reduce the processing time, the following suggestions may be adopted: 1) increasing the cell size. Cell size is the main component to be defined in the system. A small cell size can provide more detail in the virtual area, but it requires more time for the completion of the modeling. To illustrate, the smallest cell size, 1 km^2, for a small province such as Samut Songkram, requires at least 4 hours for execution without special options such as people traveling or vertical transmission of mosquitos, whereas a 139 km^2 cell size for the same province and options requires only 20 minutes for the simulation to complete. Increasing the cell size helps the simulation perform better with a large data set. 2) The second suggestion is reducing the time for selecting the mosquitos that will bite. The mosquito population is the largest component in the simulation. To reduce time necessary to account for mosquitos, the system uses a mathematical model to deal with the mosquito population.

5.4 Future Work

This research applies to the country area of Thailand and uses the actual Thai population. However, it avoids detail regarding the geographic area, including public places, parks, rivers, and other features in order to avoid complexity in representing visual space in the simulation. The varieties of land use might have different effects on human movement and the number of patients.

Rainfall is another feature which might have an effect on the mosquito population and on increases in the number of patients in the human population. Because mosquito eggs are laid in water, rainfall in a particular area might have a direct effect on the number of offspring. In 2010, there was flooding in Thailand, and the report from the Thailand Vector Borne Disease Bureau shows an increasing of number of patients with dengue fever. Rainfall could also be used as a factor in the system for the gonotrophic cycle in mosquitos.

Methods for controlling the dengue disease should be included in the system. These methods can be divided into two groups: (1) controlling the mosquito population by introducing predators for mosquitos and finding ways to control standing water, and (2) controlling the number of patients by introducing the immune system in people, such as by using a vaccine in the human population. The disease control techniques might be considered in estimating the number of surviving mosquitos in the simulation.

Time intervals in the framework are the next factor to include in the system. Certain processes in this simulation involve a gap or waiting time before the next step can begin. For example, when female mosquitoes lay eggs, they need a few days break before they can take another blood meal. Another example is when people move from one place to another; moving over a long distance should require more time than moving within the local area.

The next version of the simulation could include improved features in geographic detail, rainfall, control functions, and time intervals in the system to make the simulation results closer to reported data from the MoPH without a worsening of performance.

APPENDIX

SUPPLEMENTAL FIGURES

			Age distribution														
Province	Area in Km^2	#House	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65+	Total
Bangkok	1,569	2,263,680	293,024	339,425	417,052	395,610	383,305	445,596	474,355	485,332	493,601	466,304	397,783	312,108	203,242	426,255	5,532,992
Samut Prakan	1,004	479,503	70,305	73,679	88,471	81,473	73,406	92,296	102,140	107,960	107,820	93,734	74,265	55,487	34,665	72,752	1,128,453
Nonthaburi	622	491,795	59,511	61,073	74,194	68,576	63,007	80,217	90,393	98,063	100,334	90,438	73,751	55,328	37,118	84,266	1,036,269
Pathum Thani	1,526	427,051	63,059	60,040	68,472	65,892	62,662	74,273	88,007	94,402	90,737	72,704	54,657	40,851	26,994	54,676	917,426
Phra Nakhon Si Ayutthaya	2,557	250,256	48,394	46,186	54,681	53,081	50,245	60,746	64,749	66,400	68,030	60,101	48,627	38,378	26,621	72,941	759,180
Ang Thong	968	84,397	15,641	15,991	19,428	19,535	18,426	21,456	22,104	22,022	24,755	23,376	19,562	16,300	10,885	31,132	280,613
Lopburi	6,200	247,918	43,488	44,029	52,091	51,994	61,557	57,706	58,548	59,513	66,098	60,217	48,597	37,913	26,775	65,830	734,356
Sing Buri	822	66,744	11,448	11,557	13,708	13,980	14,001	16,009	16,066	16,142	18,352	18,427	15,701	12,980	9,241	24,298	211,910
Chainat	2,470	106,295	18,114	17,926	21,796	22,935	21,084	24,387	25,873	26,627	29,462	27,860	23,824	19,817	13,874	36,537	330,116
Saraburi	3,576	212,904	38,637	37,982	45,035	44,209	46,106	47,170	49,674	52,133	53,425	47,553	37,522	28,319	19,546	47,896	595,207
Chonburi	4,363	652,001	88,433	83,109	94,077	91,705	92,073	107,085	118,614	118,149	110,448	92,445	71,314	52,477	35,989	81,189	1,237,107
Rayong	3,552	295,931	44,960	41,257	46,122	42,733	39,947	50,540	57,850	57,629	52,705	42,150	32,713	24,415	16,975	38,250	588,246
Chanthaburi	6,338	187,923	31,121	32,033	37,530	38,093	36,403	40,954	40,728	43,823	44,554	39,620	31,836	24,610	16,682	42,961	500,948
Trat	2,819	86,925	13,714	13,778	15,710	15,841	15,253	17,551	17,721	17,657	17,406	15,863	12,892	10,414	7,357	17,620	208,777
Chachoengsao	5,351	223,508	42,989	42,218	49,587	49,685	48,375	54,849	55,690	56,328	56,726	49,359	39,278	31,740	22,218	58,078	657,120
Prachinburi	4,762	159,699	29,854	29,467	34,119	34,294	35,203	37,713	39,408	38,430	38,107	33,946	26,755	20,821	14,573	38,322	451,012
Nakhon Nayok	2,122	79,019	15,065	14,500	17,576	19,693	18,824	19,446	19,633	19,949	21,728	18,986	15,774	12,746	9,323	24,638	247,881
Sa Kaeo	7,195	167,332	37,102	37,110	43,082	42,498	42,290	46,061	46,922	46,664	45,440	38,175	29,814	22,633	15,506	34,453	527,750
Nakhon Ratchasima	20,494	763,903	158,552	163,882	190,467	189,841	189,872	216,043	227,016	227,158	216,657	185,529	150,935	118,944	88,370	197,165	2,520,431
Buriram	10,323	379,550	103,474	109,508	127,645	121,829	113,077	133,033	137,539	138,334	121,981	101,217	82,589	67,756	51,405	108,448	1,517,835
Surin	8,124	328,279	88,959	94,622	113,578	110,333	103,115	118,817	117,111	117,308	105,058	91,851	72,735	61,065	46,919	102,745	1,344,216
Sisaket	8,840	333,083	90,182	98,878	118,721	113,504	107,244	124,559	128,857	128,975	116,535	97,158	77,813	64,129	48,589	101,198	1,416,342
Ubon Ratchathani	16,113	467,182	120,188	128,418	149,950	150,114	140,481	153,310	155,337	158,150	142,998	115,926	94,203	76,294	53,593	117,961	1,756,923
Yasothon	4,162	141,941	30,824	33,911	41,582	41,171	39,943	44,626	48,285	51,796	46,859	38,324	32,253	25,539	20,308	39,186	534,607
Chaiyaphum	12,778	326,043	67,455	69,587	82,865	84,448	79,404	88,793	92,739	101,561	98,731	82,223	69,878	55,260	42,358	87,912	1,103,214
Amnat Charoen	3,161	93,878	22,996	24,476	29,959	30,313	27,763	31,078	31,825	34,030	31,746	25,614	21,129	16,740	11,869	24,727	364,265
Nong Bua Lamphu	3,859	124,849	32,210	33,999	40,312	39,990	37,959	43,901	46,383	46,060	42,619	33,873	28,384	22,437	16,142	28,028	492,297
Khon Kaen	10,886	499,450	101,660	106,218	133,430	135,902	131,902	144,937	148,681	158,891	156,362	129,336	107,766	86,867	67,329	126,082	1,735,363
Udon Thani	11,730	413,693	95,464	103,466	121,006	122,675	117,684	132,900	142,036	141,531	130,895	104,827	85,516	66,756	50,642	87,866	1,503,264
Loei	11,425	179,721	38,508	37,985	44,638	46,384	44,762	50,485	51,273	53,466	54,134	46,894	39,614	29,783	22,325	46,695	606,946
Nong Khai	3,027	244,354	60,156	63,288	72,495	69,627	64,253	79,965	84,133	84,052	75,555	62,081	50,029	37,937	28,307	56,867	888,745
Maha Sarakham	5,292	245,020	52,976	56,828	70,223	72,334	67,426	75,426	83,164	90,265	83,122	67,028	56,426	48,265	38,148	62,473	924,104
Roi Et	8,299	327,816	74,010	80,980	102,752	101,388	95,837	108,428	116,167	125,441	112,972	90,741	77,250	64,094	51,214	89,696	1,290,970
Kalasin	6,947	250,550	58,541	61,164	73,935	77,368	75,247	82,191	86,183	95,165	87,739	69,179	57,214	45,626	35,500	61,589	966,641
Sakon Nakhon	9,606	301,061	74,804	78,212	87,755	88,128	86,517	103,235	103,086	104,927	93,086	75,748	60,872	47,712	35,067	61,701	1,100,850
Nakhon Phanom	5,513	183,952	47,671	50,823	55,915	53,238	53,012	63,581	65,954	64,434	55,638	46,246	37,206	30,633	23,064	43,328	690,743
Mukdahan	4,340	90,365	22,007	22,718	27,686	25,878	27,034	30,339	30,360	30,879	27,782	22,647	17,942	14,306	10,255	21,160	330,993
Chiang Mai	20,107	636,928	81,455	83,540	105,685	116,224	119,525	121,375	110,683	110,771	127,122	139,969	128,643	89,832	52,261	140,741	1,527,826
Lamphun	4,506	156,112	18,393	18,816	25,522	28,666	27,355	30,458	28,530	29,916	36,122	39,055	35,497	25,636	15,763	40,761	400,490
Lampang	12,534	260,974	32,366	35,548	50,867	55,462	53,121	53,718	53,819	61,247	70,094	72,175	64,581	46,410	29,775	77,367	756,550
Uttaradit	7,839	149,237	24,846	26,738	31,843	31,141	30,445	34,458	37,803	39,985	40,776	38,661	33,439	26,432	17,861	44,160	458,588
Phrae	6,539	156,884	20,592	22,210	30,254	32,642	31,231	34,912	33,101	37,382	42,938	42,531	38,403	28,898	20,090	44,083	459,267
Nan	11,472	144,258	25,240	26,235	35,543	36,519	35,472	37,707	35,371	37,204	44,680	40,981	35,411	23,939	16,266	40,076	470,644
Phayao	6,335	167,010	21,946	23,887	32,911	37,741	36,981	36,756	35,425	38,578	44,642	45,923	39,415	28,903	16,829	40,384	480,321
Chiang Rai	11,678	446,346	59,928	63,859	80,401	87,324	80,776	90,026	83,387	86,555	97,821	100,079	89,332	62,499	37,554	89,852	1,109,393
Mae Hong Son	12,681	86,111	17,376	17,929	19,818	19,900	19,124	18,243	16,069	15,405	15,310	13,417	11,144	8,583	5,778	15,397	213,493
Nakhon Sawan	9,598	350,468	60,979	61,669	73,956	75,827	73,390	82,773	83,729	86,058	95,259	85,116	71,413	57,334	38,752	98,298	1,044,553
Uthai Thani	6,730	102,099	20,198	19,987	23,525	23,327	22,509	25,770	26,432	27,221	28,198	24,384	20,994	17,477	12,387	30,696	323,105
Kamphaeng Phet	8,607	226,332	45,732	45,382	54,153	53,998	50,636	59,112	61,304	61,014	63,514	55,102	44,931	35,890	23,524	53,756	708,048
Tak	16,407	167,558	41,001	41,690	42,384	39,799	36,121	38,328	37,234	36,143	36,995	31,875	26,985	20,272	14,671	31,217	474,715
Sukhothai	6,596	186,214	33,149	33,430	41,714	41,370	38,456	45,355	50,664	51,931	54,985	51,482	41,671	33,937	21,744	53,901	593,789
Phitsanulok	10,816	284,518	47,718	48,287	58,923	63,260	63,563	67,008	68,613	70,125	75,266	68,327	55,340	43,737	28,488	68,710	827,365
Phichit	4,531	166,388	32,268	32,520	39,635	38,491	36,106	43,582	45,057	44,941	48,980	43,740	37,783	31,479	19,836	51,626	546,044
Phetchabun	12,668	296,919	60,203	61,472	72,044	71,432	71,358	83,289	85,301	84,557	84,077	75,580	63,433	48,181	33,697	78,038	972,662
Ratchaburi	5,196	256,839	50,797	49,930	59,498	60,072	60,862	66,316	67,612	68,325	68,001	62,873	53,236	42,355	29,058	73,822	812,757
Kanchanaburi	19,483	275,015	52,340	50,313	57,870	59,650	63,309	64,753	65,727	64,026	62,228	55,546	45,831	35,533	23,619	53,826	754,571
Suphan Buri	5,358	250,318	49,764	48,502	58,825	60,732	60,871	68,007	67,964	66,077	70,868	66,675	54,888	45,233	32,138	82,297	832,841
Nakhon Pathom	2,168	305,855	52,137	50,800	62,115	65,600	62,971	70,635	72,182	71,159	72,929	65,974	53,537	40,594	27,745	64,984	833,362
Samut Sakhon	872	220,469	31,351	31,185	37,725	36,034	33,020	38,261	40,853	42,020	42,634	37,074	29,500	22,025	14,726	33,147	469,555
Samut Songkhram	417	56,213	10,439	10,701	12,864	12,586	12,800	15,421	15,494	16,016	16,434	14,978	13,361	11,371	8,194	21,398	192,057
Phetchaburi	6,225	160,240	27,283	27,027	32,344	32,926	34,132	36,655	37,968	38,580	39,147	34,717	29,217	23,074	16,004	42,484	451,558
Prachuap Khiri Khan	6,368	187,381	33,101	31,920	36,142	37,034	42,626	40,932	41,009	41,615	41,258	36,788	30,355	22,570	14,857	37,633	487,840
Nakhon Si Thammarat	9,943	452,972	98,332	101,945	118,341	121,331	124,226	133,447	127,081	120,460	113,543	100,908	80,348	64,334	49,649	135,626	1,489,571
Krabi	4,709	134,107	37,175	33,593	36,259	36,555	36,513	38,156	36,557	34,583	31,291	26,671	19,977	14,124	9,305	24,956	415,715
Phang Nga	4,171	90,987	18,294	17,454	19,791	18,958	18,756	21,224	20,245	20,591	20,079	17,910	15,015	11,382	7,593	20,500	247,792
Phuket	543	157,360	26,407	25,050	26,725	24,807	22,444	29,556	32,328	31,025	28,400	22,572	16,496	12,440	7,879	16,353	322,482
Surat Thani	12,891	369,432	71,159	68,062	76,445	76,932	76,904	84,472	85,315	85,623	81,358	67,679	50,993	38,721	27,577	74,184	965,424
Ranong	3,298	67,835	11,999	12,336	14,498	13,052	12,597	13,665	13,964	14,242	13,423	11,467	9,444	7,084	4,732	11,159	163,662
Chumphon	6,010	183,384	30,796	31,543	37,558	36,507	36,435	38,863	39,637	41,281	41,310	34,876	28,827	20,892	15,821	42,307	476,653
Songkhla	7,394	409,713	98,125	97,450	107,407	106,911	108,898	112,240	109,698	107,273	99,843	90,558	71,067	58,349	39,272	103,595	1,310,686
Satun	2,479	79,434	24,880	24,288	25,267	25,474	24,966	24,978	23,731	22,901	20,618	18,237	13,790	11,152	6,936	19,217	286,435
Trang	4,918	185,592	43,789	43,673	51,587	51,891	50,449	52,860	51,383	49,501	47,186	42,906	33,978	25,494	17,296	46,485	608,478
Phatthalung	3,424	154,850	32,641	32,234	39,354	39,249	38,143	43,071	42,788	42,177	39,449	34,406	28,405	23,133	18,622	45,992	499,664
Pattani	1,940	149,522	60,768	61,200	64,214	60,828	52,942	49,717	45,051	44,459	41,479	35,725	26,811	24,324	15,508	49,777	632,803
Yala	4,521	130,143	44,534	44,055	46,856	45,267	39,289	37,021	33,321	33,340	32,436	28,135	21,053	18,288	11,446	32,771	467,812
Narathiwat	4,475	168,681	66,424	66,683	68,947	67,630	63,024	58,810	51,993	52,031	48,162	41,242	29,931	26,679	17,260	46,627	705,443

FIGURE A.1. Province information and age distribution

Province	L2
Bangkok	0.0022
Samut Prakan	0.0055
Nonthaburi	0.0027
Pathum Thani	0.0138
Phra Nakhon Si Ayutthaya	0.0320
Ang Thong	0.0330
Lopburi	0.0836
Sing Buri	0.0374
Chainat	0.0753
Saraburi	0.0593
Chonburi	0.0334
Rayong	0.0599
Chanthaburi	0.1271
Trat	0.1369
Chachoengsao	0.0810
Prachinburi	0.1047
Nakhon Nayok	0.0856
Sa Kaeo	0.1343
Nakhon Ratchasima	0.0807
Buriram	0.0673
Surin	0.0599
Sisaket	0.0622
Ubon Ratchathani	0.0914
Yasothon	0.0772
Chaiyaphum	0.1162
Amnat Charoen	0.0865
Nong Bua Lamphu	0.0789
Khon Kaen	0.0622
Udon Thani	0.0798
Loei	0.1898
Nong Khai	0.0320
Maha Sarakham	0.0567
Roi Et	0.0640
Kalasin	0.0717
Sakon Nakhon	0.0865
Nakhon Phanom	0.0789
Mukdahan	0.1274
Chiang Mai	0.1299

Province	L2
Lamphun	0.1139
Lampang	0.1657
Uttaradit	0.1657
Phrae	0.1424
Nan	0.2219
Phayao	0.1343
Chiang Rai	0.1078
Mae Hong Son	0.4614
Nakhon Sawan	0.0914
Uthai Thani	0.2024
Kamphaeng Phet	0.1203
Tak	0.3200
Sukhothai	0.1096
Phitsanulok	0.1294
Phichit	0.0826
Phetchabun	0.1353
Ratchaburi	0.0640
Kanchanaburi	0.2444
Suphan Buri	0.0641
Nakhon Pathom	0.0238
Samut Sakhon	0.0158
Samut Songkhram	0.0195
Phetchaburi	0.1369
Prachuap Khiri Khan	0.1343
Nakhon Si Thammarat	0.0667
Krabi	0.1120
Phang Nga	0.1694
Phuket	0.0138
Surat Thani	0.1321
Ranong	0.1964
Chumphon	0.1271
Songkhla	0.0553
Satun	0.0873
Trang	0.0800
Phatthalung	0.0682
Pattani	0.0281
Yala	0.0969
Narathiwat	0.0622

FIGURE A.2. L2 value for each province.

REFERENCES

[1] U. Wilensky and W. Rand, *An Introduction to Agent-Based Modeling: Modeling Natural, Social, and Engineered Complex Systems with NetLogo*. The MIT Press, 2015.

[2] “WHO | Dengue and severe dengue.”

[3] “CDC - Epidemiology - Dengue.” [Online]. Available: http://www.cdc.gov/dengue/epidemiology/index.html. [Accessed: 30-Sep-2013].

[4] *Dengue Buidelines for Diagnosis, Treatment, Prevention Control.* World Health Organization, 2009.

[5] D. J. Gubler, “Dengue and Dengue Hemorrhagic Fever Dengue and Dengue Hemorrhagic Fever,” vol. 11, no. 3, 1998.

[6] D. Barmak, C. Dorso, M. Otero, and H. Solari, “Dengue epidemics and human mobility,” *Phys. Rev. E*, vol. 84, no. 1, pp. 1–11, Jul. 2011.

[7] “WHO | ITH 2012 Edition.”

[8] “WHO | Changes in reporting requirements for pandemic (H1N1) 2009 virus infection.”

[9] P. Bajardi, C. Poletto, J. J. Ramasco, M. Tizzoni, V. Colizza, and A. Vespignani, “Human mobility networks, travel restrictions, and the global spread of 2009 H1N1 pandemic.,” *PLoS One*, vol. 6, no. 1, p. e16591, Jan. 2011.

[10] P. Shirtcliffe, E. Cameron, K. G. Nicholson, and M. J. Wiselka, “Don’t forget dengue! Clinical features of dengue fever in returning travellers.,” *J. R. Coll. Physicians Lond.*, vol. 32, no. 3, pp. 235–7, Jan. .

[11] J. Muñoz *et al.*, “[Clinical and epidemiological features of imported dengue in Spain].,” *Med. Clin. (Barc).*, vol. 131, no. 1, pp. 18–21, Jun. 2008.

[12] D. Teichmann, K. Göbels, M. Niedrig, and M. P. Grobusch, “Dengue virus infection in travellers returning to Berlin, Germany: clinical, laboratory, and diagnostic aspects,” *Acta Trop.*, vol. 90, no. 1, pp. 87–95, 2004.

[13] S. Sucharit, “Epidemiological Situation of Dengue in Thailand,” *Trop. Med.*, vol. 35, no. 4, pp. 173–177, 1993.

[14] “vector borne disease bureau.” [Online]. Available: http://www.thaivbd.org/dengue.php. [Accessed: 30-Sep-2013].

[15] “Bureau of Epidemiology, Thailand.” [Online]. Available: http://www.boe.moph.go.th/. [Accessed: 30-Sep-2013].

[16] “Issue 12 - Dengue Updates | February 2013 | denguematters.info.” [Online]. Available: http://www.denguematters.info/content/issue-12-dengue-updates-february-2013. [Accessed: 01-Oct-2013].

[17] A. Wilder-Smith, “Dengue infections in travellers.,” *Paediatr. Int. Child Health*, vol. 32 Suppl 1, pp. 28–32, May 2012.

[18] “WHO | New phase in fight against neglected tropical diseases heralds universal access to health interventions for world’s poorest.”

[19] B. Adams *et al.*, “Cross-protective immunity can account for the alternating epidemic pattern of dengue virus serotypes circulating in Bangkok.,” *Proc. Natl. Acad. Sci. U. S. A.*, vol. 103, no. 38, pp. 14234–9, Sep. 2006.

[20] D. L. Chao, S. B. Halstead, M. E. Halloran, and I. M. Longini, “Controlling dengue with vaccines in Thailand.,” *PLoS Negl. Trop. Dis.*, vol. 6, no. 10, p. e1876, Jan. 2012.

[21] S. Kongsin, S. Jiamton, J. A. Suaya, and S. Vasanawathana, “Cost of dengue in Thailand,” vol. 34, pp. 77–88, 2010.

[22] L. Han *et al.*, “Immediate cost of dengue to Malaysia and Thailand : An estimate,” vol. 34, pp. 65–76, 2010.

[23] “The World Factbook :: Thailand,” *Central Intelligence Agency*, 2013. [Online]. Available: https://www.cia.gov/library/publications/the-world-factbook/geos/th.html. [Accessed: 04-Sep-2013].

[24] “Ministry of Interior.” [Online]. Available: http://www.moi.go.th/MOIWEB/MOILogin?user_id=guest&user_password=guest&flag=1#. [Accessed: 10-Apr-2013].

[25] “Thai Meteorological Department,” 2013. [Online]. Available: http://www.tmd.go.th/info/info.php?FileID=22. [Accessed: 10-Apr-2013].

[26] “Thailand Census 2012,” Bangkok, Thailand, 2012.

[27] “Bus transportation stations’ statistic in Thailand,” Bangkok, Thailand, 2012.

[28] “Railway stations in Thailand,” *State Railway of Thailand*, 2012. [Online]. Available: http://www.railway.co.th/home/srt/knowledge/route.asp. [Accessed: 11-Apr-2013].

[29] “Department of Civil Aviation,” 2012. [Online]. Available: http://www.aviation.go.th/hongson/map.htm. [Accessed: 11-Apr-2013].

[30] “Survey of Thai Travelers, 2012,” Bangkok, Thailand, 2012.

[31] “Border crossing in Thailand,” Bangkok, Thailand, 2012.

[32] Immigration Bureau, “Immigration Statistic,” *Immigration Bureau*, 2017. [Online]. Available: https://www.immigration.go.th/immigration_stats. [Accessed: 28-Feb-2018].

[33] W. Rojanapithayakorn, “Dengue Haemorrhagic Fever in Thailand Situation and trends of DHF in Thailand Dengue haemorrhagic fever was first,” vol. 22, no. 3, pp. 60–72, 1998.

[34] T. S. Asia and W. P. Region, *Dengue Bulletin (Book WHO report)*, vol. 25, no. December. World Health Organization, 2001.

[35] D. J. Gubler, “Dengue and dengue hemorrhagic fever.,” *Clin. Microbiol. Rev.*, vol. 11, no. 3, pp. 480–96, Jul. 1998.

[36] Bureau of Epidemiology, “Weekly Epidemiological Surveillance Report, Thailand,” Bangkok, Thailand, 2017.

[37] AMCA, “Mosquito Info,” *The American Mosquito Control Association*, 2017. .

[38] CDC, “Mosquito life cycle: Aedes aegypti,” pp. 1–2, 2012.

[39] Ministry of Tourism and Sport, “Internal Tourism in Whole Kingom, 2016,” *Ministry of Tourism and Sport*, 2016. [Online]. Available: http://www.mots.go.th/more_news.php?cid=438&filename=index. [Accessed: 04-Jan-2018].

[40] A. Hillier and D. Tomlin, “Agent-based Modeling of Urban Phenomena in GIS Capstone Project submitted in fulfillment of Masters in Urban Spatial Analytics University of Pennsylvania,” 2007.

[41] D. Guo, B. Ren, and C. Wang, “Integrated Agent-Based Modeling with GIS for Large Scale Emergency Simulation,” in *ISICA ’08 Proceedings of the 3rd International Symposium on Advances in Computation and Intelligence*, 2008, pp. 618–625.

[42] C. Macal and M. North, “Tutorial on Agent-Based Modeling and Simulation PART 2: How to Model with Agents,” in *Proceedings of the 2006 Winter Simulation Conference*, 2006, pp. 73–83.

[43] N. Gilbert, “AGENT-BASED MODELS,” pp. 1–20.

[44] E. Bonabeau, “Agent-based modeling: methods and techniques for simulating human systems.,” *Proc. Natl. Acad. Sci. U. S. A.*, vol. 99 Suppl 3, pp. 7280–7, May 2002.

[45] C. M. Macal and M. J. North, “Tutorial on agent-based modelling and simulation,” *J. Simul.*, vol. 4, no. 3, pp. 151–162, Sep. 2010.

[46] D. J. Barnes and D. Chu, *Introduction to Modeling for Biosciences*. London: Springer London, 2010.

[47] C. Deng, H. Tao, and Z. Ye, “Agent-based modeling to simulate the dengue spread,” *Proc. SPIE*, vol. 7143, no. 135, p. 71431O–71431O–10, 2008.

[48] C. Isidoro, N. Fachada, F. Barata, and A. Rosa, “Agent-Based Model of Aedes aegypti Population Dynamics,” in *EPIA ’09 Proceedings of the 14th Portuguese Conference on Artificial Intelligence: Progress in Artificial Intelligence*, 2009, pp. 53–64.

[49] L. F. O. Jacintho, A. F. M. Batista, T. L. Ruas, M. G. B. Marietto, and F. A. Silva, “An agent-based model for the spread of the Dengue fever: A Swarm Platform Simulation Approach,” in *Proceedings of the 2010 Spring Simulation Multiconference on - SpringSim ’10*, 2010, p. 1.

[50] S. J. De Almeida, R. P. Martins Ferreira, Á. E. Eiras, R. P. Obermayr, and M. Geier, “Multi-agent modeling and simulation of an Aedes aegypti mosquito population,” *Environ. Model. Softw.*, vol. 25, no. 12, pp. 1490–1507, Dec. 2010.

[51] A. R. Mikler, A. Bravo-Salgado, and C. D. Corley, “Global Stochastic Contact Modeling of Infectious Diseases,” *2009 Int. Jt. Conf. Bioinformatics, Syst. Biol. Intell. Comput.*, pp. 327–330, 2009.

[52] I. Bureau, “Immigration Bureau,” *Immigration Bureau of Thailand*, 2014. [Online]. Available: http://www.immigration.go.th/nov2004/en/base.php?page=stat. [Accessed: 08-Jul-2014].

[53] “National Statistic Organization:Population and Housing Census,” 2013. [Online]. Available: http://service.nso.go.th/nso/nso_center/project/search_center/23project-th.htm.

[54] “The number of District, Subdistrict for each province, 2011,” Bangkok, Thailand, 2011.

[55] I. B. of Thailand, “International Tourist Arrivals to Thailand by Nation,” 2013. [Online]. Available: http://www.immigration.go.th/. [Accessed: 11-Aug-2013].

[56] *The population and housing census survey 2011*, 1st ed. Bangkok, Thailand: Statistical Forecasting Bureau, 2011.

[57] P. Barbazan *et al.*, “Assessment of a new strategy, based on *Aedes aegypti* (L.) pupal productivity, for the surveillance and control of dengue transmission in Thailand,” *Ann. Trop. Med. Parasitol.*, vol. 102, no. 2, pp. 161–171, Mar. 2008.

[58] M. S. Sarfraz, N. K. Tripathi, T. Tipdecho, T. Thongbu, P. Kerdthong, and M. Souris, “Analyzing the spatio-temporal relationship between dengue vector larval density and land-use using factor analysis and spatial ring mapping.,” *BMC Public Health*, vol. 12, p. 853, Jan. 2012.

[59] *Practical manual and Guidelines for Dengue Vector Surveillance*. Medical Research Institute & Dengue Coordination Unit, 2011.

[60] C. Basso *et al.*, "Mosquito-producing containers, spatial distribution, and relationship between Aedes aegypti population indices on the southern boundary of its distribution in South America (Salto, Uruguay).," *Am. J. Trop. Med. Hyg.*, vol. 87, no. 6, pp. 1083–8, Dec. 2012.

[61] A. Luana Cristina Farnesi, Ademir Jesus Martins, Denise Valle and G. L. Rezende, "Embryonic development of Aedes Aegypti(Diptera:Culicidae): influence of different constant temperatures," *Mem Inst Oswaldo C*, vol. 104, no. 1, pp. 124–126, 2009.

[62] J. W. dos S. Eduardo B Beserra, Francisco P. de Castro Jnior and and C. R. M. F. Tatiana da S Santos, "Biologia e exigłncias trmicas de Aedes Aegypti (l.) (Diptera:Culicidae) provenientes de quatro regies bioclimticas da Paraba," *Neotrop. Entomol.*, vol. 35, no. 6, pp. 853–860, 2006.

[63] E. A. P. D. A. Costa, E. M. D. M. Santos, J. C. Correia, and C. M. R. De Albuquerque, "Impact of small variations in temperature and humidity on the reproductive activity and survival of Aedes aegypti (Diptera, Culicidae)," *Rev. Bras. Entomol.*, vol. 54, no. 3, pp. 488–493, 2010.

[64] A. M. Lutambi, M. A. Penny, T. Smith, and N. Chitnis, "Mathematical modelling of mosquito dispersal in a heterogeneous environment.," *Math. Biosci.*, vol. 241, no. 2, pp. 198–216, Feb. 2013.

[65] and B. H. K. W. Tun-Lin, T. R. Burkot, "Effects of temperature and larval diet on development rates and survival of the dengue vector A. Aegypti in North Queensland, Australia," *Med. Vet. Entomol.*, vol. 14, no. 1, pp. 31–37, 2000.

[66] A. N. Douglas M. Watts, Donald S. Burke, Bruce A. Harrison, Richard E. Whitmire, "Effect of Temperature on The Vector Efficiency of Aedes Aegypti for Dengue 2 Virus," *Am. J. Trop. Med. Hyg.*, vol. 36, no. l, pp. 143–152, 1987.

[67] N. K. AP Dash, Rajesh Bhatia, "Dengue in South-East Asia: an appraisal of case management and vector control," *Dengue Bull.*, vol. 36, pp. 1–13, 2012.

[68] N. S. Organization, "The Survey of Travelling in Thai People, 2013," Bangkok, Thailand, 2013.

[69] National Statistical Office, "Tourist Survey Statistic," *National Statistical Office*, 2012. [Online]. Available: http://service.nso.go.th/nso/web/statseries/statseries23.html. [Accessed: 03-Apr-2018].