

## Simulations on a Mathematical Model of Dengue Fever with a Focus on Mobility

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**ABSTRACT.** Dengue fever is a major public health threat, especially for countries in tropical climates. In order to investigate the spread of dengue fever in neighboring communities, an ordinary differential equation model is formulated based on two previous models of vector-borne diseases, one that specifically describes dengue fever transmission and another that incorporates movement of populations when describing malaria transmission. The resulting SIR/SI model is used to simulate transmission of dengue fever in neighboring communities of differing population size with particular focus on cities in Sri Lanka. Models representing connections between two communities and among three communities are investigated. Initial infection details and relative population size may affect the dynamics of disease spread. An outbreak in a highly populated area may spread somewhat more rapidly through that area as well as neighboring communities than an outbreak beginning in a nearby rural area.

### 1. Introduction

Dengue fever is a major public health threat to various countries and is difficult to prevent or control (Sirisena and Noordeen, 2014). More than 2.5 billion people living in temperate or tropical climates are at risk for dengue fever. Specific therapy treatments or effective intervention techniques have not yet been developed to fully control the virus (Laughlin et al., 2012), and the progression of more severe forms of the disease is only partially understood (Monath, 1994). Dengue fever research is imperative for public health officials around the world to better understand the virus dynamics and reduce the number of infections.

Dengue fever and dengue hemorrhagic fever belong to a group of four viruses (DEN-1, DEN-2, DEN-3, and DEN-4). Being infected by one of the virus serotypes does not mean that the infected person is immune from the other strains (Gubler and Clark, 1995; Gubler et al., 2014). The four serotypes spread and develop at different rates, which influences how quickly they cause more serious conditions (Balmaseda et al., 2006). Symptoms of dengue fever include a high fever, severe headache, severe eye pain behind the eyes, muscle and/or bone pain, rash, mild bleeding manifestation, and/or low white cell count (CDC, 2012). If not treated, the serotypes can develop into more serious forms of the disease called dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Individuals who contract a second serotype of the disease also have an increased risk of developing DHF/ DSS. Because of its severity and the significant increase of DHF reported cases in the 1980s and 1990s (Gubler, 1998), DHF is a major concern of countries with tropical climates (Monath, 1994). The virus is transmitted through the mosquitoes *Aedes aegypti* and *Aedes albopictus*, which grow and thrive in warm climates. Recent trends of urbanization and globalization have also increased the populations of these mosquitoes and the prevalence of the disease (Gubler and

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Clark, 1995; Gubler et al., 2014). The mosquitoes that transmit dengue viruses bite during the day (unlike malaria transmitting mosquitoes), which make interventions like barrier nets ineffective for reducing dengue infection. Vaccines for dengue fever have not been widely distributed, but one quadrivalent vaccine has been administered in a few countries (Maron, 2015). Additionally, the lack of antiviral drugs and effective vaccines make controlling dengue transmission difficult, and countries such as Sri Lanka currently face a much higher health threat from dengue fever than from malaria (Sirisena and Noordeen, 2014). Repellents can be used to prevent the contraction of dengue fever and may be an appropriate strategy for combating the disease (Dorsett et al., 2016).

Malaria has been shown to persist in urban areas due to human transportation to rural areas with higher malaria prevalence. This persistence suggests that control methods against vector-borne diseases should specifically consider mobile populations (Osorio et al., 2004), and risk factors for dengue may vary greatly in similar environmental areas (Van Benthem et al., 2005; Vanwambeke et al., 2006). Dengue fever was originally more prevalent in densely-populated areas, but the disease appears to have spread to rural areas in some countries (Sirisena and Noordeen, 2014). Understanding how vector-borne diseases are transmitted in a mobile population could lead to more effective interventions and hence better control of these diseases.

Changes in populations and the transmission of a disease within each population can be described using ordinary differential equation (o.d.e.) models. The original model of mosquito-borne diseases, the Ross-MacDonald model, used rates of change to describe populations of humans and mosquitoes becoming infected with malaria (Macdonald, 1957) and many subsequent models of vector-borne diseases use similar equations and assumptions (Reiner et al., 2013). The basic Ross-MacDonald model included a differential equation describing the rate of change for infected humans and one for the rate of change of infected vectors, and the overall populations remained fixed. Many vector-borne o.d.e. models use similar structures based on populations of susceptible (S) and infected (I) populations (Aneke, 2002; Rodríguez and Torres-Sorando, 2001; Torres-Sorando and Rodríguez, 1997), sometimes including additional categories for humans such as recovered or removed (R) (Esteva and Vargas, 1998), exposed or incubating (E), or both (Aron and May, 1982; Pinho et al., 2010). Other models also incorporate time delay (Aron and May, 1982) (Wei et al., 2008). Additional models have focused on movement of humans to different geographic areas (Auger et al., 2008; Rodríguez and Torres-Sorando, 2001; Torres-Sorando and Rodríguez, 1997) or incorporated discrete or probabilistic modeling techniques (Lloyd et al., 2007; MacDonald et al., 1968; Yokley et al., 2014).

Dengue fever models have been constructed to specifically involve interaction of the different serotypes (Esteva and Vargas, 2003; Feng and Velasco-Hernández, 1997) and various incubation and infection periods (Chowell et al., 2007). Other models have focused on the geographic movement of dengue using partial differential equations to describe the changes of populations as functions of time and space (Maidana and Yang, 2008) or using a discrete-time model (Nevai and Soewono, 2014). Using spatially-separated populations has more commonly been used in malaria modeling (Auger et al., 2008; Rodríguez and Torres-Sorando, 2001; Torres-Sorando and Rodríguez, 1997), and the current study will use similarly structured o.d.e. models.

The current study develops and investigates a mathematical model of dengue fever transmission in populations divided into patches. The developed model combines aspects of an existing model of dengue fever (Esteva and Vargas, 1998) with the structure representing the movement of populations from a previous malaria model (Torres-Sorando and Rodríguez, 1997). After the new model structure is established and appropriate parameters are identified, various scenarios are simulated in order to see how movement between populations affects dengue transmission. The current study

aims to simulate the effects of transportation of individuals between rural and urban settings, possibly related to employment or education. Therefore, the “visitation” model from (Torres-Sorando and Rodriguez, 1997) was used as a basis for the movement of individuals as opposed to other vector transmission models incorporating more generalized migration (Auger et al., 2008; Rodríguez and Torres-Sorando, 2001; Torres-Sorando and Rodriguez, 1997). Additionally, time was modeled continuously in the current study, which differentiates the current work from the model in (Nevai and Soewono, 2014).

## 2. Model Background

Since dengue is typically transmitted during the day, many who contract the disease do so while in their work or school setting. The transmission of dengue fever is highly affected by the mobility of individuals during the vulnerable hours of the day when the mosquitoes are biting. The objectives of the current study are to construct a model that incorporates movement of individuals in related communities and to use simulations to determine how dengue fever may spread from one of these locations to another. In order to model dengue fever transmission among separate but interacting populations, a model is developed by using the dengue fever model from (Esteva and Vargas, 1998) merged with the “visitation” concepts from the malaria model in (Torres-Sorando and Rodriguez, 1997). The model in (Esteva and Vargas, 1998) was chosen to be the starting point for the model development in this study in part for its SIR/SI structure (see Section 2.1), and interactions between communities could then be incorporated into the dengue fever model using a fractional visitation time (see Section 2.2).

### 2.1. Dengue SIR/SI Model

Esteva and Vargas (1998) developed a model of humans and mosquitoes contracting dengue fever, and assumptions used in the model include constant human population size and infection by only one serotype. The model from Esteva and Vargas (1998) is presented in equations (2.1)-(2.5).

$$\frac{dS_h(t)}{dt} = \mu_h N_h - \frac{\beta_h b}{N_h + m} S_h(t) I_v(t) - \mu_h S_h(t) \quad (2.1)$$

$$\frac{dI_h(t)}{dt} = \frac{\beta_h b}{N_h + m} S_h(t) I_v(t) - (\mu_h + \gamma_h) I_h(t) \quad (2.2)$$

$$\frac{dR_h(t)}{dt} = \gamma_h I_h(t) - \mu_h R_h(t) \quad (2.3)$$

$$\frac{dS_v(t)}{dt} = A - \frac{\beta_v b}{N_h + m} S_v(t) I_h(t) - \mu_v S_v(t) \quad (2.4)$$

$$\frac{dI_v(t)}{dt} = \frac{\beta_v b}{N_h + m} S_v(t) I_h(t) - \mu_v I_v(t) \quad (2.5)$$

$N_h$  and  $N_v$  represent the human and vector population sizes,  $\mu_h$  represents the per capita birth and death rate assuming a constant population,  $\mu_v$  is a per capita mortality rate of the mosquitoes,  $\gamma_h$  is a constant recovery rate for the humans,  $A$  is a constant recruitment rate,  $b$  is the average number of bites per mosquito per day,  $\beta_h$  is the probability that the disease is transmitted from vector to human,  $\beta_v$  is the transmission probability from human to mosquito, and  $m$  is the number of alternative hosts available for mosquitoes to bite (Esteva and Vargas, 1998).

Overall, equations (2.1)-(2.5) describe the dynamics between susceptible humans ( $S_h$ ) and mosquitoes ( $S_v$ ), infected humans ( $I_h$ ) and mosquitoes ( $I_v$ ), and recovered humans ( $R_h$ ) for a one serotype infection in a fixed population. The number of infected individuals is multiplied by the bite rate, the appropriate transition rate, and the proportion of potential hosts that are human to represent the movement from a susceptible class into an infected one. Susceptible vectors are added through a constant recruitment rate,  $A$ , and both susceptible and infected mosquitoes are modeled to die and leave the system at the same rate. Death due to dengue fever is not incorporated.

## 2.2. A Malaria Model Incorporating Mobility

Spatial and temporal factors have been previously incorporated into malaria models (Auger et al., 2008; Rodríguez and Torres-Sorando, 2001; Torres-Sorando and Rodriguez, 1997). In (Torres-Sorando and Rodriguez, 1997), two frameworks were considered to describe movement of individuals, denoted as “visitation” and “migration” models. Although the models in (Torres-Sorando and Rodriguez, 1997) describe malaria transmission, both malaria and dengue fever share similar transmission patterns based on climate and parasite-host interactions. Torres-Sorando and Rodriguez (1997) developed their models to focus on the connection between regions (which can be thought of as patches or locations on a grid) and how long humans travel to those patches in two different ways. The “migration” model assumes that individuals leave their patch and do not return. Alternatively, the “visitation” model allows individuals to travel to another patch for a certain time period,  $T$ , and then return to their patch of origin within a day. Hence, the “visitation” model provides a more appropriate framework for characterizing mosquito/human interaction when the humans are traveling for portions of each day, such as commuting to school or work. The equations of the “visitation” model from (Torres-Sorando and Rodriguez, 1997) are presented in equations (2.6)-(2.9).

$$\frac{dX_1(t)}{dt} = \beta Y_1(t) \left( \frac{N}{a} - X_1(t) \right) - \gamma X_1(t) + \beta T \left( \frac{N}{a} - X_1(t) \right) Y_2(t) \quad (2.6)$$

$$\frac{dY_1(t)}{dt} = \beta (X_1(t) + T X_2(t)) \left( \frac{M}{a} - Y_1(t) \right) - \mu Y_1(t) \quad (2.7)$$

$$\frac{dX_2(t)}{dt} = \beta Y_2(t) \left( \frac{N}{a} - X_2(t) \right) - \gamma X_2(t) + \beta T \left( \frac{N}{a} - X_2(t) \right) Y_1(t) \quad (2.8)$$

$$\frac{dY_2(t)}{dt} = \beta (X_2(t) + T X_1(t)) \left( \frac{M}{a} - Y_2(t) \right) - \mu Y_2(t) \quad (2.9)$$

$\beta$  represents the biting rate,  $N$  and  $M$  are the population sizes of the humans and mosquitoes respectively,  $\gamma$  is the per capita rate of recovery in humans,  $\mu$  is the per capita rate of mortality in mosquitoes,  $X_i(t)$  denotes the number of infected humans in patch  $i$  at time  $t$ , and  $Y_i(t)$  is the number of infected mosquitoes in patch  $i$  at time  $t$ .  $T$  represents the time period for which the humans leave their home patch and visit a neighboring patch, and two patches ( $i = 1, 2$ ) are modeled. If individuals are infected in one patch, the individuals and mosquitoes from the other patch become infected once interaction occurs between the two patches. The structure of equations (2.6)-(2.9) is similar to those presented in Section 2.1 but equations (2.6)-(2.9) only incorporate human hosts.

### 3. Developing a Dengue SIR/SI Model Connecting Related Populations

As in the previous study in (Esteva and Vargas, 1998), the human population was assumed to remain constant. The model also only represents infection with a single serotype. The two models were merged using the majority of the structure from the model in Section 2.1 and the visitation aspects of the model described in Section 2.2. A few modifications related to parameters were also made to more fully integrate the two models, and those parameters are discussed following the model equations.

#### 3.1. The SIR/SI Model

The resulting system of equations representing the three patch system is presented below.

$$\begin{aligned} \frac{dS_{h1}(t)}{dt} = & \mu_h N_{h1} - \frac{\beta_h b}{N_{h1}^* + m} (T_{11} S_{h1}(t) I_{v1}(t)) - \frac{\beta_h b}{N_{h2}^* + m} (T_{12} S_{h1}(t) I_{v2}(t)) \dots \quad (3.1) \\ & - \frac{\beta_h b}{N_{h3}^* + m} (T_{13} S_{h1}(t) I_{v3}(t)) - \mu_h S_{h1}(t) \end{aligned}$$

$$\begin{aligned} \frac{dS_{h2}(t)}{dt} = & \mu_h N_{h2} - \frac{\beta_h b}{N_{h2}^* + m} (T_{22} S_{h2}(t) I_{v2}(t)) - \frac{\beta_h b}{N_{h1}^* + m} (T_{21} S_{h2}(t) I_{v1}(t)) \dots \quad (3.2) \\ & - \frac{\beta_h b}{N_{h3}^* + m} (T_{23} S_{h2}(t) I_{v3}(t)) - \mu_h S_{h2}(t) \end{aligned}$$

$$\begin{aligned} \frac{dS_{h3}(t)}{dt} = & \mu_h N_{h3} - \frac{\beta_h b}{N_{h3}^* + m} (T_{33} S_{h3}(t) I_{v3}(t)) - \frac{\beta_h b}{N_{h1}^* + m} (T_{31} S_{h3}(t) I_{v1}(t)) \dots \quad (3.3) \\ & - \frac{\beta_h b}{N_{h2}^* + m} (T_{32} S_{h3}(t) I_{v2}(t)) - \mu_h S_{h3}(t) \end{aligned}$$

$$\begin{aligned} \frac{dI_{h1}(t)}{dt} = & \frac{\beta_h b}{N_{h1}^* + m} (T_{11} S_{h1}(t) I_{v1}(t)) + \frac{\beta_h b}{N_{h2}^* + m} (T_{12} S_{h1}(t) I_{v2}(t)) \dots \quad (3.4) \\ & + \frac{\beta_h b}{N_{h3}^* + m} (T_{13} S_{h1}(t) I_{v3}(t)) - (\mu_h + \gamma_h) I_{h1}(t) \end{aligned}$$

$$\begin{aligned} \frac{dI_{h2}(t)}{dt} = & \frac{\beta_h b}{N_{h2}^* + m} (T_{22} S_{h2}(t) I_{v2}(t)) + \frac{\beta_h b}{N_{h1}^* + m} (T_{21} S_{h2}(t) I_{v1}(t)) \dots \quad (3.5) \\ & + \frac{\beta_h b}{N_{h3}^* + m} (T_{23} S_{h2}(t) I_{v3}(t)) - (\mu_h + \gamma_h) I_{h2}(t) \end{aligned}$$

$$\begin{aligned} \frac{dI_{h3}(t)}{dt} = & \frac{\beta_h b}{N_{h3}^* + m} (T_{33} S_{h3}(t) I_{v3}(t)) + \frac{\beta_h b}{N_{h1}^* + m} (T_{31} S_{h3}(t) I_{v1}(t)) \dots \quad (3.6) \\ & + \frac{\beta_h b}{N_{h2}^* + m} (T_{32} S_{h3}(t) I_{v2}(t)) - (\mu_h + \gamma_h) I_{h3}(t) \end{aligned}$$

$$\frac{dR_{h1}(t)}{dt} = \gamma_h I_{h1}(t) - \mu_h R_{h1}(t) \quad (3.7)$$

$$\frac{dR_{h2}(t)}{dt} = \gamma_h I_{h2}(t) - \mu_h R_{h2}(t) \quad (3.8)$$

$$\frac{dR_{h3}(t)}{dt} = \gamma_h I_{h3}(t) - \mu_h R_{h3}(t) \quad (3.9)$$

$$\frac{dS_{v1}(t)}{dt} = A_1 - \frac{\beta_v b}{N_{h1}^* + m} (T_{11}S_{v1}(t)I_{h1}(t) + T_{21}S_{v1}(t)I_{h2}(t) + T_{31}S_{v1}(t)I_{h3}(t)) - \mu_v S_{v1}(t) \quad .(3.10)$$

$$\frac{dS_{v2}(t)}{dt} = A_2 - \frac{\beta_v b}{N_{h2}^* + m} (T_{22}S_{v2}(t)I_{h2}(t) + T_{12}S_{v2}(t)I_{h1}(t) + T_{32}S_{v2}(t)I_{h3}(t)) - \mu_v S_{v2}(t) \quad .(3.11)$$

$$\frac{dS_{v3}(t)}{dt} = A_3 - \frac{\beta_v b}{N_{h3}^* + m} (T_{33}S_{v3}(t)I_{h3}(t) + T_{13}S_{v3}(t)I_{h1}(t) + T_{23}S_{v3}(t)I_{h2}(t)) - \mu_v S_{v3}(t) \quad .(3.12)$$

$$\frac{dI_{v1}(t)}{dt} = \frac{\beta_v b}{N_{h1}^* + m} (T_{11}S_{v1}(t)I_{h1}(t) + T_{21}S_{v1}(t)I_{h2}(t) + T_{31}S_{v1}(t)I_{h3}(t)) - \mu_v I_{v1}(t) \quad \dots \quad (3.13)$$

$$\frac{dI_{v2}(t)}{dt} = \frac{\beta_v b}{N_{h2}^* + m} (T_{22}S_{v2}(t)I_{h2}(t) + T_{12}S_{v2}(t)I_{h1}(t) + T_{32}S_{v2}(t)I_{h3}(t)) - \mu_v I_{v2}(t) \quad \dots \quad (3.14)$$

$$\frac{dI_{v3}(t)}{dt} = \frac{\beta_v b}{N_{h3}^* + m} (T_{33}S_{v3}(t)I_{h3}(t) + T_{13}S_{v3}(t)I_{h1}(t) + T_{23}S_{v3}(t)I_{h2}(t)) - \mu_v I_{v3}(t) \quad \dots \quad (3.15)$$

$N_{hi}$  and  $N_{vi}$  represent the human and vector population sizes in patch  $i$  and  $N_h$  is the total human population size.  $\mu_h$  represents the per capita birth and death rate assuming a constant population,  $\mu_v$  is a per capita mortality rate of the mosquitoes,  $\gamma_h$  is a constant recovery rate for the humans,  $b$  is the average number of bites per mosquito per day,  $\beta_h$  is the probability that the disease is transmitted from vector to human,  $\beta_v$  is the transmission probability from human to mosquito, and  $m$  is the number of alternative hosts available for mosquitoes to bite per patch (Esteva and Vargas, 1998).

If  $T$  and  $A$  were fixed at the same value in all patches, each patch would have similar vector and traveling dynamics. In order to fully simulate communities having various vector population sizes and having differing numbers of humans leaving their home patch during the day,  $T$  and  $A$  should be specific for each patch.  $T_{ij}$  represents the fraction of the day that humans living in patch  $i$  spend visiting a different patch,  $j$ , during the day while interacting with mosquitoes in patch  $j$ . In order for a human to be in one patch at a time, the following equation must hold:

$$T_{ii} = \left( 1 - \sum_j T_{ij} \right).$$

Similarly,  $A_i$  denotes the constant recruitment rate for mosquitoes in patch  $i$ .

The number of humans within a patch at a particular time is different than the population that considers each patch ‘‘home.’’ Hence, the population present must be considered when accounting for the number of available hosts. The number of persons in a particular patch was calculated

$$N_{hj}^* = \sum_i T_{ij} N_{hi} \quad .$$

TABLE 3.1. Parameter values used in equations (3.1)-(3.16).

Parameter	Symbol	Value	Source
Per capita human birth and death rate	$\mu_h$	0.0000457	(Esteva and Vargas, 1998)
Per capita mortality rate in mosquitoes	$\mu_v$	0.25	(Esteva and Vargas, 1998)
Average number of bites per mosquito per day	$b$	0.5	(Esteva and Vargas, 1998)
Transmission probability from vector to human	$\beta_h$	0.75	(Esteva and Vargas, 1998)
Transmission probability from human to vector	$\beta_v$	1	(Esteva and Vargas, 1998)
Number of alternative hosts available per patch	$m$	0	(Esteva and Vargas, 1998)
Human recovery rate	$\gamma_h$	0.1428	(Esteva and Vargas, 1998)
Recruitment rate for patch $i$	$A_i$	$\frac{1}{3}N_{vi}$	(Soewono and Supriatna, 2001)

Because the  $T_{ij}$  values are fractions of the day and the model is based on average populations based on these fractions, the above calculation was assumed to represent the number of humans present for each patch.

### 3.2. Parameter Values

Fixed parameter values used in equations (3.1)-(3.16) are presented in Table 3.1. The number of humans in each patch,  $N_{hi}$ , were set to represent actual communities in Sri Lanka. Patch 1 will represent Colombo ( $N_{h1} = 325000$ ), patch 2 will represent Sri Jayawardenepura Kotte ( $N_{h2} = 110000$ ), and patch 3 will represent Peliyagoda ( $N_{h3} = 32000$ ). As will be discussed more fully in Section 4, values for  $T_{ij}$  were based on generalized amounts of time spent working.

The mosquito (or vector) population,  $N_{vi}$ , was assumed to be twice the human population within each patch, i.e.,  $2N_{hi} = N_{vi}$ . The proportion of mosquitoes to humans has varied in modeling with *Aedes aegypti*, including ratios close to 4 to 1 (Hughes and Britton, 2013) to close to 2 to 1 (Kuniyoshi and dos Santos, 2017).

## 4. Simulated Outbreak

In order to simulate potential outbreaks in actual settings, population sizes were incorporated representing two cities and one town in Sri Lanka. As mentioned in Section 3.2, the city of Colombo has a population of about 325,000 (worldatlas.com, 2015a), and Sri Jayawardenepura Kotte has a population size of about 110,000 (worldatlas.com, 2015b). The nearby town of Peliyagoda has a population of about 32,000 (Time.is, 2016).

In order to more accurately portray the dynamics of humans traveling in Sri Lanka, the  $T_{ij}$  values (visitation values) were estimated using information about the country and the three communities. However, the visitation parameter is a value representing how much a fraction of the day in general would be spent in another patch and would not necessarily represent every individual specifically. Hence, the values for  $T_{ij}$  were calculated incorporating the fact that not every individual will travel for work and considering the parameter as representing the portion of time the collective individuals of the patch population spent working in other areas. A little less than half of Sri Lanka's population is eligible to be in the workforce (Department of Census and Statistics Sri Lanka, 2001), and the Shop and Office Employees Act of 1954 in Sri Lanka states that workers may not work

TABLE 4.1. Visitation parameter values,  $T_{ij}$  associated with simulations in Section 4. The values are also used in generating Figures 4.1-4.4.

		$j$ TO		
		Colombo (Patch 1)	Sri Jayawardenepura Kotte (Patch 2)	Peliyagoda (Patch 3)
$i$ FROM	Colombo (Patch 1)	1	0	0
	Sri Jayawardenepura Kotte (Patch 2)	0.05	0.95	0
	Peliyagoda (Patch 3)	0.08	0.04	0.88

more than 8 hours in a day and cannot work more than 45 hours in a week (WageIndicator, 2017). Considering holidays in addition to the limitations on work hours per week, working individuals likely spend an average 25% or less of their time at work. Colombo is the commercial capital of Sri Lanka and likely has the most influx of workers from other communities. Sri Jayawardenepura Kotte, is the legislative capital of Sri Lanka and may also be a location for outsiders to travel for work. Peliyagoda is much smaller than the other two cities; therefore, fewer individuals likely travel here for work from Colombo or Sri Jayawardenepura Kotte. Based on Sri Lanka labor information and the respective sizes of the three communities, the following assumptions were used when setting the visitation times:

- 12% of the time of the population of Peliyagoda is assumed to be spent in Colombo (8%) and in Sri Jayawardenepura Kotte (4%).
- 5% of the time of the population of Sri Jayawardenepura Kotte is spent in Colombo, and the population of Sri Jayawardenepura Kotte. is assumed to spend a negligible percentage of time in Peliyagoda.
- People in Colombo are assumed to stay in Colombo.

The specific resulting values for  $T_{ij}$  are listed in Table 4.1.

Model simulations were generated representing an outbreak caused by a single infected individual in an otherwise unaffected community. Simulations were performed using Wolfram *Mathematica*<sup>®</sup>, version 11.1. Figures 4.1, 4.2, and 4.3 present simulation results when an outbreak begins in Colombo, Sri Jayawardenepura Kotte, and Peliyagoda (respectively). Figures 4.4-4.7 present overlapping simulation results when an outbreak begins in each of the patches. The proportion of the populations infected is similar for all communities. The peak of infections occurs earliest (although slightly) in the patch of the outbreak in each of the three cases. For example, when the outbreak begins in the smallest population (Peliyagoda), the delay is largest between the peak of infection in Peliyagoda to the peak of infection in Colombo.

## 5. Reproduction Number

The basic reproduction number,  $R_0$  was calculated using the method from Van den Driessche and Watmough (2002) and outlined in Browne et al. (2014). Because of the many parameters, specific parameter values were used in generating  $R_0$ . Parameter values and population numbers presented in Section 3.2 and  $T_{ij}$  values from Table 4.1 were used to calculate  $R_0$ . The resulting



## Proportion Infected

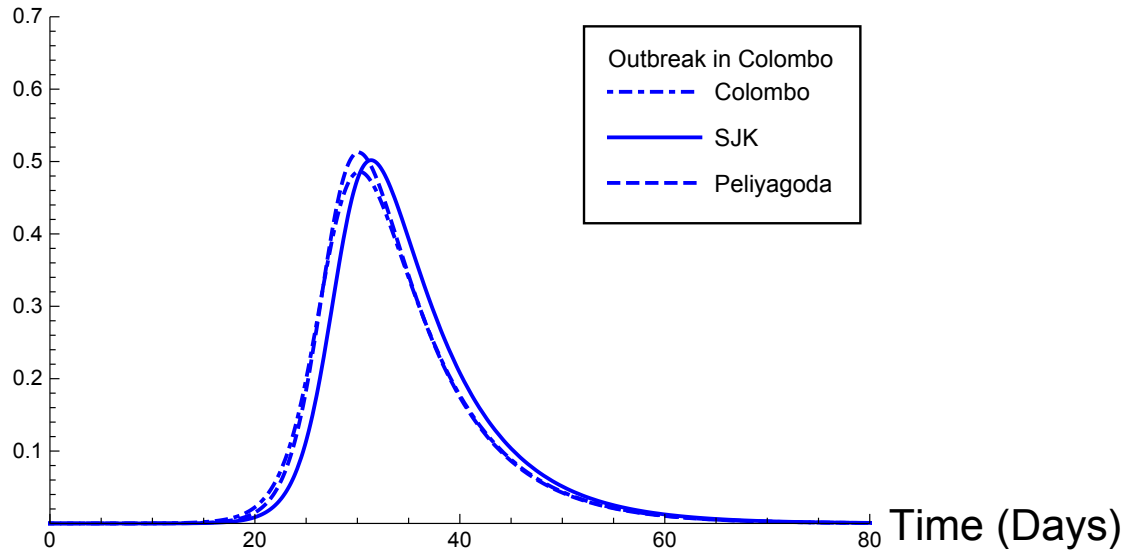


FIGURE 4.1. **Outbreak in Colombo.** Colombo (Patch One) has a population of 325,000, Sri Jayawardenepura Kotte (Patch Two) has a population of 110,000, and Peliyagoda (Patch Three) has a population of 32,000. The initial conditions were  $S_{h1}(0) = N_{h1} - 1$ ,  $S_{h2}(0) = N_{h2}$ ,  $S_{h3}(0) = N_{h3}$ ,  $I_{h1}(0) = 1$ ,  $I_{h2}(0) = 0$ ,  $I_{h3}(0) = 0$ ,  $R_{h1}(0) = 0$ ,  $R_{h2}(0) = 0$ ,  $R_{h3}(0) = 0$ ,  $S_{v1}(0) = 2N_{v1}$ ,  $S_{v2}(0) = 2N_{v2}$ ,  $S_{v3}(0) = 2N_{v3}$ ,  $I_{v1}(0) = 0$ ,  $I_{v2}(0) = 0$ ,  $I_{v3}(0) = 0$ . The simulation was run over a period of 200 days.

value, 3.29, was consistent with previously determined dengue fever values in various areas of the world Chowell et al. (2007) Hsieh and Ma (2009) Marques et al. (1994).

## 6. Discussion and Conclusions

The dynamics of the spread of dengue can be investigated when humans travel to other communities by modeling a portion of the individual's day spent elsewhere. Population size and conditions related to the initial outbreak can affect the timing of the peak of infection although proportions of communities infected appear to be similar regardless of the location of the initial outbreak. Simulation results suggest that an outbreak in a rural area can lead to significant infections in neighboring, more densely populated areas.

Different prevention methods may be more effective based on the type of community. For example, an intervention of one kind may work better in an urban setting than in a rural one. Because transmission of dengue fever in one area is affected by actions within that region as well as actions in neighboring areas, community-specific strategies for intervention may better lower infections in multiple regions. In other words, a mixed intervention strategy may have a greater impact than a single strategy over a large region.

More sophisticated modeling related to time spent in each patch could be used to improve the model. Using fractions of populations to represent movement is a simplification, and future studies could incorporate functions of time for  $T_{ij}$  or more agent-based approaches. Environmental factors were not incorporated in the current study, but rural and urban environments may have different

## Proportion Infected

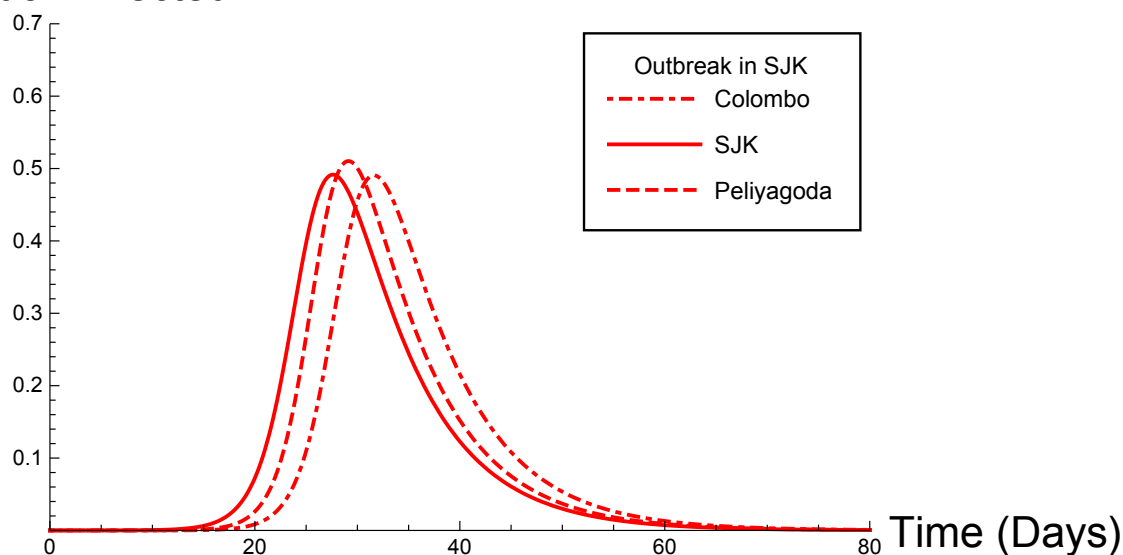


FIGURE 4.2. **Outbreak in Sri Jayawardenepura Kotte.** Colombo (Patch One) has a population of 325,000, Sri Jayawardenepura Kotte (Patch Two) has a population of 110,000, and Peliyagoda (Patch Three) has a population of 32,000. The initial conditions were  $S_{h1}(0) = N_{h1}$ ,  $S_{h2}(0) = N_{h2} - 1$ ,  $S_{h3}(0) = N_{h3}$ ,  $I_{h1}(0) = 0$ ,  $I_{h2}(0) = 1$ ,  $I_{h3}(0) = 0$ ,  $R_{h1}(0) = 0$ ,  $R_{h2}(0) = 0$ ,  $R_{h3}(0) = 0$ ,  $S_{v1}(0) = 2N_{v1}$ ,  $S_{v2}(0) = 2N_{v2}$ ,  $S_{v3}(0) = 2N_{v3}$ ,  $I_{v1}(0) = 0$ ,  $I_{v2}(0) = 0$ ,  $I_{v3}(0) = 0$ . The simulation was run over a period of 200 days.

conditions related to mosquito populations. Differences in weather conditions and mosquito habitats may affect dengue spread. Incorporation of more patch specific parameters, such as related to the recruitment rate  $A$ , could improve model predictions. Additionally, the mosquito populations may be higher per person in rural areas, which was not incorporated in the current study.

The model could additionally be improved by adding an exposed class between the susceptible and infected class because dengue does have a latency period. Conducting a stability analysis of the system of equations would also be useful in understanding the spread of the disease among patches. The work as a whole describes the dynamics in separate patches with the assumptions of fixed population sizes, uniform density, and a one serotype infection. Incorporating multiple serotype infection would more fully describe dengue transmission. The model aids in understanding the urgency needed for preventative measures in order to slow or reduce the impact of the disease on a community.

## 7. Acknowledgments

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## Proportion infected

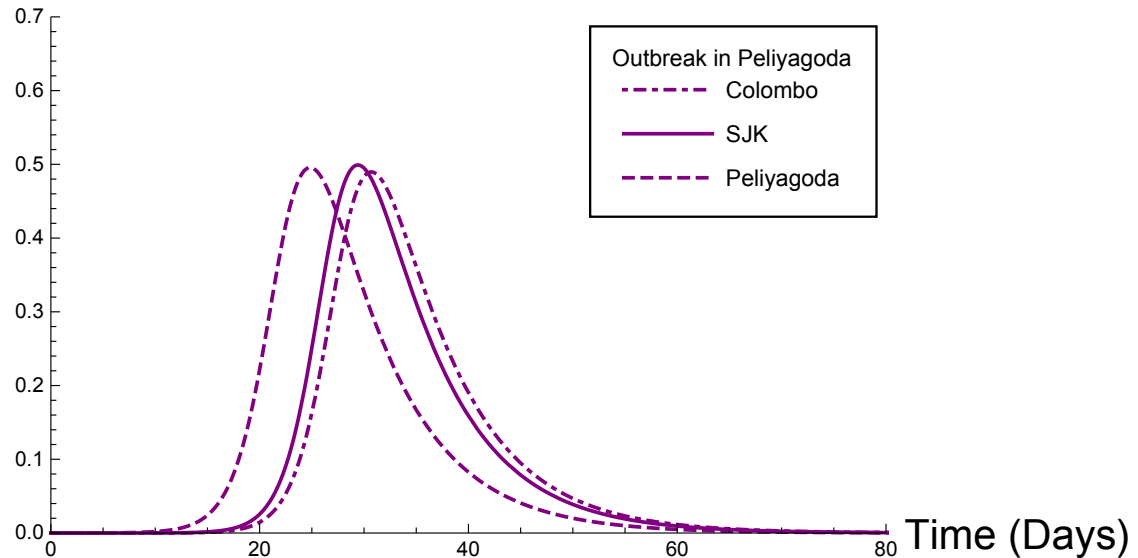


FIGURE 4.3. **Outbreak in Peliyagoda.** Colombo (Patch One) has a population of 325,000, Sri Jayawardenepura Kotte (Patch Two) has a population of 110,000, and Peliyagoda (Patch Three) has a population of 32,000. The initial conditions were  $S_{h1}(0) = N_{h1}$ ,  $S_{h2}(0) = N_{h2}$ ,  $S_{h3}(0) = N_{h3} - 1$ ,  $I_{h1}(0) = 0$ ,  $I_{h2}(0) = 0$ ,  $I_{h3}(0) = 1$ ,  $R_{h1}(0) = 0$ ,  $R_{h2}(0) = 0$ ,  $R_{h3}(0) = 0$ ,  $S_{v1}(0) = 2N_{v1}$ ,  $S_{v2}(0) = 2N_{v2}$ ,  $S_{v3}(0) = 2N_{v3}$ ,  $I_{v1}(0) = 0$ ,  $I_{v2}(0) = 0$ ,  $I_{v3}(0) = 0$ . The simulation was run over a period of 200 days.

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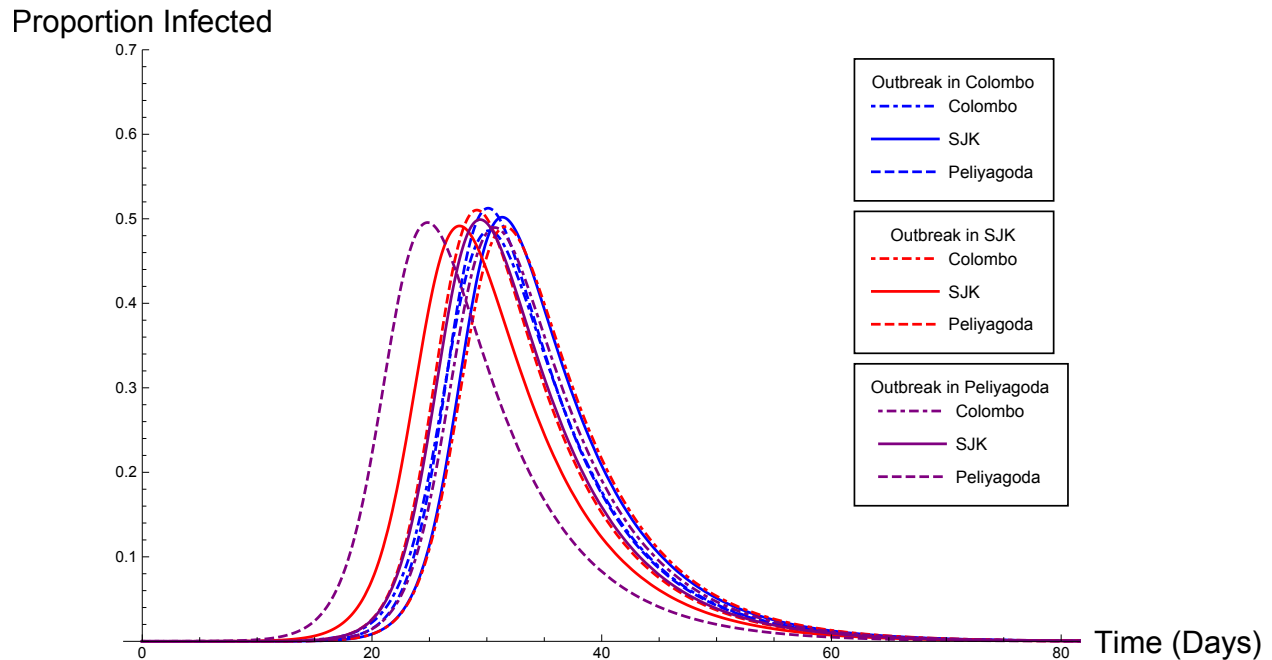


FIGURE 4.4. **Multiple Outbreaks using the Three Patch System.** Simulation results for the proportion of infected humans in each patch after an individual patch begins with one infected human. Colombo (Patch One) has a population of 325,000, Sri Jayawardenepura Kotte (Patch Two) has a population of 110,000, and Peliyagoda (Patch Three) has a population of 32,000. The initial conditions represented having one infected human in the patch of the outbreak and all other individuals being susceptible.

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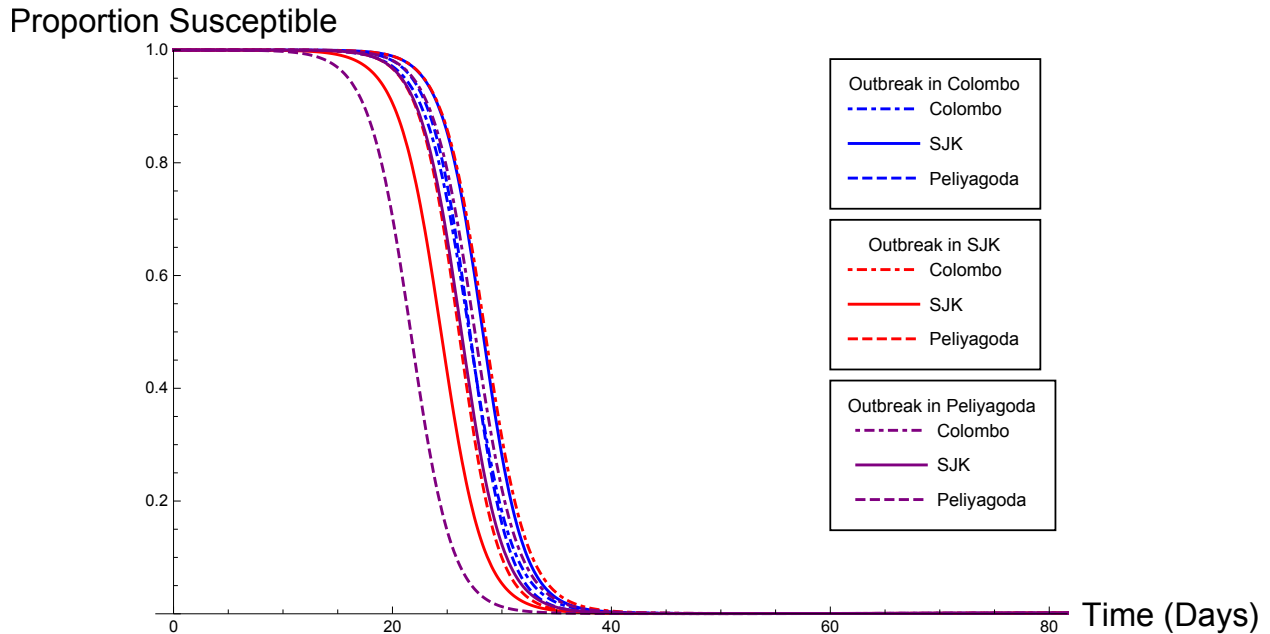


FIGURE 4.5. **Multiple Outbreaks using the Three Patch System.** Simulation results for the proportion of susceptible humans in each patch after an individual patch begins with one infected human. Colombo (Patch One) has a population of 325,000, Sri Jayawardenepura Kotte (Patch Two) has a population of 110,000, and Peliyagoda (Patch Three) has a population of 32,000. The initial conditions represented having one infected human in the patch of the outbreak and all other individuals being susceptible.

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## Susceptible Mosquitoes

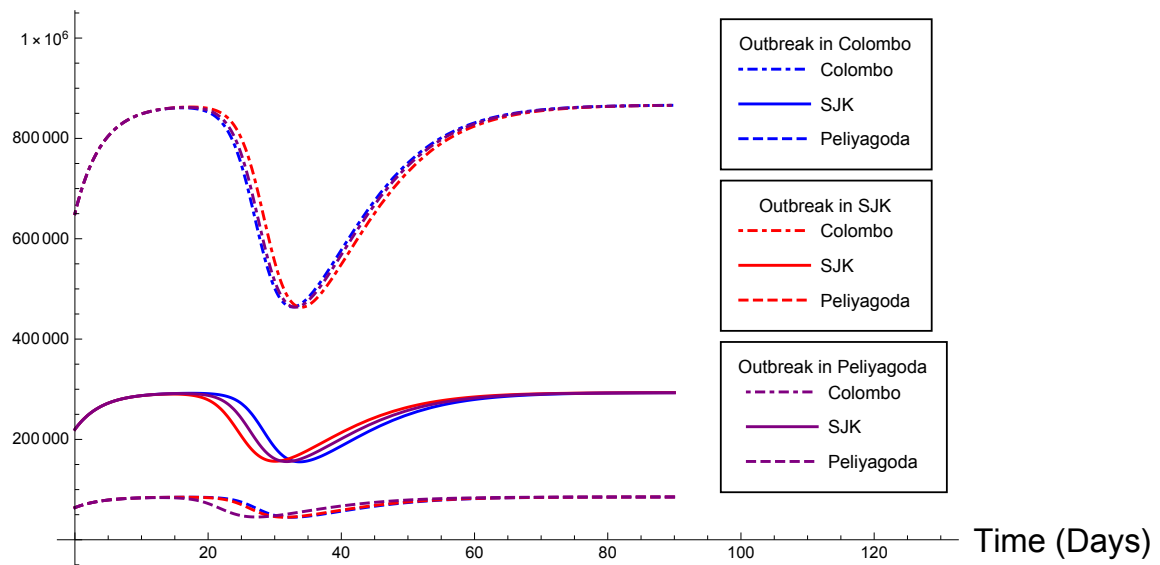


FIGURE 4.6. **Multiple Outbreaks using the Three Patch System.** Simulation results for the number of susceptible mosquitoes in each patch after an individual patch begins with one infected human. Colombo (Patch One) has a population of 325,000, Sri Jayawardenepura Kotte (Patch Two) has a population of 110,000, and Peliyagoda (Patch Three) has a population of 32,000. The initial conditions represented having one infected human in the patch of the outbreak and all other individuals being susceptible.

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## Infected Mosquitoes

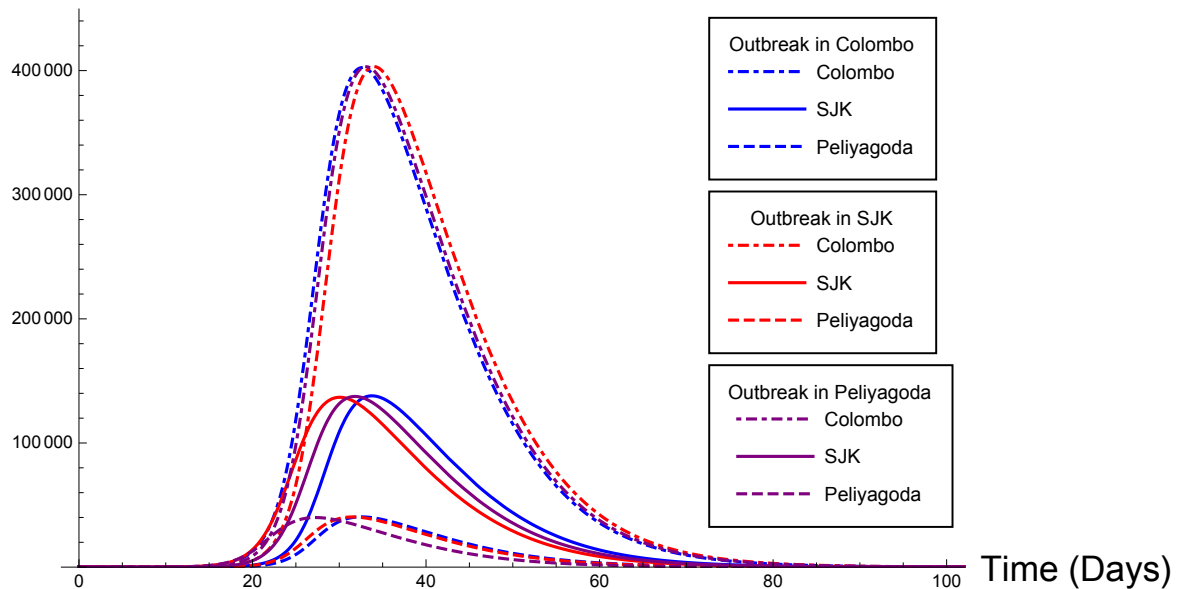


FIGURE 4.7. **Multiple Outbreaks using the Three Patch System.** Simulation results for the number of infected mosquitoes in each patch after an individual patch begins with one infected human. Colombo (Patch One) has a population of 325,000, Sri Jayawardenepura Kotte (Patch Two) has a population of 110,000, and Peliyagoda (Patch Three) has a population of 32,000. The initial conditions represented having one infected human in the patch of the outbreak and all other individuals being susceptible.

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