EUROPEAN JOURNAL OF PURE AND APPLIED MATHEMATICS
Vol. 17, No. 3, 2024, 1637-1658
ISSN 1307-5543 – ejpam.com
Published by New York Business Global

Mathematical Analysis and Numerical Simulation on Free-Living Leptospira: A Mathematical Modeling Perspective

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Abstract. A bacterial disease called leptospirosis is very typical in both tropical and subtropical regions. It is a well-known animal-borne illness that is brought on by spiral-shaped bacteria (Leptospira spp.). Both directly and indirectly, the disease can spread to humans through the urine of sick animals or polluted water, soil, or food. Two phases might appear in leptospirosis symptoms. The patient will have mild symptoms during the first phase, which is known as the Septicemic phase. In the meantime, the Immune phase, the second, is more severe. This study aimed to create a mathematical model of leptospirosis disease using free-living bacteria. In the model, interactions occur between people, free-living Leptospira, animal hosts, and animal vectors. The population's characteristics are used to build the model, and the actual issue is used to identify the disease's transmission paths. While the endemic equilibrium is investigated numerically through ODE45 solver, the disease-free equilibrium is analyzed theoretically. The paper demonstrates that for the established mathematical model with an epidemic threshold R_0, analytical and numerical solutions produced the same outcome.

2020 Mathematics Subject Classifications: 92B05, 34C11, 47H10, 00A71.

Key Words and Phrases: Mathematical Model, Leptospirosis, Free-Living Bacteria, ODE45 Solver, Environment.

1. Introduction

The Leptospira genus of spiral-shaped spirochetes is the cause of leptospirosis, a dangerous zoonotic illness that affects people worldwide. Leptospirosis is a serious zoonoses

*Corresponding author.
DOI: https://doi.org/10.29020/nybg.ejpam.v17i3.5178

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disease that affect people all over the world and is caused by spiral-shaped spirochetes belonging to the Leptospira genus. This disease spreads widely not just in tropical regions but also in subtropical regions, including Europe[9, 23], Africa [6], America [26, 31], Asia [1, 7, 29] and Australia [16, 28]. The disease is also well-known as one of the world's most typical zoonoses, with a prevalence of 1.03 million cases and 58.900 cases every year [18].

First recognized as an occupational disease, leptospirosis infected sewer workers in 1883. In 1886, German physician Adolf Weil discovered four patients with clinical manifestations of this disease, which included symptoms of severe jaundice, fever, enlarged liver, and kidney failure [27]. Subsequently, in 1987, Goldsmith named the disease Weil's disease. This disease also has other names in several countries, such as Swamp fever, Swineherd's disease, Mud fever, Redwater of Calves, Autumn fever (Akiyami), Rice-field fever, Canicola fever, Cane-cutter's fever, Hemorrhagic Jaundice, Stuttgart disease [4, 12]. Furthermore, in 1915, Inada succeeded in isolating the Leptospira icterohemorrhagiae bacterium as a cause of Weil's disease [12]. Up to now, there are 20 genus Leptospira species based on DNA hybridization studies consisting of three major, namely, pathogenic, intermediate, and saprophytic (non-pathogenic) leptospires [4, 14].

Pathogenic bacteria infect humans and animals. Rats are well-known as vector animals for this disease. Even though bacteria can infect it, rats still usually live. Almost all species of rats are a good reservoir for the spread of leptospirosis disease [2, 21]. The bacteria breed and grow well in the rat's kidney. These bacteria spread through rats' urine and then contaminate the environment. Humans and animals in contact with contaminated water, soil and mud have easily been infected by leptospirosis disease [5]. In human cases, these bacteria enter the body through mucosae such as the mouth, nose, and eye. It also enters the human body through broken skin. People who work as farmers, ranchers, gardeners, and butchers would be more susceptible to the disease [3, 15]. Some animals like cats, dogs, pigs, horses, and cows are also easily infected by the bacteria. These kinds of animals are called host animals, and the bacteria can kill them.

There are two main phases of infection in the human population. The first phase, Septicemic, occurs in 3-7 days with some symptoms like fever, rash, vomiting, muscle pain, headache, chills, and red eyes [8, 19, 24]. Some symptoms look like flu disease, such that people with these symptoms usually think that the influenza virus has infected them. It is also one reason why this disease is sometimes un-diagnosed or misdiagnosed. However, in order to know whether someone has an infection with leptospirosis or not, the patient needs to do a blood test. The second phase, Immune, occurs in 0-30 days. Some symptoms that probably appear in this phase are jaundice, acute rash, bleeding, kidney failure, heart failure, liver failure, or meningitis. In this phase, some leptospirosis patients probably will die [11, 25]. There is also interphase and defervescence, lasting 2-3 days. In this phase, someone with leptospirosis will feel better. Unfortunately, bacteria are still in their body, so after this phase, they will go to the Immune phase [20].

Some research in mathematical epidemiology has been developed to analyze the dynamics and spread of leptospirosis in a homogeneous/heterogeneous population [10, 17, 22]. Unfortunately, none of these research had considered assessing the effect of free-living leptospira in the surroundings. In the last decade, research conducted to develop mathe-

matical models of leptospirosis disease only considers the interaction between humans and animal vectors, animal hosts with animal vectors or humans with free-living leptospira alone, so this interaction model cannot describe the overall dynamics of this disease. The research gap that occurs is that a mathematical model needs to be developed that looks at all the factors that cause the spread of leptospirosis. Mathematical models of diseases that are strongly influenced by environmental factors and spread through the intermediary of several animals, both vectors and hosts and also can cause serious illness in humans, need to be constructed and analyzed so that it can be known its spread in the human population which in turn can be done effective prevention of the spread of this disease. In this paper, a framework model of leptospirosis disease with free-living bacteria in the environment is rigorously studied, which has been developed from similar research about schistosomiasis, which has been done by Garira et al. l [13].

2. Mathematical Model

The construction of a leptospirosis model in a closed population was considered a system with no seasonal effect. With regard to the characteristics of the disease, the human population at any time t was divided into susceptible human individuals S_{Hu}(t), exposed human individuals who relate to the septicemic phase E_{Hu}(t), infected human individuals who relate to the immune phase I_{Hu}(t) and recovered human individuals R_{Hu}(t). The animal population was divided into a host animal population and a vector population. Similarly with the human, the host animal population at any time t was divided into susceptible host animal individuals S_{Ho}(t), infected host animal individual I_{Ho}(t), and recovered host animal individual R_{Ho}(t), while the vector animal population at any time t was divided into susceptible vector animal individuals S_{Ho}(t) and infected vector animal individual I_{Ho}(t). Free-living leptospira at any time t is L(t).

There are three possible transmission routes for susceptible humans to become infected. They have direct interaction with free-living leptospira in the surroundings at the rate of β_{Hu1} , they have contact with infected host animals at the rate β_{Hu2} , or they have contact with infected vector animals at the rate β_{Hu3}. It was assumed that there was only one transmission route for susceptible animals to become infected. Host and vector animals have contact with free-living leptospira at the rate β_{Ho} and β_V, respectively. There are also two possibilities for the exposed human population to become infected at the rate γ_{Hu} or recover at the rate σ_{Hu}. The number of bacteria in the environment only comes from the urine of the infected population at the rate κ_{Hu},κ_{Ho}, and κ_V.

We made some assumptions to construct the model, as follows: a) each population is assumed to be closed; b) every individual in each population is blending homogeneously; c) every infected individual sheds leptospira bacteria in the environment; d) there is no recovered vector animal population; e) there is no direct transmission between host animal and vector animal; f) recovered individuals can be re-infected; and g) there is death-caused by the infection in human and host animal, whereas in vector animal population there is no death-caused by the infection.

By incorporating a few assumptions that can provide support when creating a mathe-

matical model, the spread of the illness can be illustrated in a component diagram similar to the one shown in Figure 1. With regard to the assumptions and the compartment

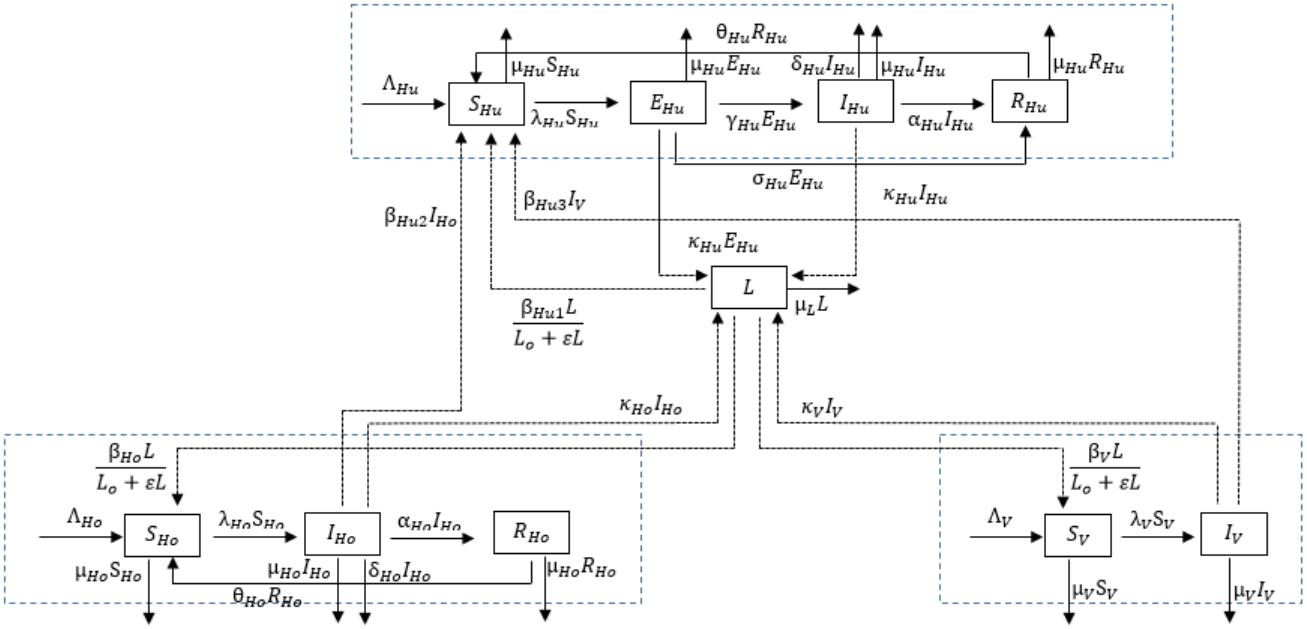

Figure 1: The route of transmission from Free-Living Leptospira into the human population, animal-host population, and animal-vector population.

diagram, the route of transmission of leptospira bacteria at time t is disempowered by the following nonlinear ordinary differential system.

Human population

$$\frac{dS_{Hu}}{dt} = \Lambda_{Hu} - (\lambda_{Hu} + \mu_{Hu})S_{Hu} + \theta_{Hu}R_{Hu}, \tag{1}$$

$$\frac{dE_{Hu}}{dt} = \lambda_{Hu}S_{Hu} - (\gamma_{Hu} + \mu_{Hu} + \sigma_{Hu})E_{Hu}, \tag{2}$$

$$\frac{dI_{Hu}}{dt} = \gamma_{Hu}E_{Hu} - (\mu_{Hu} + \delta_{Hu} + \alpha_{Hu})I_{Hu}, \tag{3}$$

$$\frac{dR_{Hu}}{dt} = \alpha_{Hu}I_{Hu} + \gamma_{Hu}E_{Hu} - (\mu_{Hu} + \theta_{Hu})R_{Hu}, \tag{4}$$

Animal-Host Population

$$\frac{dS_{Ho}}{dt} = \Lambda_{Ho} - (\lambda_{Ho} + \mu_{Ho})S_{Ho} + \theta_{Ho}R_{Ho}, \tag{5}$$

$$\frac{dI_{Ho}}{dt} = \lambda_{Ho}S_{Ho} - (\mu_{Ho} + \delta_{Ho} + \alpha_{Ho})I_{Ho}, \tag{6}$$

$$\frac{dR_{Ho}}{dt} = \alpha_{Ho} I_{Ho} - (\mu_{Ho} + \theta_{Ho}) R_{Ho}, \tag{7}$$

Animal-Vector Population

$$\frac{dS_V}{dt} = \Lambda_V - (\lambda_V + \mu_V) S_V, \tag{8}$$

$$\frac{dI_V}{dt} = \lambda_V S_V - \mu_V I_V, \tag{9}$$

Free-Living Leptospira in the environment

$$\frac{dL}{dt} = \kappa_{Hu}(E_{Hu} + I_{Hu}) + \kappa_{Ho} I_{Ho} + \kappa_V I_V - \mu_L L, \tag{10}$$

where,
$\lambda_{Hu} = (\frac{\beta_{Hu1} L}{L_0 + \in L} + \frac{\beta_{Hu2} I_{Ho}}{N_{Hu}} + \frac{\beta_{Hu3} I_V}{N_{Hu}})$,
$\lambda_{Ho} = (\frac{\beta_{Ho} L}{L_0 + \in L})$,
$\lambda_V = (\frac{\beta_V L}{L_0 + \in L})$,
All parameters for equations are assumed to be non-negative for all times t¿0 with the initial condition given by
$S_{Hu}(t_0) \geq 0, E_{Hu}(t_0) \geq 0, I_{Hu}(t_0) \geq 0, R_{Hu}(t_0) \geq 0, S_{Ho}(t_0) \geq 0, I_{Ho}(t_0) \geq 0, R_{Ho}(t_0) \geq 0, S_V(t_0) \geq 0, I_V(t_0) \geq 0, L(t_0) \geq 0$
Here, $t \geq_0$ represents the time in days and t_0 represents the beginning of the leptospirosis illness spread where each symbol can be written as follows in table 1.

Table 1: Summary of parameter's description

Parameter	**Description**
Λ_{Hu}	the rate at which the human population is being recruited
Λ_{Ho}	the rate at which animal host populations are being recruited
Λ_V	the rate at which animal vector populations are being recruited
μ_{Hu}	the rate of death in the human population
μ_{Ho}	the rate of death of animal host population
μ_V	the rate of death of animal vector population
μ_L	the rate of death of free-living leptospira in the environment
θ_{Hu}	the transmission rate of humans from the recovered population to the susceptible population
θ_{Ho}	the transmission rate of the animal host from the recovered population to the susceptible population
γ_{Hu}	the transmission rate from the septicemic phase to the immune phase
σ_{Hu}	the transmission rate of humans from the exposed population to the recovered population

Table 2: Summary of parameter's description

Parameter	**Description**
δ_{Hu}	mortality rate caused by sickness in the human population
δ_{Ho}	mortality rate caused by sickness of animal host population
α_{Hu}	the recovery rate of the human population
α_{Ho}	the recovery rate of animal host population
β_{Hu1}	the infection rate of the human population by free-living leptospires in the environment
β_{Hu2}	the infection rate of the human population by infected animal host population
β_{Hu3}	the infection rate of the human population by infected animal vector population
β_V	infection rate of animal host population by free-living leptospira in the environment
L_0	infection rate of animal vector population by free-living leptospira in the environment
ε	saturation constant of leptospires bacteria
κ_{Hu}	a reduction in the growth rate of leptospires bacteria, given the rise in cases
κ_{Ho}	the excretion rate of leptospira from the human population into the environment
κ_V	the excretion rate of leptospira from animal-host populations into the environment

3. Result and Discussion

3.1. Feasibility Region of the Equilibria of the Model

Mathematically and epidemiologically, the system is well-posed by constructed it from the real phenomenon of disease spread and the system of differential equations, meaning it is biologically meaningful when all model parameters and state variables for the model system are assumed to be non-negative and consistent with human and animal populations for all time $t \geq 0$. Additionally, it can be confirmed that for the model system, all bounded and non-negative solutions with non-negative beginning conditions continue to exist. Leptospirosis transmission dynamics model in the equations (1) - (10) shall thus be examined in a suitable, feasible area, which will be determined as follows. Letting $N_{Hu} = S_{Hu} + E_{Hu} + I_{Hu} + R_{Hu}$, and adding equations (1) - (4) in the system, it will give us.

$$\frac{dN_{Hu}}{dt} = \Lambda_{Hu} - \mu_{Hu}N_{Hu} - \delta_{Hu} \leq \Lambda_{Hu} - \mu_{Hu}N_{Hu},$$

This implies that

$$\lim_{t\to\infty} supN_{Ho} \leq \frac{\Lambda_{Ho}}{\mu_{Ho}},$$

Analogous for another two populations Letting $N_{Ho} = S_{Ho} + I_{Ho} + R_{Ho}$, and adding equations (5) - (7) in the system will give us. $\frac{dN_V}{dt} \leq \Lambda_V - \mu_V N_V$,
This implies that

$$\lim_{t\to\infty} supN_V \leq \frac{\Lambda_V}{\mu_V},$$

From equation (10), we have $\frac{dL}{dt} \leq \kappa_{Hu}(E_{Hu} + I_{Hu}) + \kappa_{Ho} I_{Ho} + \kappa_V I_V - \mu_L L$, This implies that

$$\lim_{t\to\infty} supN_V \leq \frac{\kappa_{Hu}(E_{Hu} + I_{Hu}) + \kappa_{Ho} I_{Ho} + \kappa_V I_V}{\mu_L},$$

Therefore, every possible systemic solution is positive and will eventually reach the invariant attractive area.
$\Omega = \{(S_{Hu}, E_{Hu}, I_{Hu}, R_{Hu}, S_{Ho}, I_{Ho}, R_{Ho}, S_V, I_V, L) : N_{Hu}(t) \leq \frac{\Lambda_{Hu}}{\mu_{Hu}}, N_{Ho}(t) \leq \frac{\Lambda_{Ho}}{\mu_{Ho}}, N_V(t) \leq \frac{\Lambda_V}{\mu_V}, L(t) \leq \frac{\kappa_{Hu}(E_{Hu}+I_{Hu})+\kappa_{Ho}I_{Ho}+\kappa_V I_V}{\mu_L}\}$,

Thus, whenever $\Lambda_{Hu} > \mu_{Hu}$, Ω is attractive and positively invariant, examining the system's solutions in Ω suffices. Results for the system's existence, uniqueness, and continuation hold in this area, and all solutions beginning in Ω stay there for all $t \geq 0$. Therefore, the model is well-posed both mathematically and epidemiologically. Examining the dynamics of the flow produced by the model in Ω suffices. Unless otherwise indicated, we will assume in all that follows that $\Lambda_{Hu} > \mu_{Hu}$.

3.2. Determination of disease-free equilibrium

We subsequently ascertained the solution of the system of nonlinear ordinary differential equations based on the created mathematical model (1) - (10). In order to determine this solution, the right-hand side of each equation was taken to be equal to zero. This allowed the system to admit two equilibrium states: the endemic state and the disease-free equilibrium.

$$\frac{dS_{Hu}}{dt} = \frac{dE_{Hu}}{dt} = \frac{dI_{Hu}}{dt} = \frac{dR_{Hu}}{dt} = \frac{dS_{Ho}}{dt} = \frac{dI_{Ho}}{dt} = \frac{dR_{Ho}}{dt} = \frac{dS_V}{dt} = \frac{dI_V}{dt} = \frac{dL}{dt} = 0,$$

Infection in the populations of humans, animals serving as hosts, and animal vectors occurs when there are no free-living leptospira in the environment or in a state of disease-free equilibrium. As such, the model system's disease-free equilibrium is given by
$E^0 = (\frac{\Lambda_{Hu}}{\mu_{Hu}}, 0, 0, 0, \frac{\Lambda_{Ho}}{\mu_{Ho}}, 0, 0, \frac{\Lambda_V}{\mu_V}, 0, 0)$

3.3. Calculation of the Reproduction Number

The basic reproduction number, or R_0, is the most intriguing quantity in many epidemic models that highlights the key players in the disease transmission cycle. Its definition is the mean quantity of secondary infections caused by a single infectious host that is

introduced into a population that is completely susceptible. A basic reproduction number is one of the most crucial tools for evaluating disease outbreaks. For the majority of illness outbreaks, if $R_0 < 1$, then with time, the outbreak will end, whereas if $R_0 > 1$, then The epidemic will continue at endemic proportions.

The basic reproduction number has been obtained using the operator approach of the next-generation matrix. The form can be used to write a model system.

$$\frac{dX}{dt} = f(X, Y, Z),$$
$$\frac{dY}{dt} = g(X, Y, Z),$$
$$\frac{dZ}{dt} = h(X, Y, Z),$$

where
$X = (S_{Hu}, R_{Hu}, S_{Ho}, R_{Ho}, S_V)$,
$Y = (E_{Hu}, I_{Hu})$,
$Z = (I_{Ho}, I_V, L)$,
Component X represents the quantity of vulnerable, while component Y represents the quantity of those with the infection who do not spread the illness. The component of Z represents the number of people that are able to spread the illness.
Define $\widetilde{g}(X^*, \mathrm{Z})$ by

$\widetilde{g}(X^*, \mathrm{Z}) = \widetilde{g_1}(X^*, \mathrm{Z}), \widetilde{g_2}(X^*, \mathrm{Z})$ with

$\widetilde{g_1}(X^*, \mathrm{Z}) = (\frac{\beta_{Hu1}L}{L_o+\epsilon L} + \frac{\beta_{Hu2}L_{Ho}}{N_{Hu}} + \frac{\beta_{Hu3}I_V}{N_{Hu}}) \frac{\Lambda_{Hu}}{\mu_{Hu}} \frac{1}{\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu}}$,

$\widetilde{g_2}(X^*, \mathrm{Z}) = \frac{\gamma_{Hu}}{\mu_{Hu}+\delta_{Hu}+\alpha_{Hu}} (\frac{\beta_{Hu1}L}{L_o+\epsilon L} + \frac{\beta_{Hu1}L_{Ho}}{L_o+\epsilon L} + \frac{\beta_{Hu2}I_{Ho}}{N_{Hu}} + \frac{\beta_{Hu3}I_V}{N_{Hu}}) \frac{\Lambda_{Hu}}{\mu_{Hu}} \frac{1}{\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu}}$,

Let $A = D_z\mathrm{h}(X^*, \widetilde{g}(X^*,0), 0)$ and further presume that A can be expressed as follows: A = M - D where $\mathrm{M} \geq 0$ and $\mathrm{D} > 0$, a diagonal matrix. Next, A turns into

$\frac{dI_{Ho}}{dt} = (\frac{\beta_{Ho}L}{L_0+\epsilon L}).\frac{\Lambda_{Ho}}{\mu_{Ho}}$ - $(\mu_{Ho} + \delta_{Ho} + \alpha_{Ho})I_{Ho}$,

$\frac{dI_V}{dt} = (\frac{\beta_V L}{L_0+\epsilon L}).\frac{\Lambda}{\mu}$ - $\mu_V I_V$,

$\frac{dL}{dt} = \kappa_{Hu}((\frac{\beta_{Hu1}L}{L_0+\epsilon L} + \frac{\beta_{Hu2}I_{Ho}}{N_{Hu}} + \frac{\beta_{Hu3}I_V}{N_{Hu}}).\frac{\Lambda_{Hu}}{\mu_{Hu}}.\frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})}(\frac{\beta_{Hu1}L}{L_0+\epsilon L} + \frac{\beta_{Hu2}I_{Ho}}{N_{Hu}} + \frac{\beta_{Hu3}I_V}{N_{Hu}}).\frac{\Lambda_{Hu}}{\mu_{Hu}}.\frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})}) + \kappa_{Ho}I_{Ho} + \kappa_V I_V - \mu_L L$,

$$A = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix}$$

where
$a_{11} = -(\mu_{Ho} + \delta_{Ho} + \alpha_{Ho})$,
$a_{12} = 0$,
$a_{13} = \frac{\Lambda_{Ho}}{\mu_{Ho}} \frac{\beta_{Ho} L_0}{(L_0+\epsilon L)^2}$,
$a_{21} = 0$,
$a_{22} = -\mu_V$,
$a_{23} = \frac{\Lambda_V}{\mu_v} \frac{\beta_V L_0}{(L_0+\epsilon L)^2}$,
$a_{31} = \frac{\kappa_{Hu}\beta_{Hu2}}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}\beta_{Hu2}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \kappa_{Ho}$,
$a_{32} = \frac{\kappa_{Hu}\beta_{Hu3}}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}\beta_{Hu3}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \kappa_V$,
$a_{33} = \kappa_{Hu}((\frac{\beta_{Hu1} L_0}{(L_0+\epsilon L)^2}) . \frac{\Lambda_{Hu}}{\mu_{Hu}} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})} (\frac{\beta_{Hu1} L_0}{L_0+\epsilon L)^2}) . \frac{\Lambda_{Hu}}{\mu_{Hu}} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})}) - \mu_L$,

Since A = M - D, we deduce matrices M and D to be

$$M = \begin{bmatrix} m_{11} & m_{12} & m_{13} \\ m_{21} & m_{22} & m_{23} \\ m_{31} & m_{32} & m_{33} \end{bmatrix}$$

where
$m_{11} = 0$,
$m_{12} = 0$,
$m_{13} = \frac{\Lambda_{Ho}}{\mu_{Ho}} \frac{\beta_V L_0}{(L_0+\epsilon L)^2}$,
$m_{21} = 0$,
$m_{22} = 0$,
$m_{23} = \frac{\Lambda_V}{\mu_V} \frac{\beta_V L_0}{(L_0+\epsilon L)^2}$,
$m_{31} = \frac{\kappa_{Hu}\beta_{Hu2}}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}\beta_{Hu2}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \kappa_{Ho}$,
$m_{32} = \frac{\kappa_{Hu}\beta_{Hu3}}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}\beta_{Hu3}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \kappa_V$,
$m_{33} = \kappa_{Hu}((\frac{\beta_{Hu1} L_0}{(L_0+\epsilon L)^2}) . \frac{\Lambda_{Hu}}{\mu_{Hu}} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})} (\frac{\beta_{Hu1} L_0}{(L_0+\epsilon L)^2}) . \frac{\Lambda_{Hu}}{\mu_{Hu}} \cdot \frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})})$,

$$D = \begin{bmatrix} d_{11} & d_{12} & d_{13} \\ d_{21} & d_{22} & d_{23} \\ d_{31} & d_{32} & d_{33} \end{bmatrix}$$

$d_{11} = \mu_{Ho} + \delta_{Ho} + \alpha_{Ho}$,
$d_{11} = 0$,
$d_{12} = 0$,
$d_{13} = 0$,
$d_{21} = 0$,
$d_{22} = \mu_v$,
$d_{23} = 0$,

$d_{31} = 0,$
$d_{32} = 0,$
$d_{33} = \mu_L,$

The basic reproduction number is the spectral radius (dominant eigenvalue) of the matrix MD^{-1}, that is

$$R_0 = \rho(MD^{-1}) = \sqrt{\frac{r}{a}.\frac{p}{c} + \frac{s}{b}.\frac{q}{c}},$$

where
$a = \frac{1}{\mu_{Ho}+\delta_{Ho}+\alpha_{Ho}},$
$b = \frac{1}{\mu_V},$
$c = \frac{1}{\mu_L},$
$p = \frac{\Lambda_{Ho}}{\mu_{Ho}} \frac{\beta_{Ho} L_0}{(L_0+\epsilon L)^2},$
$q = \frac{\Lambda_V}{\mu_V} \frac{\beta_V L_0}{(L_0+\epsilon L)^2},$
$r = \frac{\kappa_{Hu}\beta_{Hu2}}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}\beta_{Hu2}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})}.\frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \kappa_{Ho},$
$s = \frac{\kappa_{Hu}\beta_{Hu3}}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \frac{\gamma_{Hu}\beta_{Hu3}}{(\mu_{Hu}+\delta_{Hu}+\alpha_{Hu})}.\frac{1}{(\gamma_{Hu}+\mu_{Hu}+\sigma_{Hu})} + \kappa_V,$

3.4. Local Stability of the Disease Free Equilibrium

Based on the theorem proposed by van den Dreissche and Watmough [30], The disease cannot spread throughout the population if the basic reproduction number R_0 is smaller than one, indicating that the disease-free equilibrium is locally asymptotically stable. This is condensed into the subsequent theorem.
Theorem The point E^0, When $R_0 < 1$, the model system is locally asymptotically stable; otherwise, it is unstable.
Proof Since local stability of the disease-free equilibrium is a result of the van den Driessche and Warmough theorem, there is no need for the proof.

3.5. Global Asymptotic Stability of Disease-Free Equilibrium

The theorem proposed by van den Dreissche and Watmough [30] states that when $R_0 < 1$ and $R_0 > 1$, the disease-free equilibrium is locally asymptotically stable and unstable, respectively. In order to ensure the global asymptotic stability of the disease-free equilibrium, we must first enumerate two conditions. Fill out the form with the system's information.

$$\frac{dX}{dt} = F(X, Z),$$
$$\frac{dZ}{dt} = G(X, Z), G(X, 0) = 0,$$

with $X = (S_{Hu}, R_{Hu}, S_{Ho}, R_{Ho}, S_V)$ comprises of the uninfected components
$Z = (E_{Hu}, I_{Hu}, I_{Ho}, I_V, L)$ comprises of infected and infectious components
$E^0 = (X^*, 0) = (\frac{\Lambda_{Hu}}{\mu_{Hu}}, 0, 0, 0, \frac{\Lambda_{Ho}}{\mu_{Ho}}, 0, 0, \frac{\Lambda_V}{\mu_V}, 0, 0)$ denotes the disease-free equilibrium
To ensure asymptotic global stability, the condition H_1 and H_1 must be hold
$\mathbf{H_1}$: For $\frac{dX}{dt} = F(X, Z), X^*$ is globally asymptotically stable (g.a.s)
$\mathbf{H_2}$: $G(X, Z) = AZ - G(X, Z), G(X, Z) \geq 0$ for $R(X, Z) \in R_{10}^+$ where $A = D_Z G(X^*, 0)$ is an M-matrix and R_{10}^+ is the area in which the biological model makes sense. Here, we have

$$F(X,0) = \begin{bmatrix} \Lambda_{Hu} - \mu_{Hu}.S_{Hu} \\ 0 \\ \Lambda_{Hu} - \mu_{Hu}.S_{Hu} \\ 0 \\ \Lambda_V - \mu_V.S_V \\ 0 \end{bmatrix} \text{ and}$$

$$A = \begin{bmatrix} -(\gamma_{Hu} + \mu_{Hu} + \sigma_{Hu}) & 0 & \frac{\beta_{Hu2}}{N_{Hu}}.\frac{\Lambda_{Hu}}{\mu_{Hu}} & \frac{\beta_{Hu3}}{N_{Hu}}.\frac{\Lambda_{Hu}}{\mu_{Hu}} & \frac{\beta_{Hu1}}{L_0}.\frac{\Lambda_{Hu}}{\mu_{Hu}} \\ \gamma_{Hu} & -(\mu_{Hu} + \delta_{Hu} + \alpha_{Hu}) & 0 & 0 & 0 \\ 0 & 0 & -(\mu_{Ho} + \delta_{Ho} + \alpha_{Ho}) & 0 & \frac{\beta_{Ho}}{L_0}.\frac{\Lambda_{Ho}}{\mu_{Ho}} \\ 0 & 0 & 0 & -\mu_V & \frac{\beta_V/}{L_0}.\frac{\Lambda_V}{\mu_V} \\ \kappa_{Hu} & \kappa_{Hu} & \kappa_{Ho} & \kappa_V & -\mu_L \end{bmatrix}$$

$$Z = \begin{bmatrix} E_{Hu} \\ I_{Hu} \\ I_{Ho} \\ I_V \\ L \end{bmatrix}$$

Next, we have to find $\tilde{G}(X, Z)$ from $G(X, Z) = AZ - \tilde{G}(X, Z)$

$$\tilde{G}(X,Z) = \begin{bmatrix} (\frac{1}{L_0}.\frac{\Lambda_{Hu}}{\mu_{Hu}} - \frac{1}{L_0+\epsilon L}S_{Hu})\beta_{Hu1}L \\ 0 \\ (\frac{1}{L_0}.\frac{\Lambda_{Ho}}{\mu_{Ho}} - \frac{1}{L_0+\epsilon L}S_{Ho})\beta_{Ho}L \\ (\frac{1}{L_0}.\frac{\Lambda_V}{\mu_V} - \frac{1}{L_0+\epsilon L}S_V)\beta_V L \\ 0 \end{bmatrix}$$

Since $S_{Hu}^0 = \frac{\Lambda_{Hu}}{\mu_{Hu}}$ then $\frac{1}{L_0} \geq \frac{1}{L_0+\epsilon L}, S_{Hu}^0 = \frac{\Lambda_{Ho}}{\mu_{Hu}}$ then $\frac{1}{L_0 \geq \frac{1}{L_0+\epsilon L}}$, and $S_V^0 = \frac{\Lambda_V}{\mu_V}$ then $\frac{1}{L_0} \geq \frac{1}{L_0+\epsilon L}$ therefore, it is clear that $\widetilde{G}(X, Z) \geq 0$ for all $(X, Z) \in \mathbb{R}_{10}^+$. It is also clear that matrix A is an M-matrix since the off-diagonal elements of A are non-negative. This result can be summarized that the disease-free equilibrium $E^0 = (\frac{\Lambda_{Hu}}{\mu_{Hu}}, 0, 0, 0, \frac{\Lambda_{Ho}}{\mu_{Ho}}, 0, 0, \frac{\Lambda_V}{\mu_V}, 0, 0)$ is globally asymptotically stable of the system if and the condition $\mathbf{H_1}$ and $\mathbf{H_2}$ are fulfilled.

3.6. The Endemic Equilibrium State

This section contains our findings regarding the presence of a constant solution or endemic equilibrium for the model system. We'll use a threshold parameter, which we've already designated as R_0, to do this. There is one endemic equilibrium in the proportionately specified model solution given by $E^1 = (S_{Hu} = S^*_{Hu}, E_{Hu} = E^*_{Hu}, I_{Hu} = I^*_{Hu}, R_{Hu} = R^*_{Hu}, S_{Ho} = S^*_{Ho}, I_{Ho} = I^*_{Ho}, R_{Ho} = R^*_{Ho}, S_V = S^*_V, I_V = I^*_V, L = L^*)$; with $(S^*_{Hu}, E^*_{Hu}, I^*_{Hu}, R^*_{Hu}, S^*_{Ho}, I^*_{Ho}, R^*_{Ho}, S^*_V, I^*_V, L^*)$ all non-negative, the threshold parameter determining their existence and characteristics $R_0 > 1$ or more specific determined by the existence of free-living Leptospira in the environment. Suppose we have L^* from the system, and then we have the endemic equilibrium presented.

$$S^*_{Hu} = \frac{\Lambda_{Hu} + \theta_{Hu} R^*_{Hu}}{(\lambda^*_{Hu} + \mu_{Hu})},$$

$$E^*_{Hu} = \frac{\lambda^*_{Hu} S^*_{Hu}}{(\gamma_{Hu} + \mu_{Hu} + \sigma_{Hu})},$$

$$I^*_{Hu} = \frac{\gamma_{Hu} E^*_{Hu}}{(\mu_{Hu} + \delta_{Hu} + \alpha_{Hu})},$$

$$R^*_{Hu} = \frac{\alpha_{Hu} I^*_{Hu} + \sigma_{Hu} E^*_{Hu}}{(\mu_{Hu} + \theta_{Hu})},$$

$$S^*_{Ho} = \frac{\Lambda_{Ho} + \theta_{Ho} R^*_{Ho}}{\lambda^8_{Ho} + \mu_{Ho}},$$

$$I^*_{Ho} = \frac{\lambda^*_{Ho}}{(\mu_{Ho} + \delta_{Ho} + \alpha_{Ho})} S^*_{Ho},$$

$$R^*_{Ho} = \frac{\alpha_{Ho} I^*_{Ho}}{(\mu_{Ho} + \theta_{Ho})},$$

$$S^*_V = \frac{\Lambda_V}{\lambda^*_V + \mu_V},$$

$$I^*_V = \frac{\lambda^*_V}{\mu_V} S^*_V,$$

where
$\lambda^*_{Hu} = (\frac{\beta_{Hu1} L^*}{L_0 + \epsilon L^*} + \frac{\beta_{Hu2} I_{Ho}}{N_{Hu}} + \frac{\beta_{Hu3} I_V}{N_{Hu}})$,

$\lambda^*_{Ho} = (\frac{\beta_V L}{L_0 + \epsilon L^*})$,

$\lambda^*_V = (\frac{\beta_V L}{L_0 + \epsilon L^*})$,

The analysis for this equilibrium could not be written in this article due to the complexity of the results, and it will be explored in the numerical simulation in the next

section.

3.7. Numerical Simulation

This section displays the system's result as a graphics produced by ODE45 Solver. The parameter value is given in Table 2.

Table 3: Summary of parameters used in the system

Parameter	**Value**	**Units**	**Reference/Rational**
Λ_{Hu}	10451	Human day^{-1}	$\frac{247.949.975}{65x365}$
Λ_{Ho}	1000	Animal-Host $day^{-}1$	Assumed
Λ_{Ho}	5000	Animal-Vector $day^{-}1$	Assumed
μ_{Hu}	0.000042	$day^{-}1$	$\frac{1}{65x365}$ (Lifespan of human with average lifespan about 65 years)
μ_{Ho}	0.00027	$day^{-}1$	$\frac{1}{10x365}$ (Lifespan of animal host about ten years)
μ_V	0.0013	$day^{-}1$	$\frac{1}{2x365}$ (Lifespan of animal vector about two years)
μ_L	0.07	$day^{-}1$	$\frac{1}{14}$ (Lifespan of leptospire bacteria about 14 days)l
θ_{Hu}	0.01	$day^{-}1$	$\frac{1}{100}$ (re-infection could be happen after three months)
θ_{Ho}	0.01	$day^{-}1$	$\frac{1}{100}$ (re-infection could be happen after three months)
γ_{Hu}	0.05	$day^{-}1$	$\frac{1}{20}$ (Septicemic phase to immune phase occurs in 20 days)
σ_{Hu}	0.005	$day^{-}1$	$\frac{1}{200}$ (Exposed to recovered population occurs in 6 months)
δ_{Hu}	0.0003	$day^{-}1$	$\frac{30}{100,000}$ (it is about 30 individual human deaths over 100,000 population)
δ_{Ho}	0.0005	$day^{-}1$	$\frac{50}{100,000}$ (it is about 50 individual animal host deaths over 100,000 population)
α_{Hu}	0.1	$day^{-}1$	$\frac{1}{10}$ (Human recovery in 10 days)
κ_{Hu}	0.007	$day^{-}1$	Estimated
κ_{Ho}	0.007	$day^{-}1$	Estimated
κ_V	0.005	$day^{-}1$	Estimated
α_{Ho}	0.3	$day^{-}1$	$\frac{1}{3}$ (Animal Host recovery in 3 days)
β_{Hu1}	0.001	$day^{-}1$	Fitted
β_{Hu2}	0.009	$day^{-}1$	Fitted
β_{Hu3}	0.005	$day^{-}1$	Fitted
β_{Ho}	0.0005	$day^{-}1$	Fitted
β_V	0.0005	$day^{-}1$	Fitted
Ł$_0$	10000	-	Estimated
ϵ	0.001	-	Estimated

Figure 2 illustrates the solution profile for all populations when $R_0 < 1$ (disease-free equilibrium). This condition means that there are no free-living bacteria in the environment for an extended period, so then no infected population will be found in the human and animal populations. The numerical solution shows that only the susceptible human, animal host and animal vector population will exist.

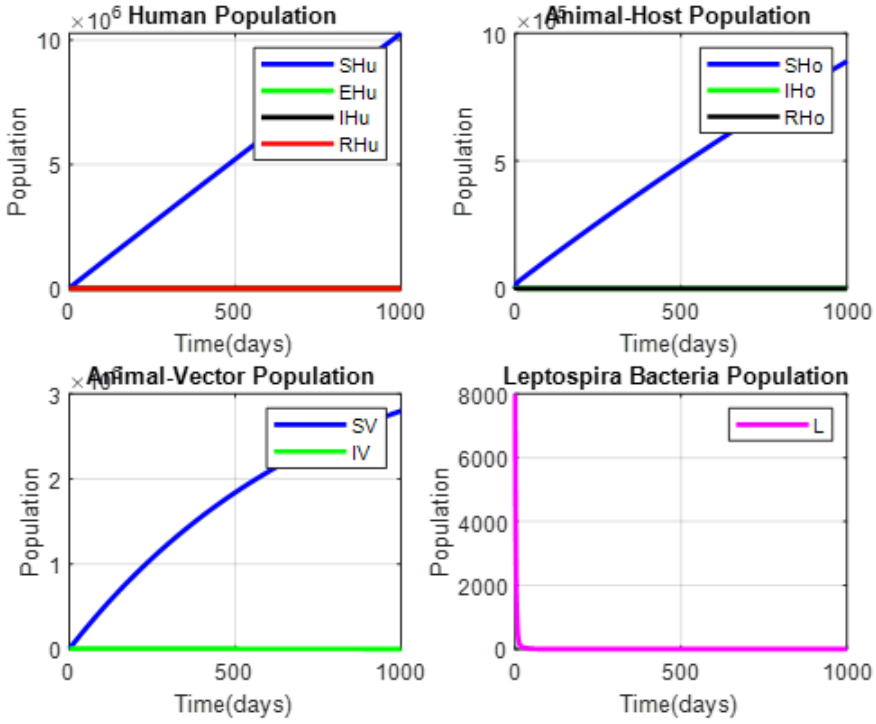

Figure 2: The simulation for each population in which disease-free equilibrium exists (The condition when $R_0 < 1$).

Figure 3 illustrates the dynamics of the human population, animal-host population, animal-vector population and free-living leptospires in the environment with condition $R_0 > 1$. This result demonstrates a correlation between the existence of free-living bacteria in the environment and the existence of leptospirosis disease in human, animal-host and animal vectors. When the bacteria exist, the disease will exist in all populations. This implies that the improvement in the free-living leptospires in the environment can reduce the risk of the spread of disease in all populations. As the route of transmission depends on the infection rate parameter (β), which is the infection occurs not only in the human population but also in the animal host and animal vector population then, the next figures will illustrate the numerical solution for several values of infection rate ($\beta_{Hu1}, \beta_{Hu2}, \beta_{Hu3}, \beta_{Ho}, \beta_V$). Figure 4 shows the graph of the numerical solution model for the infected human population, recovered human population, animal host population, and animal vector population with parameters $\beta_{Hu1} = 0.1$, $\beta_{Hu1} = 0.01$, and $\beta_{Hu1} = 0.0001$. In the infected human population, there is no significant difference between $\beta_{Hu1} = 0.1$ and $\beta_{Hu1} = 0.01$, whereas,

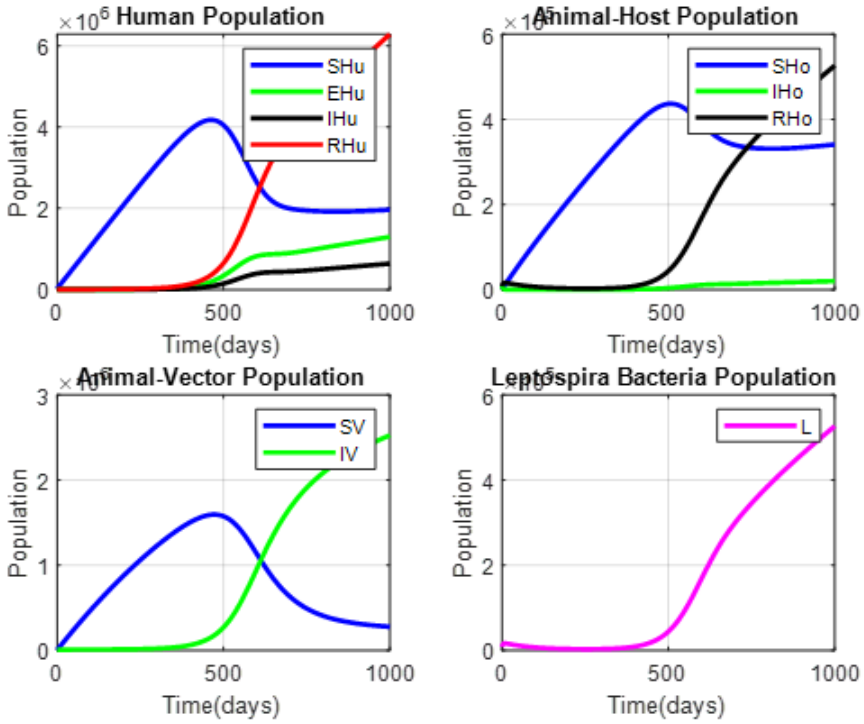

Figure 3: The simulation for each population in which endemic equilibrium exists (The condition when $R_0 > 1$)

for $\beta_{Hu1} = 0.0001$, the spread of disease is quite slow in the beginning, then increases to the endemic equilibrium. This phenomenon also occurs in the animal host and vector population. It slowly increases in the beginning for $\beta_{Hu1} = 0.0001$. The graph of the recovered human population indicates the same thing as the other graph in Figure 4.
Figure 5 illustrates the graph of the numerical solution model for the infected human population, recovered human population, animal host population, and animal vector population with parameters $\beta_{Hu2} = 0.9$, $\beta_{Hu2} = 0.09$, and $\beta_{Hu2} = 0.009$. All population in figure 5 shows the same phenomenon that any difference value of β_{Hu2} does not have a significant result. Infected-human, animal-host and animal-vector population increase almost in the same interval time. Figure 6 illustrates the numerical solution model for the infected human population, recovered human population, animal host population, and animal vector population with parameters $\beta_{Hu3} = 0.5$, $\beta_{Hu3} = 0.05$, and $\beta_{Hu3} = 0.005$. All populations show the same thing for the first interval time, and all of them increase to the endemic equilibrium. However, in the first interval time, all of the three parameters show a significant difference for each population dynamic.
Figure 7 illustrates the numerical solution of the model for the infected human population, recovered human population, animal-host population, and animal-vector population with parameters $\beta_{Ho} = 0.05$, $\beta_{Ho} = 0.005$, and $\beta_{Ho} = 0.0005$. For the infected-human population, recovered-human population, and animal vector population, the parameter does not have a great effect on the dynamic, whereas, for the infected-animal host population,

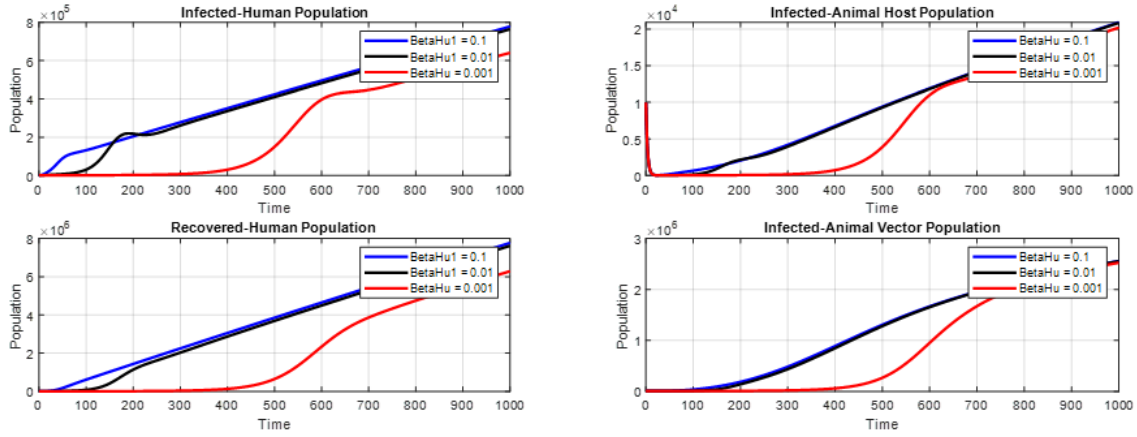

Figure 4: The simulation numeric for infected recovered human population and infected animal host and animal vector with several values of β_{Hu1} ($\beta_{Hu1} = 0.1, \beta_{Hu1} = 0.01, \beta_{Hu1} = 0.001$)

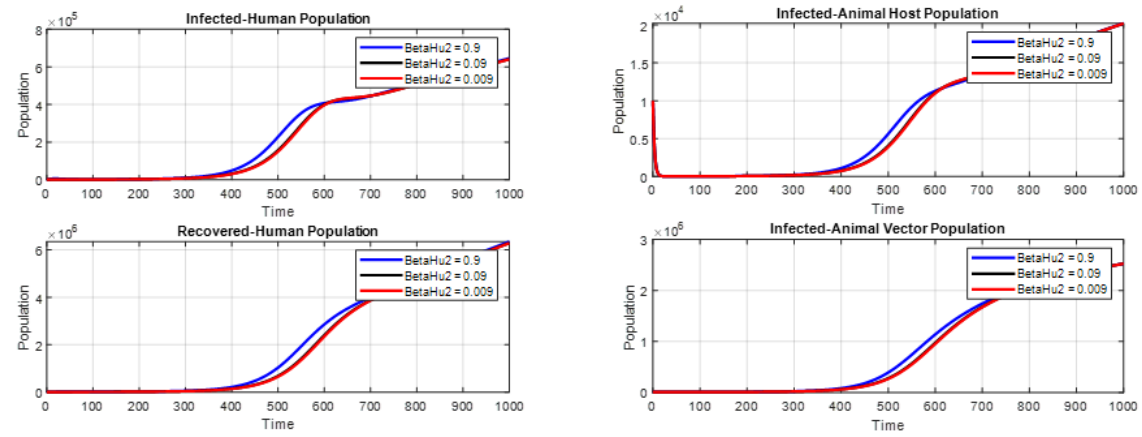

Figure 5: The simulation numeric for infected recovered human population and infected animal host and animal vector with several values of $\beta_{Hu2}(\beta_{Hu2} = 0.9, \beta_{Hu2} = 0.09, \beta_{Hu2} = 0.009)$

this parameter has a significant effect on the dynamic. Figure 8 shows the graph of the numerical solution model for the infected human population, recovered human population, animal host population, and animal vector population with parameters $\beta_V = 0.05$, $\beta_V = 0.005$, and $\beta_V = 0.0005$. Almost all of the population have the same dynamic behavior with several values of parameter β_V. However, the infected animal vector population has significant results compared to the other population, precisely when β_V=0.0005.

4. Conclusions

In conclusion, our work has built and investigated the mathematical modeling of leptospirosis using free-living microorganisms in the environment. With free-living microbes in the environment, various infectious diseases can theoretically be replicated using the generic modeling approach. This study established the disease reproduction number R_0

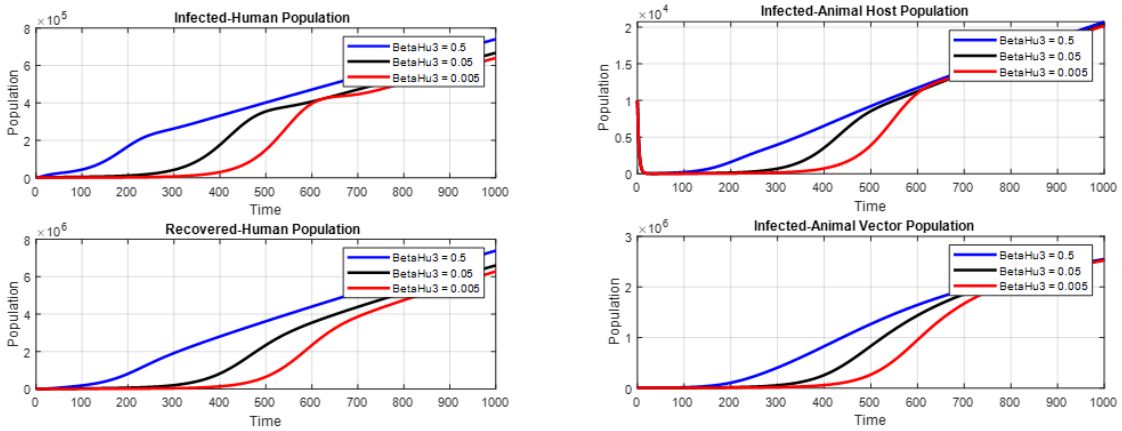

Figure 6: The simulation numeric for infected recovered human population and infected animal host and animal vector with several values of $\beta_{Hu3}(\beta_{Hu3} = 0.5, \beta_{Hu3} = 0.05, \beta_{Hu3} = 0.005)$

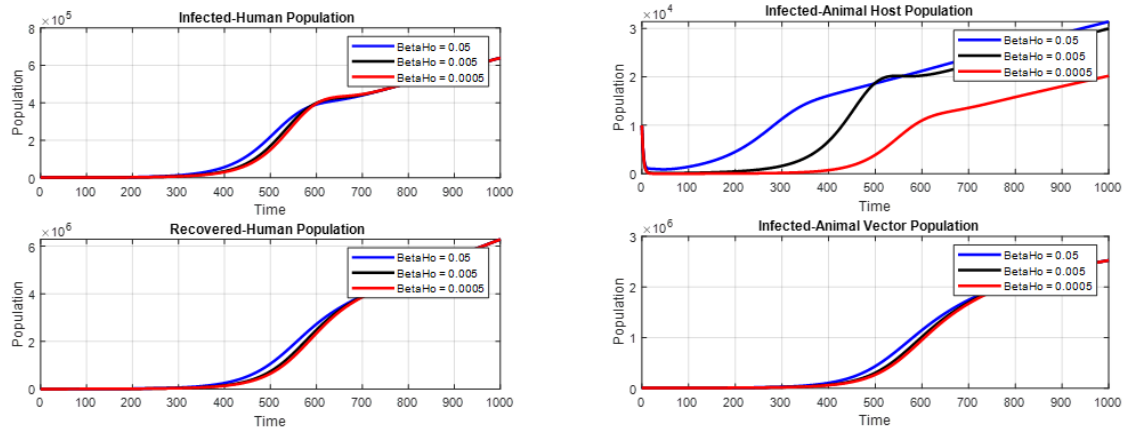

Figure 7: The simulation numeric for infected recovered human population and infected animal host and animal vector with several values of $\beta_{Ho}(\beta_{Ho} = 0.5, \beta_{Ho} = 0.05, \beta_{Ho} = 0.005)$

and the connected within-animal host and between-animal vector models of human leptospirosis using numerical simulations of the whole model and results from the analysis of the endemic equilibrium expression. The endemic equilibrium point and the disease-free equilibrium point are the two equilibrium points that are calculated. Additionally, this work provided a stability analysis for the disease-free equilibrium, which is stable if all of the parameters are assumed to be positive and the stability conditions are met. This is consistent with the numerical simulation that shows a disease-free equilibrium exists. The next generation matrix, which is assessed at the disease-free equilibrium point, is used to compute the basic reproduction number or R_0. The presence of the disease in the human population was identified by the state of each basic reproduction number pair. The presence of the endemic and disease-free equilibriums, which rely on the threshold parameter R_0, is confirmed through numerical simulation. The presence of the endemic and

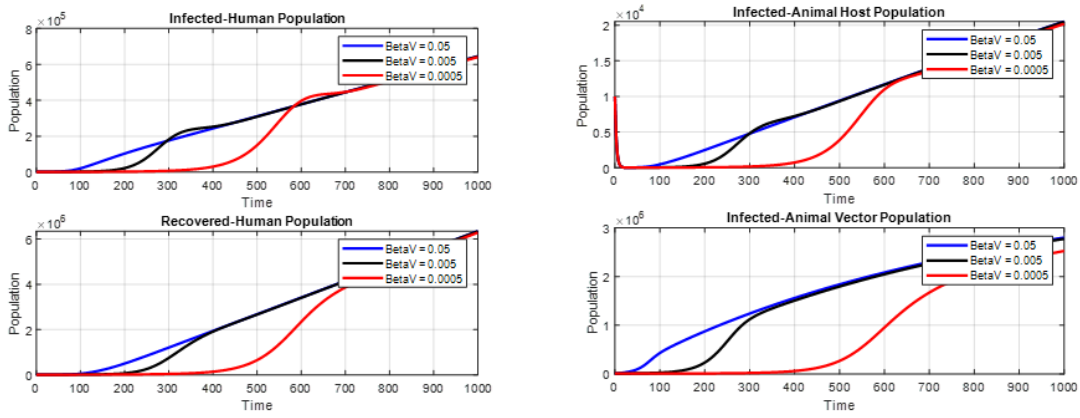

Figure 8: The simulation numeric for infected recovered human population and infected animal host and animal vector with several values of $\beta_V (\beta_V = 0.5, \beta_V = 0.05, \beta_V = 0.005)$

disease-free equilibriums, which rely on the threshold parameter R_0, is confirmed through numerical simulation. The numerical results also provide a simulation of the dynamics for the selected populations, that is, the populations of infected humans, recovered humans, infected animal hosts, and infected animal vectors.

Conflicts of Interest

The Author (s) declare(s) that there is no conflict of interest regarding the publication of this paper.

Acknowledgements

The authors acknowledge the Dean of Mathematics and Natural Sciences Universitas Negeri Surabaya and the Head of the School of Mathematical Sciences, College of Computing, Informatics and Media, UiTM Shah Alam, Malaysia, for financial support to do this research. The authors also thank the reviewers for all their valuable comments and suggestions.

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