

Transmission Dynamics of Two Co-Circulating Strains of Dengue Virus and Effective Vaccination Strategy using Deep Learning

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ABSTRACT

We develop and analyze a deterministic ODE-based model for the transmission dynamics of two cocirculating strains of dengue virus. The model takes into account the interaction between the host and vector populations and also incorporates the effects of partial and temporary cross-immunity and antibody-dependent-enhancement (ADE). The associated basic reproduction numbers for the model are calculated, and it is shown that the disease-free equilibrium is locally asymptotically stable if the maximum of the associated reproduction numbers is less than unity. Our analysis also shows the existence of a backward bifurcation, indicating the possibility of co-existence of a stable endemic equilibrium and a stable disease-free equilibrium even when the basic reproduction number is less than one. The existence and local stability of the partial endemic equilibria are also shown. Numerical exploration of the model shows the existence of oscillatory behavior (limit cycles) under certain parameter regimes. Finally, we examine efficient vaccination protocols by setting up an optimal control problem and using deep neural networks to find the optimal vaccination strategy for a variety of scenarios depending on the model parameters. Besides informing policymakers, this part of the study also demonstrates the potential of machine learning techniques in public health applications.

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1. Introduction

Historically, dengue epidemics were recorded in North America, Asia, and Africa in the late 18th century, but cases remained rare until the mid-1900s (Gubler, 1998). Since the 1970s, incidence has surged, with the WHO reporting a thirty-fold increase between 1960 and 2010, driven by rapid urbanization, population growth, and international travel (Gubler, 1998; Whitehorn & Farrar, 2010). Now endemic in nearly 110 countries across Southeast Asia, the Americas, Africa, and the Eastern Mediterranean, dengue threatens approximately 2.5 billion people. This resurgence highlights the need to better understand the disease dynamics. Dengue is a mosquito-borne disease that has now become the second most deadly mosquito-borne disease after malaria, with 50 to 100 million annual cases and 10,000 to 20,000 deaths (Halstead et al., 1970; Kautner et al., 1997; Ranjit & Kissoon, 2011; Shekhar, 2007).

Dengue transmission occurs through *Aedes aegypti* mosquitoes, which acquire the virus from infected human blood and transmit it to susceptible hosts after a 7–10 day incubation period (Garba et al., 2008; Gubler & Kuno, 1997). Infected humans recover within 1–2 weeks, gaining lifelong immunity to the infecting serotype but only temporary, partial protection against others (Esteva & Vargas, 2003; Garba & Gumel, 2010; Halstead et al., 1970; Wearing & Rohani, 2006). Dengue is caused by the dengue virus (DENV), a single positive-stranded RNA virus of the Flavivirus genus, with four serotypes (DENV1–4) (Gubler, 1998; Holmes & Twiddy, 2003). Developing a vaccine against all serotypes remains challenging, limiting immunization options (Garba et al., 2008; Shekhar, 2007; Whitehorn & Farrar, 2010). Recovery from one serotype confers lifelong immunity to that serotype but only temporary, partial cross-immunity to others, leading to ADE in secondary infections with a different serotype, which increases the risk of severe outcomes like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) (Ferguson et al., 1999; Garba & Gumel, 2010; Halstead et al., 1970; Wearing & Rohani, 2006). These virological complexities inform our two-strain model. Dengue exhibits a wide clinical spectrum, with approximately 80% of primary infections being asymptomatic or causing mild fever (Whitehorn & Farrar, 2010). The disease

progresses through febrile, critical, and recovery phases, with the febrile phase marked by high fever, rash, and muscle pain, earning the name “break bone fever” (Whitehorn & Farrar, 2010). Most cases resolve with low mortality, but a small percentage enter the critical phase, characterized by low blood pressure, plasma leakage, and organ impairment (Gubler & Kuno, 1997; Gubler, 1998; Kautner et al., 1997). Severe cases develop DHF or DSS, with mortality rates of 5–15%, primarily linked to secondary infections via ADE (Gubler & Kuno, 1997; Gubler, 1998; Kautner et al., 1997; Whitehorn & Farrar, 2010). A number of deterministic mathematical models have been put forth in recent years to examine the dynamics of dengue transmission in urban areas (Esteva & Vargas, 1999, 2003; Ferguson et al., 1999; Garba & Gumel, 2010; Garba et al., 2008; Kautner et al., 1997; Wearing & Rohani, 2006). Using a deterministic ODE model, (Esteva & Vargas, 2003) has examined the coexistence of two dengue virus serotypes. Additionally, Ferguson et al. (1999) have looked into how ADE affects the spread of several dengue virus serotypes. Furthermore, a standard incidence ODE model for a single dengue virus strain has demonstrated the presence of a backward bifurcation by Garba et al. (2008). The impact of cross-immunity on the dynamics of transmission of two dengue virus strains has also been investigated by Garba and Gumel (2010). The effects of ADE and cross-immunity on various dengue virus serotypes have also been studied by Wearing and Rohani (2006). Lastly, Chowell et al. (2007) used spatial epidemic data to estimate the basic reproduction number for dengue. Zheng and Nie (2018) proposed a two-strain dengue transmission model incorporating human awareness and vector control, analyzed equilibrium stability using the next generation matrix, and identified optimal control strategies emphasizing self-protection and mosquito reduction to curb disease spread. Ghosh et al. (2020) present a two-strain dengue model with co-infection and bilinear infection rates, incorporating time-dependent control strategies: awareness, treatment, and mosquito eradication, and apply Pontryagin’s maximum principle to optimize interventions, demonstrating that human awareness combined with treatment is the most effective control strategy. Saha et al. (2023) investigated a co-infected two-serotype dengue model with three control measures, analyzing equilibrium stability and bifurcation using the center manifold theorem and optimal control theory, concluding that combining protection and treatment is more effective than mosquito killing with treatment. Ndi et al. (2024) developed a two-strain dengue model incorporating antibody-dependent enhancement, vaccination, and Wolbachia interventions, demonstrating through simulations that temperature-sensitive mosquito dynamics and deployment of the wAu Wolbachia strain effectively reduce secondary infections.

A growing body of literature demonstrates the use of these methods for diagnosis, forecasting, and serotype evolution analysis. For example, Andrade Girón et al. (2025) presented a systematic review highlighting the application of deep learning models in the prediction of dengue diagnosis, covering a wide range of architectures and data types. Z. Mumtaz et al. (2024) proposed a deep learning-based predictive framework that accounts for the evolving nature of dengue virus serotypes, addressing one of the key challenges in long-term surveillance. Dhaked et al. (2025) investigated the predictive capacity of deep learning under complex environmental conditions, showing improved detection of dengue cases based on weather patterns in Jaipur, India. The purpose of the current study is to formulate and analyze a deterministic compartmental model for the transmission dynamics of two strains of dengue virus, which simultaneously incorporates the effects of both temporary and partial cross-immunity as well as antibody-dependent enhancement (ADE), which is widely hypothesized to cause DHF and DSS, the primary cause of death due to the disease (Ferguson et al., 1999; Garba & Gumel, 2010; Halstead et al., 1970; Wearing & Rohani, 2006). This has been built into our model by incorporating both a latency (exposed) class as well as an explicit cross-immunity class for the host population. We also incorporate the disease dynamics of the vector population in the model. We have modeled the effects of ADE by allowing for an increase in the transmissibility of host individuals suffering from a secondary heterotypic infection. Finally, we have assumed a standard incidence force of infection for this study. As demonstrated in Garba and Gumel (2010), Garba et al. (2008), there is reason to believe that a standard incidence model adds more richness to the dynamical behavior of an epidemic model for the Dengue virus. This study, therefore, extends the previous works of Garba and Gumel (2010), Esteva and Vargas (2003), Wearing and Rohani (2006), and Ferguson et al. (1999). In addition to the analytical and qualitative analysis, we extend the study to explore optimal intervention strategies by introducing vaccination as a control variable. The optimal control problem is formulated to minimize both the disease burden and the cost of interventions. A neural network-based framework is employed to approximate the optimal control trajectories, and the results are benchmarked against those obtained via the classical Pontryagin’s Maximum Principle (PMP). This approach demonstrates the potential of artificial intelligence techniques in solving complex optimal control problems, particularly when traditional analytical methods become intractable. The inclusion of a vaccinated host compartment with waning immunity, inspired by real-world vaccines such as Qdenga, enhances the model’s practical relevance for designing cost-effective public health strategies. Our modeling framework remains biologically grounded, capturing clinical and entomological realities such as incubation, temporary cross-immunity, and reinfection, while retaining analytical tractability to connect mathematical thresholds and bifurcation structures with epidemiologically interpretable outcomes, including elimination, coexistence, and oscillations.

2. Epidemic Model Formulation

We formulate a deterministic compartmental model described by a system of seventeen ordinary differential

equations, incorporating the dynamics of both the host as well as the vector population. The model is essentially an extension of the standard deterministic Susceptible, Exposed, Infectious, and Recovered (SEIR) compartmental model with two serotypes of the virus assumed to be prevalent in the population. In addition, as mentioned previously, the model will incorporate the effects of cross-immunity. It is assumed that individuals recovered from infection with a particular serotype of dengue attain lifelong immunity to that serotype and partial immunity to different serotypes (Ferguson et al., 1999). This phenomenon has been incorporated into the model by adding the cross-immunity compartments $C_i, i = 1, 2$ to the model. Individuals enter compartment C_i , having recovered from infection with serotype i , and are then partially immune to the other serotype (Ferguson et al., 1999; Garba & Gumel, 2010). Furthermore, the model will also incorporate the effects of Antibody Dependent Enhancement (ADE). Following Ferguson et al. (1999), it is assumed that ADE increases the viral load of host individuals experiencing a secondary, heterotypic infection. Biologically, this occurs as after a primary infection, the body produces antibodies against that specific serotype and in a subsequent infection with a different serotype these antibodies can bind to the new virus but are unable to neutralize it, this facilitates the virus's entry into immune cells leading to enhanced viral replication and thus a more severe, pro-inflammatory immune response, which can lead to hemorrhaging and dengue shock syndrome. Thus, secondary infections with a second serotype of dengue virus act to increase the force of infection associated with the second infecting serotype and hence for this study, ADE is assumed to increase the transmissibility of secondary infections of serotype i by a factor η_i . Thus, $\eta_i = 1$ corresponds to no enhancement effects, whereas $\eta_i > 1$ implies that individuals with secondary infection of serotype i contribute towards the force of infection η_i -times more than individuals with primary infection of the same serotype (Ferguson et al., 1999; Wearing & Rohani, 2006). For the model considered in the current study, the total host population at time t , denoted by $N_H(t)$, is subdivided into fourteen mutually exclusive compartments. These compartments consist of hosts susceptible to both strains of the dengue virus, denoted by $S(t)$, hosts exposed to the infection- infected but not yet infectious- with strain $i = (1, 2)$ of the dengue virus, denoted by $E_i(t)$, hosts infectious with strain $i = (1, 2)$, denoted by $I_i(t)$, hosts recovered from primary infection with strain $i = (1, 2)$ and with full immunity to both strains of dengue virus, denoted by $R_i(t)$, hosts recovered from strain $i = (1, 2)$ with full immunity to strain i and partial cross-immunity to strain $j \neq i$, denoted by $C_i(t)$, hosts exposed to secondary infection of strain $i = (1, 2)$ having recovered from strain $j \neq i$, denoted by $E_{ji}(t)$, hosts infectious with secondary infection of strain $i = (1, 2)$ having recovered from strain $j \neq i$, denoted by $I_{ji}(t)$ and finally, hosts no longer susceptible to both strains of the dengue virus, denoted by $R(t)$. Similarly, the vector population denoted by $N_V(t)$ is subdivided into three main compartments, namely the fraction of the vector population susceptible to both strains of the dengue virus, denoted by $S_V(t)$ and the fractions of the vector population infected with strain $i = (1, 2)$, denoted by $(V_i(t))$. Mathematically, therefore,

$$\begin{aligned} N_H(t) &= S(t) + E_1(t) + E_2(t) + E_{12}(t) + E_{21}(t) + I_1(t) + I_2(t) + I_{12}(t) + I_{21}(t) \\ &\quad + R_1(t) + R_2(t) + C_1(t) + C_2(t) + R(t) \\ N_V(t) &= S_V(t) + V_1(t) + V_2(t) \end{aligned} \quad (2.1)$$

2.1 Incidence Functions

As mentioned previously, the model that we shall formulate in this study will consider the dynamics of both the host as well as the vector population. Therefore, our model will involve four different forces of infection: the force of infection exerted by the vectors infected with strain $i = (1, 2)$ of the dengue virus on the hosts, denoted by λ_{V_i} , and the force of infection exerted by the hosts infected with strain $i = (1, 2)$ of the dengue virus on the vectors, denoted by λ_{H_i} . Here,

$$\begin{aligned} \lambda_{V_i} &= \frac{\alpha_{V_i}}{N_H} V_{Hi} \\ \lambda_{H_i} &= \frac{\alpha_{H_i}}{N_H} H_{Hi} \end{aligned}$$

Where α_{V_i} is the effective contact rate for vectors, which depends on the biting rate of mosquitoes (the vectors) and the transmission probability from vectors to hosts, and V_{Hi} represents the total number of vectors infected with serotype i of the dengue virus (Esteva & Vargas, 2003). Similarly, α_{H_i} is the effective contact rate for hosts, which depends on the biting rate of susceptible mosquitoes (vectors) and the transmission probability from hosts to vectors, and H_{Hi} represents the total number of hosts infected with serotype i of the dengue virus. We point out that H_{Hi} includes host individuals from two groups: host individuals suffering from a primary infection and host individuals suffering from a secondary infection with strain i of the dengue virus, that is I_i and I_{ji} , respectively. However, to incorporate the increased infectivity of secondary heterotypic infectives as a consequence of ADE, we assume that the class of individuals suffering from secondary infection with serotype i transmit the disease at an increased rate $\eta_i \geq 1$. Thus, mathematically, $H_{Hi} = (I_i +$

$\eta_i I_{ji}$). Therefore, the forces of infection exerted by vectors and hosts are given by

$$\begin{aligned}\lambda_{V_i} &= \frac{\alpha_{V_i}}{N_H} V_{Ii} \\ \lambda_{H_i} &= \frac{\alpha_{H_i}}{N_H} (I_i + \eta_i I_{ji})\end{aligned}\quad (2.3)$$

2.2 The Host Component of the Epidemic Model

The population of individuals susceptible to both strains of dengue virus is generated at a constant birth rate Π_H and is diminished by exposure to infection with strain 1 or 2 at the rate λ_{vi} ($i = 1, 2$), and by natural death.

$$\frac{dS}{dt} = \Pi_H - (\lambda_{V_1} + \lambda_{V_2})S - \mu_H S$$

Individuals exposed to primary infection (but not yet infectious) with strain $i = (1, 2)$ are generated at the rate λ_{V_i} . They are diminished by becoming infectious at the rate ϕ_i and by natural death.

$$\frac{dE_i}{dt} = \lambda_{V_i} S - (\phi_i + \mu_H) E_i \quad i, j = (1, 2) \quad i \neq j$$

Individuals infected with strain $i = (1, 2)$ are generated at the rate ϕ_i (where $1/\phi_i$ is the latency period of the virus of serotype i). They are diminished by recovery from strain i at the rate γ_i , by disease-induced death at the rate δ_i , and by natural death.

$$\frac{dI_i}{dt} = \phi_i E_i - (\gamma_i + \delta_i + \mu_H) I_i \quad i, j = (1, 2) \quad i \neq j$$

Hosts recovered from primary infection with strain $i = (1, 2)$ are generated at the rate γ_i upon recovery from and lifelong immunity to strain i . This population is diminished at the rate w_i as the individuals move to the refractory class and by natural death.

$$\frac{dR_i}{dt} = \gamma_i I_i - (w_i + \mu_H) R_i \quad i, j = (1, 2) \quad i \neq j$$

Once recovered from strain i , individuals gain temporary cross immunity to heterologous strain j (given by the class C_i ($i = 1, 2$)), which wanes in time. With probability u_i , the individuals in this class are exposed and then infected with a heterologous strain j , while with probability $(1 - u_i)$, the individuals in this class transition to the recovered class without a breakthrough infection during this time. Natural death also contributes to the depletion of C_i .

$$\frac{dC_i}{dt} = w_i R_i - (u_i \lambda_{vi} + (1 - u_i) k_i + \mu_H) C_i \quad i, j = (1, 2) \quad i \neq j$$

The population of individuals exposed to secondary infection with strain i that have recovered from strain $j \neq i$ is generated at a rate $u_i \lambda_{vi}$. It decreases as individuals become infectious at the rate ϕ_i and as they undergo natural death.

$$\frac{dE_{ij}}{dt} = u_i \lambda_{vi} C_i - (\phi_i + \mu_H) E_{ij} \quad i, j = (1, 2) \quad i \neq j$$

The population of individuals infectious with secondary infection with strain i that have recovered from strain $j \neq i$ is generated at a rate ϕ_i . It is reduced by recovery from infection at the rate γ_i , by disease-induced death at the rate δ_i , and by natural death.

$$\frac{dI_{ij}}{dt} = \phi_i E_{ij} - (\gamma_i + \delta_i + \mu_H) I_{ij} \quad i, j = (1, 2) \quad i \neq j$$

Individuals susceptible to neither strain are generated at the rate γ_i as individuals with secondary infection with strain $i = (1, 2)$ recover, and at the effective rate $(1 - u_i) k_i$ individuals immune to strain i in the refractory class C_i do not acquire secondary infection in their lifetime. This population is diminished by natural death.

$$\frac{dR}{dt} = \gamma_1 I_{21} + \gamma_1 I_{12} + (1 - u_1) k_1 C_1 + (1 - u_2) k_2 C_2 - \mu_H R$$

In addition, it is assumed that individuals in each of the fourteen compartments die at a constant per capita mortality rate μ .

2.3 The Vector Component of the Epidemic Model

The susceptible vectors are generated at a constant birthrate Π_V . They are diminished by natural death at the rate μ_V .

and by infection at the rate λ_{H1} and λ_{H2} with strain 1 and 2, respectively

$$\frac{dS_v}{dt} = \Pi_v - (\lambda_{H1} + \lambda_{H2} + \mu_H)S_v$$

Vectors infectious with serotype i are generated at the rate λ_{Hi} . They are diminished by natural death and disease-induced death at the rates μ_v and δ_{vi} , respectively. It is assumed, following Garba and Gumel (2010), Wearing and Rohani (2006) and Ferguson et al. (1999), that once a vector acquires an infection with one particular serotype of the virus, it remains infected for life and cannot be infected by a second serotype of the dengue virus.

$$\frac{dV_{ii}}{dt} = \lambda_{Hi}S_v - (\delta_{vi} + \mu_v)V_{ii} \quad i, j = (1, 2) \quad i \neq j$$

2.4 The Epidemic Model

The non-linear system of ordinary differential equations that governs the time evolution of each compartment of the epidemic model is given below

$$\begin{aligned} \frac{dS}{dt} &= \Pi_H - (\lambda_{v1} + \lambda_{v2})S - \mu_H S \\ \frac{dE_1}{dt} &= \lambda_{v1}S - (\Phi_1 + \mu_H)E_1 \\ \frac{dE_2}{dt} &= \lambda_{v2}S - (\Phi_2 + \mu_H)E_2 \\ \frac{dI_1}{dt} &= \Phi_1 E_1 - (\gamma_1 + \delta_1 + \mu_H)I_1 \\ \frac{dI_2}{dt} &= \Phi_2 E_2 - (\gamma_2 + \delta_2 + \mu_H)I_2 \\ \frac{dR_1}{dt} &= \gamma_1 I_1 - (\omega_1 + \mu_H)R_1 \\ \frac{dR_2}{dt} &= \gamma_2 I_2 - (\omega_2 + \mu_H)R_2 \\ \frac{dC_1}{dt} &= w_1 R_1 - (u_1 \lambda_{v2} + (1 - u_1)k_1 + \mu_H)C_1 \\ \frac{dC_2}{dt} &= w_2 R_2 - (u_2 \lambda_{v1} + (1 - u_2)k_2 + \mu_H)C_2 \\ \frac{dE_{21}}{dt} &= u_2 \lambda_{v1} C_2 - (\Phi_1 + \mu_H)E_{21} \\ \frac{dE_{12}}{dt} &= u_1 \lambda_{v2} C_1 - (\Phi_2 + \mu_H)E_{12} \\ \frac{dI_{21}}{dt} &= \Phi_1 E_{21} - (\gamma_1 + \delta_1 + \mu_H)I_{21} \\ \frac{dI_{12}}{dt} &= \Phi_2 E_{12} - (\gamma_2 + \delta_2 + \mu_H)I_{12} \\ \frac{dR}{dt} &= \gamma_1 I_{21} + \gamma_2 I_{12} + (1 - u_1)k_1 C_1 + (1 - u_2)k_2 C_2 - \mu_H R \\ \frac{dS_v}{dt} &= \Pi_v - (\lambda_{H1} + \lambda_{H2} + \mu_H)S_v \\ \frac{dV_{I1}}{dt} &= \lambda_{H1}S_v - (\delta_{v1} + \mu_v)V_{I1} \\ \frac{dV_{I2}}{dt} &= \lambda_{H2}S_v - (\delta_{v2} + \mu_v)V_{I2} \end{aligned} \tag{2.4}$$

The description of variables and parameters of the model (2.4) is as follows

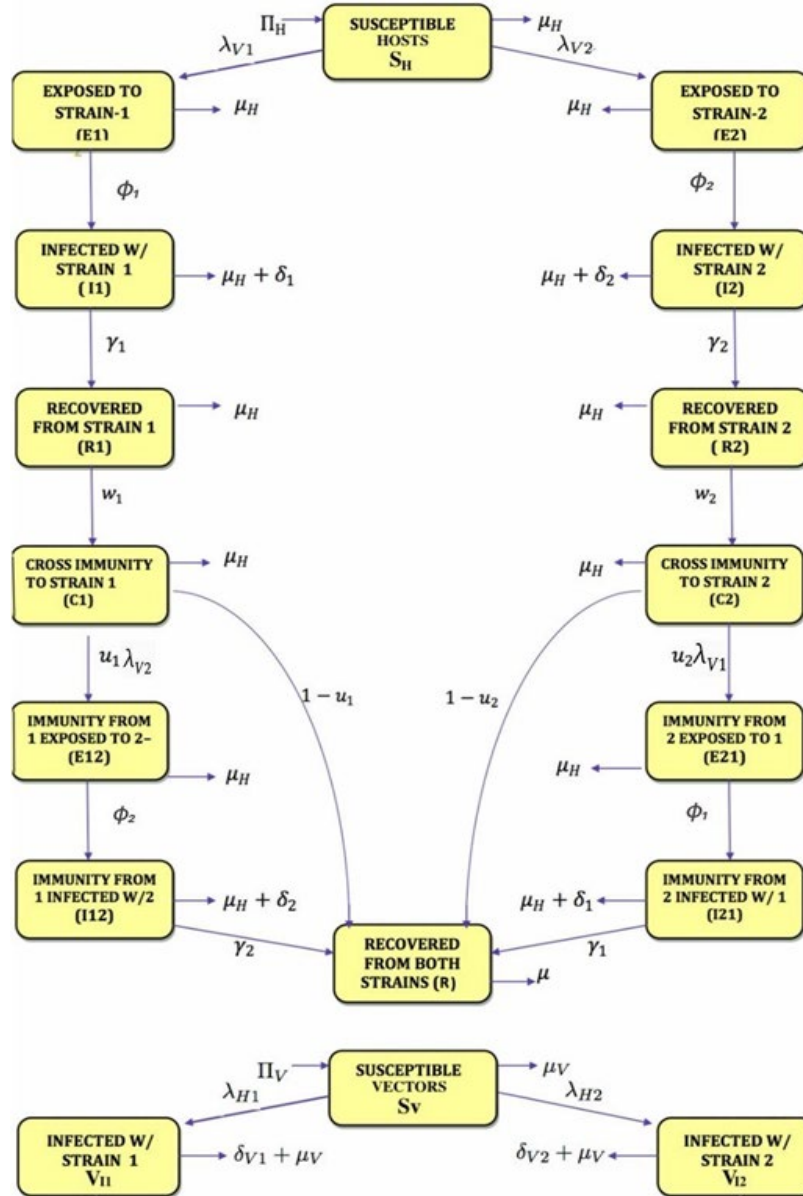


Figure 1: Flow Diagram of the Model (2.4). The Model Consists of 17 Mutually Exclusive Compartments

Table 1: Variables and their Description $i = 1, 2, j \neq i$

Variables	Description
S	Hosts Susceptible to both Strains of the Dengue Virus
E_i	Hosts Suffering Primary Exposure to Strain i of the Dengue Virus
E_{ij}	Hosts Suffering Secondary Exposure to Strain j of the Dengue Virus
I_i	Hosts Suffering Primary Infection with Strain i of the Dengue Virus
I_{ij}	Hosts Suffering Secondary Infection with Strain j of the Dengue Virus
R_i	Hosts Recovered from Infection with Strain i with Temporary Complete Cross-Immunity to Strain j
C_i	Hosts Recovered from Infection with Strain i with Partial Cross-Immunity to Strain j
R	Hosts no Longer Susceptible to infection with either Strain of the Dengue Virus
S_V	Vectors Susceptible to Infection with both Strains of the Dengue Virus
V_{ii}	Vectors Infected with Strain i of the Dengue Virus

Since (2.4) is a model for human populations, all the associated parameters are non-negative. Furthermore, the following non-negativity results holds. The variables of the model (2.4) are non-negative.

Table 2: Parameters with Base Line Values

Parameters	Description	Baseline Value (Units)	Source
μ_H	Natural death rate of hosts	$\frac{1}{65 \times 365} \text{ day}^{-1}$	(Garba & Gumel, 2010)
μ_V	Natural death rate of vectors	$\frac{26}{365} \text{ day}^{-1}$	(Garba & Gumel, 2010)
Π_H	Recruitment rate of susceptible host population	$26 \text{ persons day}^{-1}$	(Garba & Gumel, 2010; Garba et al., 2008)
Π_V	Recruitment rate of susceptible vector population	$2600 \text{ vectors day}^{-1}$	(Garba & Gumel, 2010)
$\alpha_{Hi} (i = 1, 2)$	Effective contact rate for hosts infected with strain i	$\alpha_{H1} = \frac{100}{365}, \alpha_{H2} = \frac{20}{365} \text{ day}^{-1}$	(Garba & Gumel, 2010)
$\alpha_{Vi} (i = 1, 2)$	Effective contact rate for vectors infected with strain i	$\alpha_{V1} = \frac{1000}{365}, \alpha_{V2} = \frac{800}{365} \text{ day}^{-1}$	(Garba & Gumel, 2010)
$\eta_i (i = 1, 2)$	ADE factor for strain i	$\eta_1 = 1.4, \eta_2 = 28$	Assumed*
$\phi_i (i = 1, 2)$	Rate of transfer from exposed to infectious for strain i	$\phi_1 = \phi_2 = \frac{73}{365} \text{ day}^{-1}$	(Garba & Gumel, 2010; Garba et al., 2008)
$\gamma_i (i = 1, 2)$	Rate of recovery from infection with strain i	$\gamma_1 = \gamma_2 = \frac{52}{365} \text{ day}^{-1}$	(Garba & Gumel, 2010; Garba et al., 2008)
$\delta_i (i = 1, 2)$	Disease induced death rate of hosts infected with strain i	$\delta_1 = \delta_2 = \frac{0.18}{365} \text{ day}^{-1}$	Assumed*
$\delta_{Vi} (i = 1, 2)$	Disease induced death rate of vectors infected with strain i	$\delta_{V1} = 0, \delta_{V2} = 0$	(Garba et al., 2008)
$w_i (i = 1, 2)$	Rate at which recovered from strain i gain partial immunity to strain j	$w_1 = w_2 = \frac{12}{365} \text{ day}^{-1}$	Assumed*
$u_i (i = 1, 2)$	Dimensionless scaling parameter	$u_1 = 0.6, u_2 = 0.3$	Assumed*
$k_i (i = 1, 2)$	Transition rate at which individuals recovered from strain i move to the recovered class	$k_1 = 1, k_2 = 1$	Assumed*

*These Parameter Values were Chosen to Explore Different Dynamical Behaviour of the Model.

for all time $t > 0$. In other words, solutions of the system (2.4) with positive initial data will remain positive for all $t > 0$.

Theorem 2.1. *The variables of the model (2.4) are non-negative for all time $t > 0$. In other words, solutions of the system (2.4) with positive initial data will remain positive for all $t > 0$.*

Proof. The proof is given in the Appendix.

LEMMA 1. *The closed sets*

$$D_1 = \left\{ (S, E_1, I_1, R_1, C_1, E_{12}, I_{12}, E_2, I_2, R_2, C_2, E_{21}, I_{21}, R) \in R_+^{14} : \right. \\ \left. S + E_1 + I_1 + R_1 + C_1 + E_{12} + I_{12} + E_2 + I_2 + R_2 + C_2 + E_{21} + I_{21} + R \leq \frac{\Pi_H}{\mu_H} \right\}$$

and

$$D_2 = \left\{ (S_V + V_{I1} + V_{I2}) \in R_+^3 : S_V + V_{I1} + V_{I2} \leq \frac{\Pi_H}{\mu_H} \right\}$$

are positively invariant.

Proof. The proof is given in the Appendix.

3. Stability of Disease-free Equilibrium (DFE) of System (2.4)

In this section, we discuss the existence and stability of the disease-free equilibrium (DFE).

3.1 Local Stability

The model (2.4) has a DFE, obtained by setting the right-hand sides of the equations in (2.4) to zero, given by

$$\begin{aligned} \mathfrak{N}_0 &= (S^*, E_1^*, E_2^*, I_1^*, I_2^*, R_1^*, R_2^*, C_1^*, C_2^*, E_{12}^*, E_{21}^*, I_{12}^*, I_{21}^*, R^*, S_V^*, C_{I1}^*, V_{I2}^*) \\ &= \left(\frac{\Pi_H}{\mu_H}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, \frac{\Pi_V}{\mu_V}, 0, 0 \right) \end{aligned} \quad (2.7)$$

The local stability of $\mathbb{N}_0$ will be determined using the next generation operator method described in [Van den Driessche and Watmough \(2002\)](#). The non-negative matrix F , of the new infection terms, and the M-matrix, V , of the transition terms associated with the model (2.1) are given by

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_{V1} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_{V2} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{\alpha_{H1}\mu_H\Pi_V}{\mu_V\Pi_H} & 0 & 0 & 0 & \frac{\alpha_{H1}\eta_1\mu_H\Pi_V}{\mu_V\Pi_H} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\alpha_{H2}\mu_H\Pi_V}{\mu_V\Pi_H} & 0 & 0 & 0 & \frac{\alpha_{H2}\eta_2\mu_H\Pi_V}{\mu_V\Pi_H} & 0 & 0 \end{pmatrix}$$

and,

$$V = \begin{pmatrix} k_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & k'_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\phi_1 & 0 & k_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\phi_2 & 0 & k'_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & k'_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & k_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\phi_2 & 0 & k'_2 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\phi_1 & 0 & k_2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & k_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & k'_4 \end{pmatrix}$$

Where:

$$k_1 = (\phi_1 + \mu_H) \quad k_2 = (\gamma_1 + \delta_1 + \mu_H) \quad k_3 = (w_1 + \mu_H) \quad \text{and} \quad k_4 = (\delta_{V1} + \mu_V) \quad (2.8)$$

$$k'_1 = (\phi_2 + \mu_H) \quad k'_2 = (\gamma_2 + \delta_2 + \mu_H) \quad k'_3 = (w_2 + \mu_H) \quad \text{and} \quad k'_4 = (\delta_{V2} + \mu_V) \quad (2.9)$$

The eigenvalues of the matrix FV^{-1} are

$$\left\{ 0, 0, 0, 0, 0, 0, -\sqrt{\frac{\phi_1\alpha_{H1}\mu_H\Pi_V\alpha_{V1}}{k_1k_2k_4\Pi_H\mu_V}}, \sqrt{\frac{\phi_1\alpha_{H1}\mu_H\Pi_V\alpha_{V1}}{k_1k_2k_4\Pi_H\mu_V}}, -\sqrt{\frac{\phi_2\alpha_{H2}\mu_H\Pi_V\alpha_{V2}}{k'_1k'_2k'_4\Pi_H\mu_V}}, \sqrt{\frac{\phi_2\alpha_{H2}\mu_H\Pi_V\alpha_{V2}}{k'_1k'_2k'_4\Pi_H\mu_V}} \right\}$$

It follows that the basic reproduction number $R_0 = \rho(FV^{-1})$, is given by

$$R_0 = \max \left\{ 0, 0, 0, 0, 0, 0, -\sqrt{\frac{\phi_1\alpha_{H1}\mu_H\Pi_V\alpha_{V1}}{k_1k_2k_4\Pi_H\mu_V}}, \sqrt{\frac{\phi_2\alpha_{H2}\mu_H\Pi_V\alpha_{V2}}{k'_1k'_2k'_4\Pi_H\mu_V}} \right\} = \max\{R_1, R_2\} \quad (2.10)$$

The total basic reproduction number, denoted by R_0 , is defined as the maximum of the two strain specific reproduction numbers, each corresponding to the spectral radius of the one-strain next generation block. Biologically, $R_i > 1$ implies that strain i can successfully invade a wholly susceptible host-vector system in the absence of the other strain. When $\max(R_1, R_2) < 1$ all small outbreaks die out and the disease-free equilibrium remains locally asymptotically stable. Conversely, when $\max(R_1, R_2) > 1$, at least one strain can persist in the population. Because reinfection and antibody-dependent enhancement (ADE) enter the model nonlinearly, a backward bifurcation may occur: for some intermediate range $R_c < \max(R_1, R_2) < 1$, a stable endemic equilibrium can coexist with the disease-free state, implying that the condition $R_0 < 1$ is necessary but not sufficient for complete disease elimination. We observe that the expression for the basic reproduction number R_0 for our model (2.4) is closely related to the expression obtained by [Garba and Gumel \(2010\)](#) in. Furthermore, as described in more detail in [Van den Driessche and Watmough \(2002\)](#) in the section on multi-strain epidemic models, (2.10) is essentially the maximum of the two eigenvalues corresponding to the two strains of the dengue virus. Each of

these eigenvalues is completely independent of the other and depends only on the parameters governing the dynamics of one particular serotype of the dengue virus. [Esteva and Vargas \(2003\)](#) have explored in detail this phenomenon and studied its implications on the co-existence of different strains of dengue in a population. The local stability of the DFE now holds due to Theorem 2 of [Van den Driessche and Watmough \(2002\)](#).

3.2 Sensitivity Analysis of R_0

In order to explore the model's robustness and determine the factors that most influence dengue transmission, a global sensitivity analysis of the basic reproduction number (R_0) is performed using the partial rank correlation coefficient (PRCC) approach. All key epidemiological parameters were simultaneously varied within a range of their baseline values mentioned in Table 2 using Latin Hypercube Sampling (LHS). The PRCC quantifies the monotonic relationship between each input parameter and the output R_0 .

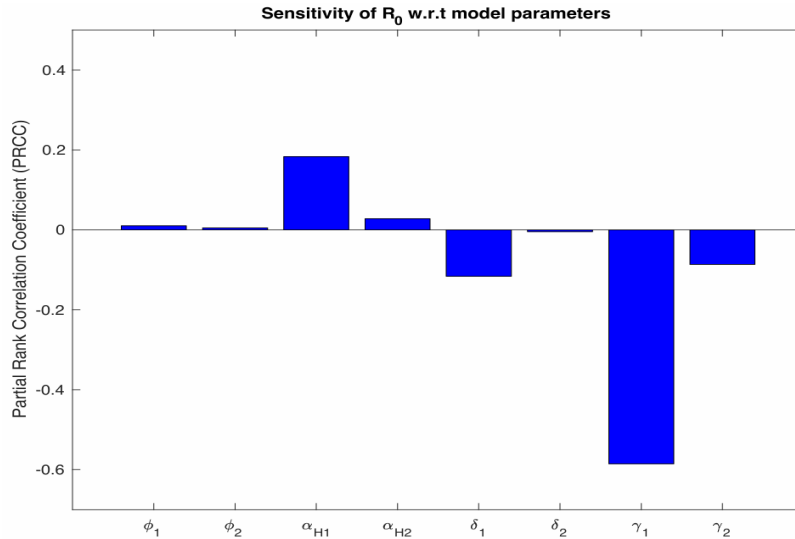


Figure 2: Sensitivity of the Basic Reproduction Number R_0 with Respect to key Model Parameters using the Partial Rank Correlation Coefficient (PRCC) Method.

Figure 2 shows that transmission coefficients (α_{H1}) exhibit the strongest positive correlations with R_0 , indicating that increases in host contact rates directly enhance the potential for disease spread. This confirms that higher host contact rates or stronger enhancement effects substantially increase dengue transmissibility. The recovery rates (γ_1) are negatively correlated to R_0 as the faster recovery will decrease the effective reproduction number.

LEMMA 2. The DFE, $\mathfrak{N}_0$, of the model (2.4) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$

Lemma 2 implies that, for $R_0 < 1$, a small influx of infectious individuals will not lead to a large outbreak of the disease. The epidemiological implication of the above result is that, given a sufficiently small influx of infectives, the disease can be eliminated from the population if the basic reproduction number R_0 can be brought down to and maintained at a value less than unity. To ensure that disease elimination is independent of the initial sizes of sub-populations, however, it is necessary to show that the DFE is globally asymptotically stable if $R_0 < 1$. As shall be shown later, the DFE is not globally asymptotically stable for $R_0 < 1$. Thus, lowering the basic reproduction number R_0 to a value less than unity is a necessary but not sufficient condition to ensure disease elimination.

4. Existence of Endemic Equilibria

In this section, the existence of endemic equilibria of the model (2.4) will be discussed. We define endemic equilibria to be those fixed points of the system (2.4) in which at least one of the infected compartments $E_1, I_1, E_{12}, I_{12}, E_2, I_2, E_{21}, I_{21}, V_{I1}, V_{I2}$ of the model is non-empty.

4.1 Existence of Partial Endemic Equilibria and Backward Bifurcations in Model (2.4)

We define partial endemic equilibria of the system (2.4) to be those fixed points of the system in which only one serotype of the dengue virus persists in the population. Mathematically, Let $\mathfrak{N}_1 =$

$(S^*, E_1^*, E_2^*, I_1^*, I_2^*, R_1^*, R_2^*, C_1^*, C_2^*, E_{12}^*, E_{21}^*, I_{12}^*, I_{21}^*, R^*, S_V^*, V_{I1}^*, V_{I2}^*)$ denote an arbitrary endemic equilibrium of the model (2.4). Then $\aleph_1$ is said to be a partial endemic equilibrium if

$$\min\{E_i^*, I_j^*, E_{ji}^*, I_{ji}^*, V_{Ii}^*\} \neq 0 \quad (2.11)$$

and

$$\max\{E_j^*, I_j^*, E_{ij}^*, I_{ij}^*, V_{Ij}^*\} = 0 \quad \text{for } i = (1, 2), j \neq i \quad (2.12)$$

We shall first prove the existence of such partial endemic equilibria of the system (2.4). Let $\aleph_2 = (S^{**}, E_1^{**}, E_2^{**}, I_1^{**}, I_2^{**}, R_1^{**}, R_2^{**}, C_1^{**}, C_2^{**}, E_{12}^{**}, E_{21}^{**}, I_{12}^{**}, I_{21}^{**}, R^{**}, S_V^{**}, V_{I1}^{**}, V_{I2}^{**})$ denote an arbitrary partial endemic equilibrium of the model (2.4). We may assume, without loss of generality, that conditions (2.11) and (2.12) hold for $i = 1$. The case for $i = 2$ will be identical. Therefore,

$$\aleph_2 = (S^{**}, E_1^{**}, 0, I_1^{**}, 0, R_1^{**}, 0, C_1^{**}, 0, 0, E_{21}^{**}, 0, I_{21}^{**}, R^{**}, S_V^{**}, V_{I1}^{**}, 0)$$

Solving the equations of the model (2.4) at steady-state in terms of the equilibrium value of the forces of infection $\lambda_{V1}^{**}, \lambda_{V2}^{**}, \lambda_{H1}^{**}, \lambda_{H2}^{**}$ gives

$$\begin{aligned} S^{**} &= \frac{\Pi_H}{\mu_H + \lambda_{V1}^{**}} \\ E_1^{**} &= \frac{\Pi_H \lambda_{V1}^{**}}{k_1(\mu_H + \lambda_{V1}^{**})} \\ I_1^{**} &= \frac{\phi_1 \Pi_H \lambda_{V1}^{**}}{k_1 k_2 (\mu_H + \lambda_{V1}^{**})} \\ R_1^{**} &= \frac{\gamma_1 \phi_1 \Pi_H \lambda_{V1}^{**}}{k_1 k_2 k_3 (\mu_H + \lambda_{V1}^{**})} \\ C_1^{**} &= \frac{\gamma_1 \omega_1 \phi_1 \Pi_H \lambda_{V1}^{**}}{k_1 k_2 k_3 (\mu_H + (1 - u_1) k_1) (\mu_H + \lambda_{V1}^{**})} \\ E_{21}^{**} &= 0 \\ I_{21}^{**} &= 0 \\ R^{**} &= \frac{\gamma_1 (1 - u_1) \omega_1 \phi_1 \Pi_H \lambda_{V1}^{**}}{k_1 k_2 k_3 (\mu_H + (1 - u_1) k_1) (\mu_H + \lambda_{V1}^{**})} \\ S_V^{**} &= \frac{\Pi_V}{\lambda_{H1}^{**} + \mu_V} \\ V_{I1}^{**} &= \frac{\lambda_{H1}^{**} \Pi_V}{k_4 (\lambda_{H1}^{**} + \mu_V)} \\ \lambda_{H1}^{**} &= 0 \\ \lambda_{H2}^{**} &= 0 \end{aligned} \quad (2.13)$$

From the definition of the force of infections λ_{V1} and λ_{H1} , we have

$$\lambda_{V1}^{**} N_H^{**} - \alpha_{V1} V_{I1}^{**} = 0$$

$$\lambda_{H1}^{**} N_H^{**} - \alpha_{H1} (I_{I1}^{**} + \eta_1 I_{21}^{**}) = 0$$

Now substituting the expressions in (2.1) and (2.13) into equations (2.14) and solving for λ_{H1}^{**} in terms of λ_{V1}^{**} yields:

$$\lambda_{H1}^{**} = \frac{k_3 \phi_1 \mu_H \alpha_{H1} \lambda_{V1}^{**}}{k_1 k_2 k_3 \mu_H + k_3 \phi_1 \mu_H \lambda_{V1}^{**} + k_2 k_3 \mu_H \lambda_{V1}^{**} + \gamma_1 \phi_1 \mu_H \lambda_{V1}^{**} + \gamma_1 \omega_1 \phi_1 \lambda_{V1}^{**}} \quad (2.15)$$

For brevity, we define the following constants:

$$\begin{aligned} Q_1 &= k_3 \phi_1 \mu_H \alpha_{H1} \\ Q_2 &= k_3 \phi_1 \mu_H + k_2 k_3 \mu_H + \gamma_1 \phi_1 \mu_H + \gamma_1 \omega_1 \phi_1 \\ Q_3 &= k_1 k_2 k_3 \mu_H \end{aligned} \quad (2.16)$$

so that (2.15) reduces to:

$$\lambda_{H1}^{**} = \frac{Q_1 \lambda_{v1}^{**}}{Q_3 + Q_2 \lambda_{v1}^{**}}$$

Now, plugging in the expression for λ_{H1}^{**} into equations (2.14) and simplifying yields a quadratic equation in terms of the force of infection λ_{v1}^{**} :

$$A(\lambda_{v1}^{**})^2 + B\lambda_{v1}^{**} + C = 0 \quad (2.17)$$

where

$$\begin{aligned} A &= \gamma_1 k_3 k_4 w_1 \phi_1^2 \mu_H \Pi_H \alpha_{H1} + \gamma_1 k_3 k_4 \phi_1^2 \mu_H^2 \Pi_H \alpha_{H1} + k_3^2 k_4 \phi_1^2 \mu_H^2 \Pi_H \alpha_{H1} + k_2 k_3^2 k_4 \phi_1 \mu_H^2 \Pi_H \alpha_{H1} \\ &+ 2\gamma_1^2 k_4 w_1 \phi_1^2 \mu_H \Pi_H \mu_V + 2\gamma_1 k_3 k_4 w_1 \phi_1^2 \mu_H \Pi_H \mu_V + 2\gamma_1 k_2 k_3 k_4 w_1 \phi_1 \mu_H \Pi_H \mu_V + \gamma_1^2 k_4 w_1^2 \phi_1^2 \Pi_H \mu_V \\ &+ \gamma_1^2 k_4 \phi_1^2 \mu_H^2 \Pi_H \mu_V + 2\gamma_1 k_3 k_4 \phi_1^2 \mu_H^2 \Pi_H \mu_V + 2\gamma_1 k_2 k_3 k_4 \phi_1 \mu_H^2 \Pi_H \mu_V + k_3^2 k_4 \phi_1^2 \mu_H^2 \Pi_H \mu_V \\ &+ 2k_2 k_3^2 k_4 \phi_1 \mu_H^2 \Pi_H \mu_V + k_3^2 k_3^2 k_4 \mu_H^2 \Pi_H \mu_V \\ B &= k_1 k_2 k_3^2 k_4 \phi_1 \mu_H^2 \Pi_H \alpha_{H1} + k_1 k_2 k_3^2 \phi_1 \mu_H^2 \alpha_{H1} \Pi_H \mu_V + 2\gamma_1 k_1 k_2 k_3 k_4 w_1 \phi_1 \mu_H \Pi_H \mu_V \\ &+ 2\gamma_1 k_1 k_2 k_3 k_4 \phi_1 \mu_H^2 \Pi_H \mu_V + 2k_1 k_2 k_3^2 k_4 \phi_1 \mu_H^2 \Pi_H \mu_V + 2k_1 k_3^2 k_3^2 k_4 \mu_H^2 \Pi_H \mu_V \\ C &= k_1^2 k_2^2 k_3^2 k_4 \mu_H^2 \Pi_H \mu_V - k_1 k_2 k_3^2 \phi_1 \mu_H^2 \alpha_{H1} \Pi_v \alpha_{1v} \\ &= k_1^2 k_2^2 k_3^2 k_4 \mu_H^2 \Pi_H \mu_V (1 - R_0^2) \end{aligned}$$

Therefore, similar to Garba et al. (2008) and Garba and Gumel (2010), we have established the following result:

Theorem 4.1. Let $\aleph_2$ represent an arbitrary partial equilibrium of the system (2.4) which satisfies conditions (2.11) and (2.12) for the case $i = 1$. Then $\aleph_2$ is

- a unique partial endemic equilibrium if $C < 0 \Leftrightarrow R_0 > 1$
- a unique partial endemic equilibrium if $B < 0$, and $C = 0$ or $B^2 - 4AC = 0$
- two distinct partial endemic equilibria if $C > 0, B < 0$ and $B^2 - 4AC > 0$
- no endemic equilibrium otherwise.

Furthermore, if case (iii) from above holds and we define RC as follows

$$R_c = \sqrt{1 - \frac{B^2}{4Ak_1^2 k_2^2 k_3^2 k_4 \mu_H^2 \Pi_H \mu_V}} \quad (2.18)$$

Then a backward bifurcation of the system (2.4) occurs for values of the basic reproduction number R_0 such that $R_c < R_0 < 1$ for the case when only one strain of the dengue virus is persisting in the population.

A similar result holds for partial endemic equilibria $\aleph_3$ which satisfy conditions (2.11) and (2.12) for the case $i = 2$.

5. Numerical Simulations

The model (2.4) exhibits extremely interesting behavior from a dynamical systems perspective. This includes non-trivial fixed points, bifurcations, and limit cycles. We shall use numerical simulations to show the existence of each of these. Here, we have defined the basic reproduction number R_0 of the model (2.4) as:

$$R_0 = \max \{R_1, R_2\}$$

Where:

$$\begin{aligned} R_1 &= \sqrt{\frac{\phi_1 \alpha_{H1} \mu_H \Pi_v \alpha_{v1}}{k_1 k_2 k_4 \Pi_H \mu_V}} \\ R_2 &= \sqrt{\frac{\phi_2 \alpha_{H2} \mu_H \Pi_v \alpha_{v2}}{k'_1 k'_2 k'_4 \Pi_H \mu_v}} \end{aligned}$$

We use numerical simulations to verify the theoretical results obtained in the previous sections. We first look at the behavior of the system for different values of R_0 and observe that the system is driven to the endemic, disease-free, and partial endemic states depending on the value of R_0 .

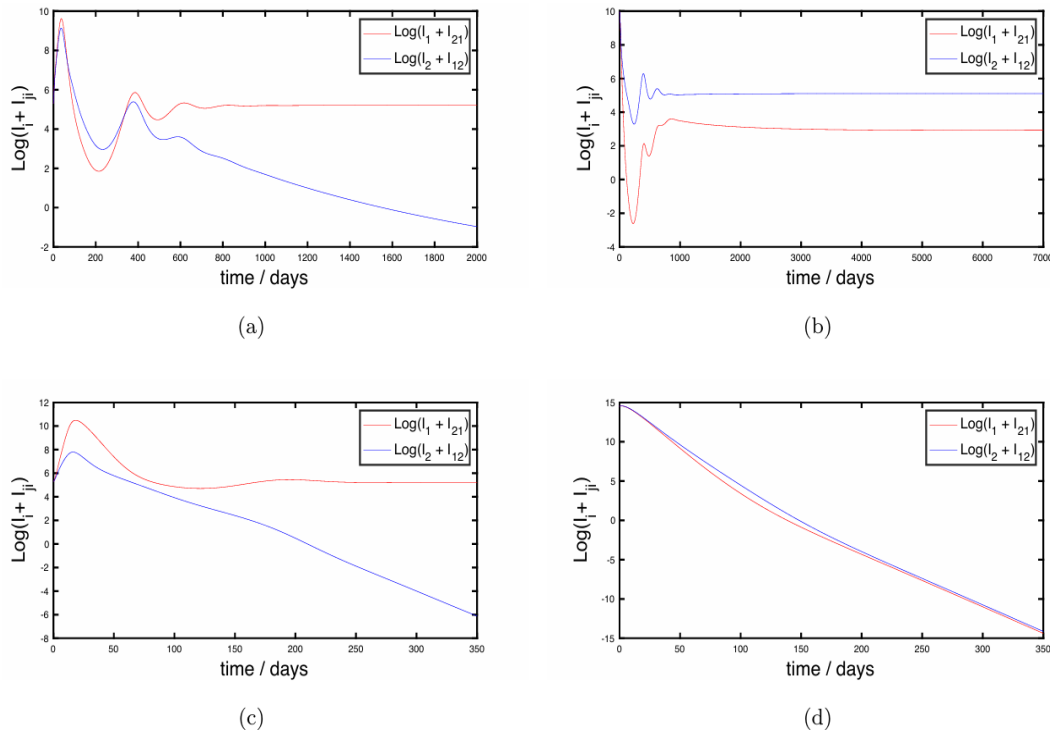


Figure 3: (a) Steady State Behavior of the Model (2.4) in which Strain 1 is Endemic while Strain 2 Dies Out for $1 > R_1 > R_2$, (b) both Strain 1 and Strain 2 are Endemic for $1 > R_1 > R_2$, (c) Strain 1 is Endemic while Strain 2 Dies Out for $R_1 > 1 > R_2$, (d) Disease-Free Behavior in which both Strains Die Out for $R_2 < R_1 < 1$. where $\eta_2 > \eta_1 > 1$ is for all Four Cases

In Figure 3, the steady-state behavior of a two-strain epidemic model is illustrated under different parameter regimes. In 3(a), the red curve representing strain 1 remains elevated while the blue curve for strain 2 declines over time, indicating that strain 1 becomes endemic while strain 2 dies out. Here 3(b) shows that both curves stabilize at nonzero levels, suggesting that both strains coexist and become endemic in the population. Similarly, 3(c) reveals that strain 1 persists while strain 2 rapidly diminishes, confirming the competitive exclusion of strain 2 despite both reproduction numbers being greater than one. In contrast, 3(d) is a disease-free state in which both strains die out.

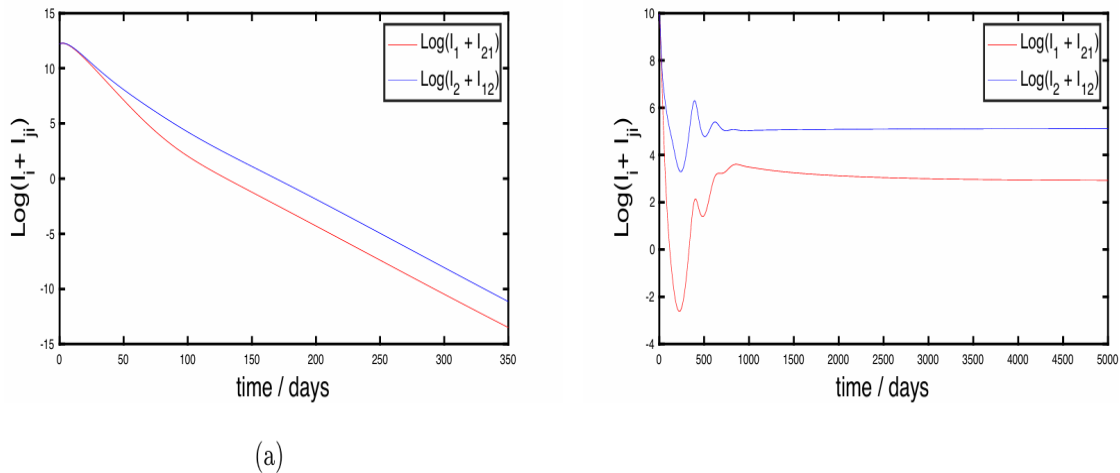


Figure 4: Bi-Stability Behavior of Model (2.4): (a) For a Lower Initial Infected Population, $I(0) = 10^2$, Both Strains Converge to the Disease-Free Equilibrium (DFE). (b) For a Higher Initial Infected Population, $I(0) = 10^4$, the System Evolves Toward an Endemic Equilibrium (Coexistence Via Backward Bifurcation), Epidemiologically Indicating Reinfection Risk in Populations with Partial Immunity, Despite Both Reproduction Numbers Being Below Unity $R_2 = 0.5905 < R_1 = 0.6602 < 1$).

Figure 4 ((a), (b)) illustrates the bi-stability behavior observed in the two-strain dengue model (2.4). Although both

basic reproduction numbers are below one ($R_2 = 0.5905 < R_1 = 0.6602 < 1$), the system exhibits qualitatively different outcomes based on the initial infected population. For a lower initial infection, the solution converges to the disease-free equilibrium (DFE), with both strains dying out. However, for a higher initial infection, the system evolves toward an endemic equilibrium. This behavior reflects a backward bifurcation phenomenon, where disease persistence is possible even when reproduction numbers are subcritical, due to nonlinear effects such as reinfection or antibody-dependent enhancement (ADE). These results highlight the importance of initial conditions in determining long-term disease dynamics and underscore the need for early intervention to prevent persistent outbreaks.

The following parameter values were used for Figure 5:

$$\begin{aligned} \Pi_H = 26; \quad \Pi_V = 2600; \quad \eta_1 = 1.4; \quad \eta_2 = 200; \quad \mu_H = \frac{1}{65} \frac{1}{365}; \quad \mu_V = \frac{26}{365}; \quad \phi_1 = \frac{73}{365}; \quad \phi_2 = \frac{73}{365}; \\ \gamma_1 = \frac{52}{365}; \quad \gamma_2 = \frac{52}{365}; \quad \delta_1 = \frac{0.18}{365}; \quad \delta_2 = \frac{0.18}{365}; \quad \delta_{V1} = 0; \quad \delta_{V2} = 0; \quad w_1 = \frac{12}{365}; \quad w_2 = \frac{12}{365}; \end{aligned}$$

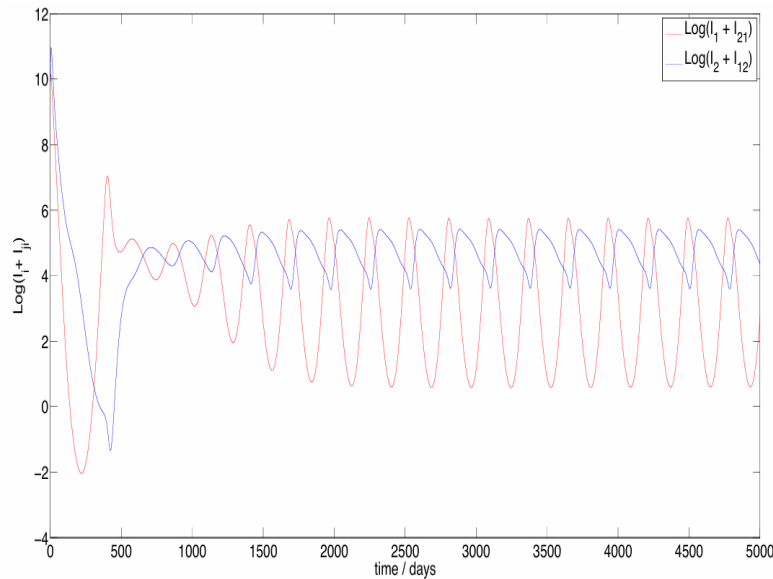


Figure 5: Steady State Behavior of the Model (2.4) in which the Total Number of Individuals Infected with Strain i of the Dengue Virus Over Time for $R_1 > 1 > R_2$

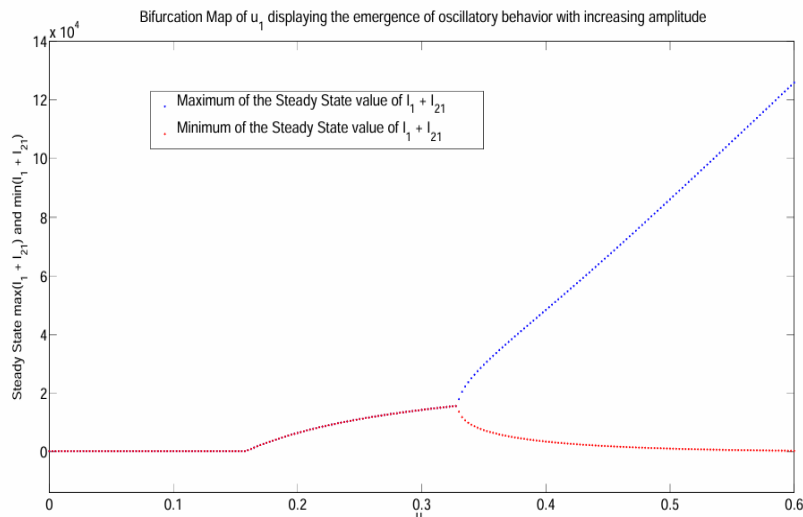


Figure 6: Bifurcation Diagram of u_1 which Shows the Emergence of Oscillations of Increasing Amplitudes as u_1 is Increased from Zero

The bifurcation diagram 6 illustrates how the system transitions from a stable steady state to oscillatory behavior as the cross-immunity parameter u_1 increases. Initially, $I_1 + I_{21}$ remains constant, but beyond a critical value of u_1 (around

0.33), sustained oscillations emerge, with their amplitude increasing as u_1 continues to rise. This indicates the onset of a Hopf bifurcation.

6. Optimal Vaccination Strategy

Optimal control theory has been used to make decisions in biological models; in particular, it has been very useful in formulating effective control strategies in epidemic models. Some examples of optimal control in epidemiological models from the literature are now discussed. [Fister et al. \(1998\)](#) used optimal control to design the treatment strategies in an HIV model. [Jung et al. \(2002\)](#) provide a very good example of deciding how to divide the efforts between two treatment strategies (case holding and case finding) of the two-strain TB model.

[K. Mumtaz et al. \(2024\)](#) examine the most effective vaccination strategy for an HPV model, when multiple vaccines are available by balancing cost, coverage, and efficacy. [Imran et al. \(2014\)](#) study optimal quarantine strategies in a two-population model for the transmission of Hep C.

When formulating an optimal control problem, the modeler needs to decide how and where to introduce the control (through vaccination, drug treatment, quarantine, etc.). The formulation of the optimal control problem must be a reasonable and practical representation of the situation to be considered so that the results are useful in informing public health authorities as to how to best control the epidemic. The form of optimal control depends on the system being analyzed and the objective function to be optimized. We will consider a quadratic dependence on the control in the objective function; this will be briefly justified when we discuss our formulation of the problem.

Control theory for models defined as a system of differential equations was formulated by [Pontryagin \(1918\)](#) and separately as an extension of initial work by Bellman in dynamic programming ([Naidu, 2018](#)). Initially applied to problems in engineering control theory, the applications of optimal control have grown considerably. The usual approach to optimal control in epidemiology has been to use Pontryagin's maximum principle. This technique optimizes a performance criterion (mostly cost and efficiency functional) that depends on control parameters appearing as time-dependent coefficients in the model. A different approach using neural nets has recently appeared in literature. [Yin et al. \(2023\)](#) represent optimal control functions using neural networks and train them via adjoint sensitivity analysis embedded in differential equations. Their approach enables both control and forecasting in epidemic models, offering insights into complex system dynamics.

In this study, we will find the most effective vaccination strategy by extending our original model to include a compartment for vaccinated hosts. We consider an imperfect vaccine and incorporate the effects of waning immunity. Recent advancements, such as the development of the Qdenga vaccine, which offers protection against all four dengue virus serotypes regardless of prior infection, highlight the relevance of studying vaccination strategies in models of Dengue transmission. We will use deep neural nets to establish an optimal control policy that minimizes the burden of infection while minimizing the cost of control.

6.1 Extended Model and Control Setup

The system of equations is defined by 18 compartments, with an additional vaccinated host compartment V_H included, and a waning immunity rate ω allowing the transition from V_H to the susceptible host compartment S , where ϵ is the vaccine efficacy rate ($0 < \epsilon \leq 1$). The force of infection for the vector and host is given by:

$$\lambda_{Vi} = \frac{\alpha_{Vi}}{N_H} V_{Ii} \quad (1)$$

$$\lambda_{Hi} = \frac{\alpha_{Hi}}{N_H} (I_i + \eta_i I_{ji}) \quad (2)$$

The differential equations governing the dynamics of the system are:

$$\begin{aligned} \frac{dS}{dt} &= \Pi_H - (\lambda_{V1} + \lambda_{V2})S - \phi(t)S - \mu_H S + \omega V_H \\ \frac{dV_H}{dt} &= \phi(t)S - (1 - \epsilon)(\lambda_{V1} + \lambda_{V2})V_H - (\mu_H + \omega)V_H \\ \frac{dE_1}{dt} &= \lambda_{V1}S + (1 - \epsilon)\lambda_{V1}V_H - (\phi_1 + \mu_H)E_1 \\ \frac{dE_2}{dt} &= \lambda_{V2}S + (1 - \epsilon)\lambda_{V2}V_H - (\phi_2 + \mu_H)E_2 \end{aligned}$$

$$\begin{aligned}
\frac{dI_1}{dt} &= \phi_1 E_1 - (\gamma_1 + \delta_1 + \mu_H) I_1 \\
\frac{dI_2}{dt} &= \phi_2 E_2 - (\gamma_2 + \delta_2 + \mu_H) I_2 \\
\frac{dR_1}{dt} &= \gamma_1 I_1 - (w_1 + \mu_H) R_1 \\
\frac{dR_2}{dt} &= \gamma_2 I_2 - (w_2 + \mu_H) R_2 \\
\frac{dC_1}{dt} &= w_1 R_1 - (u_1 \lambda_{V2} + (1 - u_1) \kappa_1 + \mu_H) C_1 \\
\frac{dC_2}{dt} &= w_2 R_2 - (u_2 \lambda_{V1} + (1 - u_2) \kappa_2 + \mu_H) C_2 \\
\frac{dI_{21}}{dt} &= \phi_1 E_{21} - (\gamma_1 + \delta_1 + \mu_H) I_{21} \\
\frac{dI_{12}}{dt} &= \phi_2 E_{12} - (\gamma_2 + \delta_2 + \mu_H) I_{12} \\
\frac{dR}{dt} &= \gamma_1 I_{21} + \gamma_2 I_{12} + (1 - u_1) \kappa_1 C_1 + (1 - u_2) \kappa_2 C_2 - \mu_H R \\
\frac{dS_V}{dt} &= \Pi_V - (\lambda_{H1} + \lambda_{H2} + \mu_H) S_V \\
\frac{dV_{I1}}{dt} &= \lambda_{H1} S_V - (\delta_{V1} + \mu_V) V_{I1} \\
\frac{dV_{I2}}{dt} &= \lambda_{H2} S_V - (\delta_{V2} + \mu_V) V_{I2}
\end{aligned} \tag{3}$$

The vaccination rate is the control variable and is denoted by $\phi(t) \in [0,1]$. The goal is to minimize the following objective functional

$$J(\phi) = \int_0^T \left[I_1 + I_{12} + I_2 + I_{21} + \frac{W}{2} \phi(t)^2 \right] dt \tag{4}$$

The functional involves the total number of infected individuals and the cost of vaccination. Since the cost involves not only the price of the vaccine but also the cost of organizing and managing vaccinations, a nonlinear cost function has been proposed. In particular, we take a quadratic function used for measuring control cost, which is very common in the literature. The coefficient W is a balancing cost factor due to the scales of the different terms in the functional.

To determine the optimal control $\phi(t)$, a neural network is employed to establish the optimal vaccination. This function determines the rate at which susceptible individuals are vaccinated over time and is optimized to minimize both the number of infected individuals and the cost of vaccination. To determine $\phi(t)$, we use a fully connected feedforward neural network with the following architecture:

- Input: Model parameters, initial conditions, time horizon T
- Hidden Layers: Two layers with 128 neurons each, using the Tanh activation function
- Output Layer: Single neuron with Sigmoid activation, scaled by a constant factor (0.7)

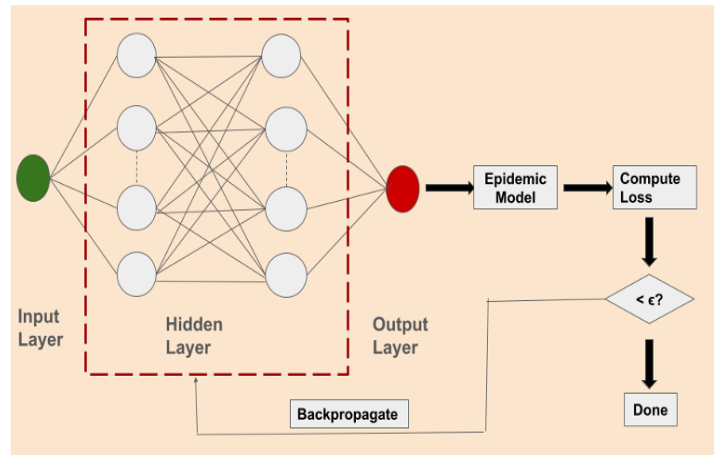


Figure 7: Neural Network Architecture

Algorithm 1: Optimal Vaccination Control for Two-Strain Epidemic Model (3)

-
- Input: Model Parameters, Initial Conditions, Time Horizon T , Number of Time Steps N_t
-
- Initialize Neural Network $\phi(t; \theta)$ with parameters θ (Weights and Biases), which Outputs the Control value ϕ at each Time t
 - Define the Objective Functional:
$$J(\theta) = \int_0^T \left[I_{total}(t) + \frac{W}{2} \phi(t)^2 \right] dt$$
where, $I_{total}(t) = I_1(t) + I_2(t) + I_{12}(t) + I_{21}(t)$
 - Repeat Until Convergence:
 1. Simulate the ODE System with Current Control $\phi(t; \theta)$
 2. Compute $J(\theta^k)$
 3. Backpropagate: Compute $\nabla_{\theta} J(\theta^k)$ using Automatic Differentiation
 4. Update Parameters:
$$\theta^{k+1} = \theta^k - \eta \cdot \nabla_{\theta} J(\theta^k)$$
where η is the Learning Rate
-
- Return: Optimal Control $\phi(t)$, Simulated Infection Curves $I_{total}(t)$, and Final Functional Value J
-

Note: (3) we optimize the neural network parameters θ using modern optimizers. These include first-order methods such as Adam (2014); Kochenderfer and Wheeler (2019), Chapter 5), second-order methods such as L-BFGS Nocedal and Wright (2006); and Kochenderfer and Wheeler (2019), Chapter 6). All the ODEs are computed by numerically integrating the system dynamics using the odeint function from the torchdiffeq package. Integral terms appearing in the cost functional are approximated using discrete summation over time steps, effectively acting as a simple quadrature method.

6.2 Results

The system of ordinary differential equations is constructed and solved in Python using the PyTorch library and the torchdiffeq package, which provides an adaptive time-step ODE solver based on high order Runge–Kutta methods. The neural network parameters are optimized using the Adam optimizer with a learning rate of 0.001 for 2500 epochs to minimize the total infection functional. All simulations were run on Google Colab with GPU compute, allowing for automatic differentiation during optimization. The numerical integration was done over the interval $[0, T]$ with $T = 100$ days using 1000 time points and was generalized and processed in Pandas and visualized in Matplotlib. The loss function corresponds to a discretized version of $J(\phi)$ over a time grid. We also use Pontryagin's Maximum Principle for benchmarking and comparison purposes to determine the optimal control.

The comparison in Figures 8, 9 demonstrates that the neural network control produces a smoother and more consistent vaccination trajectory, closely approximating the *PMP* solution while maintaining slightly stronger vaccination efforts in the later phase. Both approaches lead to similar infection trends, with the neural network control slightly outperforming *PMP* in reducing total infections after the peak period.

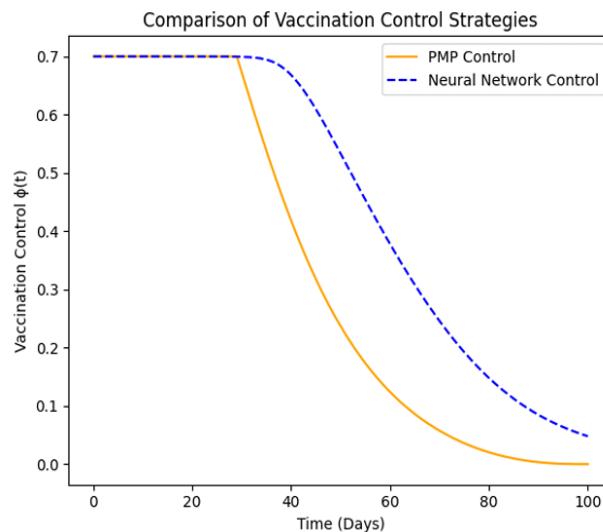


Figure 8: Comparative Result of Dengue Optimal Control using PMP and Neural Network Approach

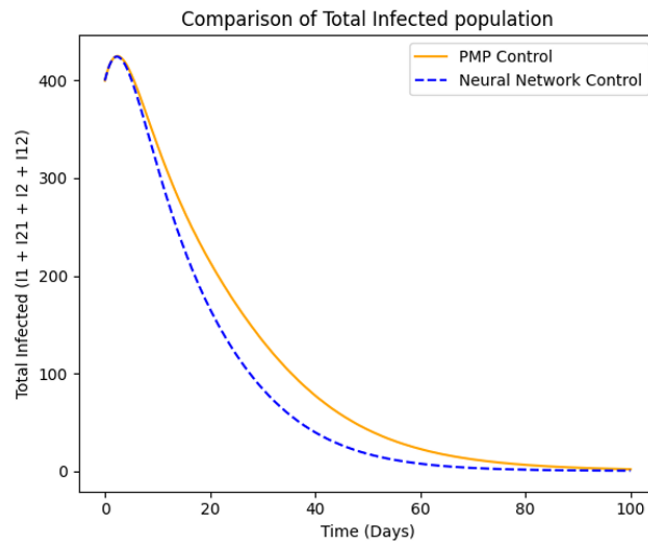


Figure 9: Comparative Result of Total Infected Population using PMP and Neural Network Approach

Although the NN method requires roughly twice the computational time, as shown in Table 3, its performance in terms of the functional is comparable. The additional cost is due to iterative training of the neural network. However, the NN approach offers a key advantage: it provides an alternative.

Table 3: Computational Time of PMP and NN.

PMP Functional $J(\phi)$		Time (s)		NN Functional $J(\phi)$	NN Time (s)
$\Delta t = 0.0001$	$\Delta t = 0.01$	$\Delta t = 0.0001$	$\Delta t = 0.01$	34620.94	2905
32989.36	35160.89	1322	957		

to PMP in situations where deriving and solving the adjoint system is challenging or impractical. This is particularly relevant for models with PDE constraints, higher-dimensional systems, or strong nonlinearities, where PMP can become analytically intractable and numerically unstable. In such cases, NN-based optimal control serves as a flexible and robust approximation tool despite its higher computation time.

Figure 10 illustrates the impact of varying vaccine efficacy on the optimal vaccination control strategy over time. In all cases, the vaccination control $\phi(t)$ starts at its maximum value of 0.7 and gradually decreases over 100 days. As efficacy increases, the rate at which the control decreases become steeper. This indicates, as expected, that higher vaccine efficacy allows for a more rapid relaxation of vaccination efforts since a more effective vaccine provides better protection with less frequent or intensive administration. Conversely, lower efficacy demands sustained higher control to achieve similar outcomes.

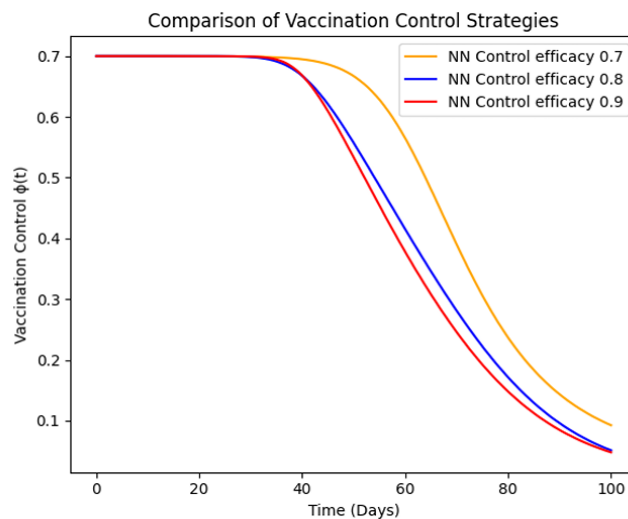


Figure 10: Dengue Optimal Control Using Neural Network Approach with Different Efficacy.

Figure 11 compares the control curves for different rates of waning. Similarly to the efficacy figure, all scenarios start with $\phi(t) = 0.7$, but the decline patterns differ based on the speed with which immunity diminishes. A higher waning rate (0.02) causes a slower decline in control, indicating the need for a more prolonged vaccination effort due to faster loss of immunity. In contrast, a lower waning rate (0.005) allows for a quicker reduction in vaccination control, as immunity persists longer. These results highlight that longer-lasting immunity reduces the need for sustained vaccination interventions.

Table 4: Values of the Functional at Waning Rate 0.005 for Different Efficacy.

Efficacy Rate	PMP Functional $J(\phi)$	NN Functional $J(\phi)$
0.7	36384.39	37297.27
0.8	32989.36	34620.94
0.9	27629.81	29210.67

Across scenarios, PMP achieved the lowest cost $J(\phi)$; the NN control matched PMP within 1–5% while offering better extensibility when costs or constraints are non-quadratic or when system parameters

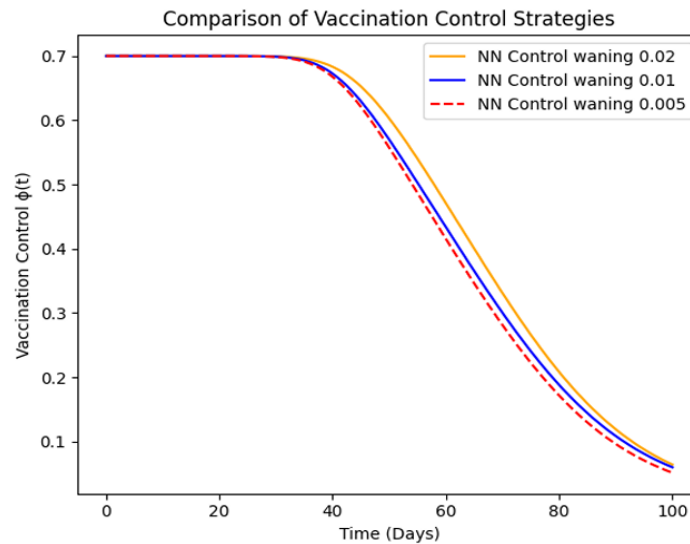


Figure 11: Dengue Optimal Control using Neural Network Approach with efficacy 0.8 and Different Waning Rates.

Table 5: Values of the Functional at Efficacy Rate 0.8 for Different Waning Rates.

Waning Rate	PMP Functional $J(\phi)$	NN Functional $J(\phi)$
0.005	32989.36	34620.78
0.01	33164.52	34831.01
0.02	33502.68	35227.94

are repeatedly varied.

7. Conclusion

In this work, we have considered a model for the transmission dynamics of two co-circulating strains of Dengue Virus. We include the effects of antibody-dependent enhancement, which has been shown to cause a more severe secondary infection from a different strain post-infection from the other.

We establish some basic properties of the model that show it is a feasible epidemiological model. We then derive an expression for the basic reproduction number R_0 and show that the disease-free equilibrium (DFE) is locally asymptotically stable when $R_0 < 1$. Numerical simulations are run to verify the result.

We determine the endemic states and boundary equilibria. We show that the system undergoes a backward bifurcation and the system is driven to the endemic state when $R_c < R_0 < 1$, i.e., the disease is endemic even though $R_0 < 1$ as long as $R_0 > R_c$, where R_c is the 'critical reproduction number'. Numerical simulations show that the system goes to the endemic or boundary equilibria depending on the value of R_0 . Bi-stable behavior established by the backward bifurcation is also shown numerically.

Further numerical exploration shows oscillatory behavior in the system, which shows the presence of a Hopf bifurcation and the existence of limit cycles for certain parameter values.

We extend the model to include a vaccinated compartment, taking into account an imperfect vaccine and waning vaccine efficacy. We set up an optimal control problem to determine the most efficient vaccination strategy. Such problems

have been mostly approached in the epidemiology literature using Pontryagin's maximum principle. We explore an alternative approach using deep neural networks. After establishing the neural network architecture and setting up the problem, we determine the optimal strategy. To benchmark our results, we compare them to those obtained using PMP and note good agreement, indicating that the NN approach can provide a viable alternative method for such problems in epidemiology. This will be particularly useful for problems with PDE constraints where PMP becomes rather difficult to apply. Finally, we determine the optimal vaccination strategies for different vaccine efficacies and waning rates. They can provide general guidelines to public health authorities to roll out Dengue vaccination programs in areas where the disease is endemic.

Our work shows that rich dynamics that can arise due interaction between heterologous strains of Dengue virus. In particular partial cross immunity can lead to oscillatory dynamics which have been observed for Dengue outbreaks. Furthermore, reinfection (due to partial cross immunity and ADE can lead to the infection being endemic in a population despite the basic reproduction number being less than unity. From a public health perspective this calls for a more robust year-round surveillance of the strains co-circulating in the population and more an informed vaccination strategies for disease control as simply bringing R_0 below unity may not ensure disease eradication.

As future extension of the work, we would like to extend the model to include age structure, as it has been shown that severe symptoms are more likely to arise in younger children and the elderly, leading to higher mortality. Another possible direction to extend the current study is to consider a patch model, where a severe outbreak has occurred in one of the patches and investigate the effective control strategies. As mentioned, determining the optimal vaccination strategy for such models is difficult using PMP, and the NN approach may find good use here. We would also like to explore whether the existence of a Hopf bifurcation observed numerically in the current study can be proved theoretically using dynamical systems theory. Finally, it would be interesting to see the effects of adding seasonality to the model and observe any qualitative changes to the dynamics that may occur.

8. Additional Information

Supplementary Information All codes and parameter files are available at: https://github.com/kinzamumtaz/Dengue_NN.git

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Appendix

A1: Theorem 2.1

Proof: Let $t_1 = \sup \{t > 0: S > 0, E_1 > 0, I_1 > 0, R_1 > 0, C_1 > 0, E_{12} > 0, I_{12} > 0, E_2 > 0, I_2 > 0, R_2 > 0, C_2 > 0, E_{21} > 0, I_{21} > 0, R > 0, S_V > 0, V_{11} > 0, V_{12} > 0\}$. Thus, $t_1 > 0$. It follows from the first equation of the model (2.1) that

$$\begin{aligned}\frac{dS}{dt} &= \Pi_H - (\lambda_{v1} + \lambda_{v2})S(t) - \mu_H S(t), \\ \frac{dS}{dt} + (\lambda_{v1} + \lambda_{v2})S(t) + \mu_H S(t) &= \Pi_H. \\ \frac{d}{dt} \{S(t)e^{\mu_H t + \int_0^t \lambda_{v1}(\tau) + \lambda_{v2}(\tau) d\tau}\} &= \Pi_H e^{\mu_H t + \int_0^t \lambda_{v1}(\tau) + \lambda_{v2}(\tau) d\tau} \\ \Rightarrow S(t_1)e^{\mu_H t_1 + \int_0^{t_1} \lambda_{v1}(\tau) + \lambda_{v2}(\tau) d\tau} - S(0) &= \int_0^{t_1} [\Pi_H e^{\mu_H y + \int_0^y (\lambda_{v1} + \lambda_{v2}) d\tau}] dy\end{aligned}$$

Therefore,

$$S(t_1) = S(0)e^{-\mu_H t_1 - \int_0^{t_1} (\lambda_{v1} + \lambda_{v2}) d\tau} + e^{-\mu_H t_1 - \int_0^{t_1} (\lambda_{v1} + \lambda_{v2}) d\tau} \int_0^{t_1} [\Pi_H e^{\mu_H y + \int_0^y (\lambda_{v1} + \lambda_{v2}) d\tau}] dy > 0$$

Similarly, it can be shown that $E_1 > 0, I_1 > 0, R_1 > 0, C_1 > 0, E_{12} > 0, I_{12} > 0, E_2 > 0, I_2 > 0, R_2 > 0, C_2 > 0, E_{21} > 0, I_{21} > 0, R > 0, S_V > 0, V_{11} > 0, V_{12} > 0$ for all $t > 0$.

We now prove a useful lemma.

A2: LEEMA 1

Proof: Adding the first 14 equations of the model (2.4) gives

$$\frac{dN_H}{dt} = \Pi_H - \mu_H N_H - \delta_1 I_1 - \delta_1 I_{21} - \delta_2 I_2 - \delta_2 I_{12} \leq \Pi_H - \mu_H N_H \quad (2.5)$$

Similarly, adding the last 3 equations of the model (2.4) gives

$$\frac{dN_V}{dt} = \Pi_V - \mu_V N_V - \delta_{v1} V_{I1} - \delta_{v2} V_{I2} \leq \Pi_V - \mu_V N_V \quad (2.6)$$

It follows from (2.5) that $\frac{dN_H}{dt} \leq 0$ if $N_H \geq \frac{\Pi_H}{\mu_H}$. Similarly, it follows from (2.6) that $\frac{dN_V}{dt} \leq 0$ if $N_V \geq \frac{\Pi_V}{\mu_V}$. Thus, a standard comparison theorem can be used to show that $N_H \leq N_H(0)e^{-\mu_H t} + \left(\frac{\Pi_H}{\mu_H}\right)(1 - e^{-\mu_H t})$ and $N_V \leq N_V(0)e^{-\mu_V t} + \left(\frac{\Pi_V}{\mu_V}\right)(1 - e^{-\mu_V t})$. In particular, $N_H(t) \leq \frac{\Pi_H}{\mu_H}$ if $N_H(0) \leq \frac{\Pi_H}{\mu_H}$, and $N_V(t) \leq \frac{\Pi_V}{\mu_V}$ if $N_V(0) \leq \frac{\Pi_V}{\mu_V}$. Thus, the regions D_1 and D_2 are positively invariant. Furthermore, if $N_H(0) > \frac{\Pi_H}{\mu_H}$, then either the solution of the first 14 equations of system (2.4) either D_1 in finite time, or $N_H(t)$ approaches $\frac{\Pi_H}{\mu_H}$ asymptotically. Similarly, if $N_V(0) > \frac{\Pi_V}{\mu_V}$, then either the solution of the last 3 equations of system (2.4) enters D_2 in finite time, or $N_V(t)$ approaches $\frac{\Pi_V}{\mu_V}$ asymptotically. Since the regions D_1 and D_2 are positively invariant, it is sufficient to consider the dynamics of the flow generated by model (2.4) in regions D_1 and D_2 , where the usual existence and uniqueness results hold for the system.