Advances in Differential Equations and Control Processes 2025, 32(4), 3720.
doi: https://doi.org/10.59400/adecp3720

Article

Global stability of antibody–based and CTL–based PDE models for secondary dengue infection

Ebtehal Almohaimeed[1], Ahmed Elaiw[2,*], Reem Aldubiban[2], Aatef Hobiny[2]

[1] Department of Mathematics, College of Science, Qassim University, P.O. Box 6644, Buraydah 51452, Saudi Arabia
[2] Department of Mathematics, Faculty of Science, King Abdulaziz University, P.O. Box 80203, Jeddah 21589, Saudi Arabia
*** Corresponding author:** Ahmed Elaiw, aelaiwksu.edu.sa@kau.edu.sa

CITATION

Almohaimeed E, Elaiw A, Aldubiban R, et al. Global stability of antibody–based and CTL–based PDE models for secondary dengue infection. Advances in Differential Equations and Control Processes. 2025; 32(4): 3720. https://doi.org/10.59400/adecp3720

ARTICLE INFO

Received: 12 October 2025
Revised: 1 November 2025
Accepted: 11 November 2025
Available online: 24 November 2025

Abstract: Infections caused by Flavivirus species, such as dengue virus (DENV), remain a significant public health concern. Because DENV has four antigenically distinct serotypes, a person can be reinfected after a first exposure. Existing within–host models, mostly based on ODEs, describe viral behavior during primary and secondary DENV infection but generally assume uniform mixing and ignore the spatial motion of cells and virions. The present work introduces two PDE models for secondary DENV infection. One captures antibody action against free virus, while the other represents cytotoxic T lymphocyte (CTL) destruction of infected cells. Immune cell production combines an intrinsic source term with a predator–prey–type activation mechanism. The study begins by verifying well-posedness through proofs of global existence and uniform bounds on all solutions. Equilibria are then determined, and the basic reproduction number is calculated to characterize the threshold separating clearance from persistence of infection. Lyapunov techniques, together with LaSalle's invariance principle, show that the infection–free equilibrium is globally asymptotically stable for $\mathcal{R}_0 \leq 1$, while the endemic state attracts all trajectories for $\mathcal{R}_0 > 1$. Numerical tests confirm the analytical results. A sensitivity investigation highlights the parameters with the greatest impact on secondary DENV dynamics.

Keywords: DENV infection; antibody immunity; CTL immunity; global stability; Lyapunov function; diffusion; latency; sensitivity analysis

1. Introduction

Dengue virus (DENV), the causative agent of dengue fever, continues to pose a major health burden in tropical and subtropical regions. It is one of the most widespread arboviruses worldwide and remains difficult to control. Recent reports show a sharp rise in infections: an estimated 14.1 million cases were documented globally in 2024, more than twice the 7 million recorded in 2023 and nearly twelve times higher than the 1.2 million reported in 2014 [1]. In the same year, 9508 deaths were attributed to dengue, corresponding to a case–fatality rate of 0.07% [1]. DENV is a positive–sense, single–stranded RNA virus belonging to the Flavivirus genus [2]. DENV comes from four known serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. A person infected with one type stays immune to that same type for life, but the resistance to the other types lasts only for a short time [3]. A second infection with a different serotype often leads to more severe disease [4]. The immune system of human body is the primary defense against DENV. When a human is infected with DENV, the body's innate and adaptive

immune responses work together to combat DENV. The innate immune response acts quickly, within hours, providing general protection against infections. The adaptive response takes longer to develop but targets the virus specifically and creates lasting memory [2]. Adaptive immunity has two main parts. The humoral part, controlled by B cells, generates antibodies that attach to and neutralize the virus. The cell–mediated part, led by cytotoxic T lymphocytes (CTLs), destroys DENV-infected cells directly.

1.1. Mathematical models for DENV infection

Within–host dengue models describe how the virus, healthy cells, and immune cells interact over time. By following infection growth and immune response, one can track how the disease develops and how it might be controlled. Examining the model allows the calculation of threshold levels, steady states, stability ranges, and how each parameter affects the outcome. From this, one can judge whether a treatment can clear the virus or if the infection is likely to persist. Several studies have focused on constructing within–host models for primary DENV infection (e.g., Sasmal et al. [2], Nuraini et al. [5], S. D. Perera and S. S. N. Perera [6–8], Clapham et al. [9], Ansari and Hesaaraki [10], Thibodeaux et al. [11], Modak and Muthu [12], Mishra and Gakkhar [13], Cerón Gómez and Yang [14]). On the other hand, several models have explored secondary DENV infections. Sasmal et al. [15] incorporated both humoral and CTL responses, while Boisov et al. [16] considered infectious and noninfectious virus particles alongside humoral and CTL immunity. Camargo et al. [17] examined the interplay between infection–enhancing and infection–neutralizing antibodies. Nikin–Beers and Ciupe [18] proposed models highlighting T cell cross–reactivity in disease severity, with the role of cross–reactive antibodies further analyzed in their study [19]. Ben–Shachar and Koelle [20] demonstrated how T cell–driven cytokine production may elevate disease severity. Alves Rubio et al. [21] investigated antibody–dependent enhancement during heterologous secondary infections and examined the impact of limited plasma cell cloning. Rashid et al. [22] combined deterministic and stochastic modeling with logistic cell growth, nonlinear transmission, and piecewise fractional differential equations. Gujarati and Ambika [23] developed a model considering two distinct antibody types. Alshaikh et al. [24] modeled the virus's capacity to infect multiple host cell types.

Elaiw et al. [25] introduced a viral infection model that accounts for two antibody groups. The model follows six time–dependent variables: uninfected cells $M(t)$, latently infected cells $E^L(t)$, actively infected cells $E^A(t)$, free virus $V(t)$, non–specific antibodies $W^N(t)$, and strain–specific antibodies $W^S(t)$. Their interaction is described by:

$$
\begin{cases}
\dfrac{dM}{dt} = \overbrace{\phi}^{\text{recruitment of uninfected cells}} - \overbrace{\varrho M}^{\text{death}} - \overbrace{\kappa\, MV}^{\text{infectious transmission}}, \\
\dfrac{dE^L}{dt} = \overbrace{(1\,-\,\xi)\,\kappa\, M\, V}^{\text{establishment of latent infection}} - \overbrace{\varphi E^L}^{\text{death}} - \overbrace{\mu E^L}^{\text{reactivation of latent cells}}, \\
\dfrac{dE^A}{dt} = \overbrace{\xi\,\kappa\, M\, V}^{\text{establishment of active infection}} + \overbrace{\mu E^L}^{\text{reactivation of latent cells}} - \overbrace{\delta E^A}^{\text{death}}, \\
\dfrac{dV}{dt} = \overbrace{\eta E^A}^{\text{production of viruses}} - \overbrace{\rho V}^{death} - \overbrace{\beta_N V W^N}^{\text{neutralization mediated by W}^{\text{N}}} - \overbrace{\beta_S V W^S}^{\text{neutralization mediated by W}^{\text{S}}}, \\
\dfrac{dW^N}{dt} = \overbrace{\gamma_N}^{\text{baseline production of non-specific antibodies}} + \overbrace{\lambda_N V W^N}^{\text{antibody activation}} - \overbrace{\psi_N W^N}^{death}, \\
\dfrac{dW^S}{dt} = \overbrace{\gamma_S}^{\text{baseline production of strain-specific antibodies}} + \overbrace{\lambda_S V W^S}^{\text{antibody activation}} - \overbrace{\psi_S W^S}^{\text{death}}.
\end{cases}
\tag{1}
$$

In a related study, Raezah et al. [26] analyzed secondary dengue infection by distinguishing two cytotoxic T–cell responses: T^N, triggered during primary infection and broadly reactive, and T^s, activated only by heterologous serotypes during reinfection. Their proliferation, decay, and cytolytic action were modeled through the rates $\alpha_N,\ \alpha_S$, (production), $\vartheta_N v_N T^N,\ \vartheta_S v_s T^s$ (stimulation), $v_N T^N$, $v_s T^s$ (decay), and $\zeta_N E^A T^N$, $\zeta_S E^A T^S$ (killing of infected monocytes). The resulting system is:

$$
\begin{cases}
\frac{dM}{dt} = \phi - \varrho M - \kappa MV, \\
\frac{dE^L}{dt} = (1-\xi)\kappa MV - (\mu+\varphi)E^L, \\
\frac{dE^A}{dt} = \xi\kappa MV + \mu E^L - \delta E^A - \zeta_N E^A T^N - \zeta_S E^A T^S, \\
\frac{dV}{dt} = \eta E^A - \rho V, \\
\frac{dT^N}{dt} = \alpha_N + \vartheta_N E^A T^N - v_N T^N, \\
\frac{dT^S}{dt} = \alpha_S + \vartheta_S E^A T^S - \nu_S T^S.
\end{cases}
\tag{2}
$$

Both studies [25,26] established that all state variables stay positive and bounded over time. Reproduction-like threshold values were identified to distinguish between infection clearance and persistence. The equilibria were examined for global stability using the Lyapunov approach. Numerical simulations were presented to illustrate how antibody and CTL responses influence the progression of infection. Models (1) and (2) assume that cells and viruses are evenly distributed, neglecting spatial movement and local interactions. This approach does not capture heterogeneity such as clustering of infected cells, formation of hotspots, or restricted viral spread, which can strongly affect infection dynamics and immune response. Including spatial dynamics provides a more realistic depiction of viral behavior. T cells have been shown to move along concentration gradients [27,28], and recent studies indicate that infected cells, immune cells, and virions may also migrate from areas of high to low density [29]. Elaiw and Alofi [30] accounted for the mobility of cells and viruses, and this approach was later extended by Raezah [31] to include multiple DENV target cell types. In both studies [30, 31], the dynamics of non-specific and strain-specific antibodies were described solely through virus-induced proliferation and natural degradation:

$$\frac{dW^N}{dt} = \lambda_N V W^N - \psi_N W^N,$$

$$\frac{dW^S}{dt} = \lambda_S V W^S - \psi_S W^S,$$

That is, antibody populations were assumed to expand only in response to viral stimulation, with no intrinsic or baseline production. The omission of self-regulated generation terms (γ_N and γ_S) simplifies the formulation but alters key threshold quantities. These formulations result in the survival of just a single antibody type, meaning that both types cannot persist simultaneously. When such terms are included, they explicitly contribute to the basic reproduction number, which becomes a decreasing function of and γ_S. Hence, baseline antibody recruitment enhances infection control, underscoring the relevance of incorporating these parameters in immune response models.

1.2. Aims and objectives of the present paper

The main contributions of this study are summarized below:

1. Two mathematical models are constructed to describe secondary DENV infection. One incorporates antibody–mediated immunity, while the other focuses on CTL responses. Both models are formulated as PDE systems that extend (1) and (2) by accounting for the spatial movement of cells and viral particles.
2. The basic reproduction numbers for the two systems are derived via the next–generation matrix approach.
3. Global stability of all equilibria is established through appropriately designed Lyapunov functions.
4. A sensitivity analysis is carried out to determine which parameters most strongly influence viral persistence through their effect on the reproduction numbers.
5. Numerical experiments are presented to support and illustrate the theoretical findings.

This work provides insight into critical components of the adaptive immune response to DENV, emphasizing how antibodies neutralize circulating virus and how CTLs target and remove actively infected monocytes. A deeper understanding of these mechanisms contributes to the rational design of effective antiviral therapies and vaccines.

The remainder of this paper is organized as follows. Sections 2 and 3 present two DENV infection models: one incorporating the antibody response and the other incorporating the CTL response. For each model, we establish well-posedness by proving the existence, uniqueness, and boundedness of solutions, and we perform a qualitative analysis that includes identifying the equilibria and examining their stability properties. Section 4 provides numerical simulations to illustrate and support the analytical findings. Finally, Section 5 summarizes the main results and outlines potential directions for future research.

2. DENV model with antibody response

2.1. Model formulation

This section formulates and introduces a PDEs model to capture the dynamics of secondary DENV infection. We start by examining the following key factors:

A1: DENV mainly targets uninfected monocytes and gains entry into these cells via direct virus–to– cell interaction.

A2: Infected monocytes can be classified into two categories: latently infected monocytes and actively infected monocytes.

A3: Two separate antibody populations exist: non–specific antibodies, generated during the primary infection in response to one DENV serotype, and strain–specific antibodies, which specifically target the new serotype encountered during reinfection.

A4: The model consists of six populations: uninfected monocytes $(M(x,\ t))$, latently infected monocytes $(E^L(x,\ t))$, actively infected monocytes $(E^A(x,\ t))$, free DENV particles $(V(x,\ t))$, non–specific antibodies $(W^N(x,\ t))$, and strain–specific antibodies $(W^S(x,\ t))$, where $t > 0$ represent time and $x \in \Omega$ denote spatial position. The spatial domain $\Omega \subset$ Rm, m $\geq$ 1, is assumed to be bounded, connected, and to have a smooth boundary $\partial\Omega$. The compartments $(M,\ E^L\ , E^A\ ,\ V, W^N, W^S)$ diffuse according to Fick's law, with diffusion terms given by $(D_M\Delta M, D_{E^L}\Delta E^L, D_{E^A}\Delta E^A, D_V\Delta V, D_{W^N}\Delta W^N, D_{W^S}\Delta W^S)$, respectively, where $\Delta = \frac{\partial^2}{\partial x^2}$ denotes the Laplacian operator [27,28].

A5: Uninfected monocytes are generated at a constant rate ϕ and are exposed to DENV at an infection rate kMV (refer to Equation (3)). Upon infection, a proportion $\xi \in [0, 1]$ transitions into the activated state, whereas the complementary fraction $1 - \xi$ stays in a latent form.

A6: Latent monocyte infections occur at a rate of $(1 - \xi)kMV$ and transition to the active state at μE^L, as shown in Equation (4). In contrast, actively infected monocytes are formed directly at a rate ξkMV (see Equation (5)).

A7: Virus particles are released from actively infected monocytes at a rate ηE^A. They are subsequently removed by immune mechanisms involving non–specific antibodies and strain–specific antibodies, acting at rates $\beta_N VW^N$ and $\beta_S VW^S$, respectively (refer to Equation (6)).

A8: Non–specific and strain–specific antibodies are generated at baseline rates and γ_S, respectively, while their expansion is driven by viral presence at $\lambda_N VW^N$and $\lambda_S VW^N$(see Equations (7)–(8)).

A9: The compartments $(M,\ E^L\ , E^A\ ,\ V, W^N, W^S)$ undergo natural decay, clearance, or death at rates $\varrho M, \varphi E^L, \delta E^A, \rho V, \psi_N W^N$, and $\psi_S W^S$, respectively.

Based on assumptions A1–A9, we formulate the dynamics of the DENV model

with diffusion as a system of six partial differential equations (PDEs):

$$\frac{\partial M(x,t)}{\partial t} = D_M \Delta M(x,t) + \phi - \varrho M(x,t) - \kappa M(x,t) V(x,t), \tag{3}$$

$$\frac{\partial E^L(x,t)}{\partial t} = D_{E^L} \Delta E^L(x,t) + (1-\xi)\kappa M(x,t) V(x,t) - (\mu + \varphi) E^L(x,t), \tag{4}$$

$$\frac{\partial E^A(x,t)}{\partial t} = D_{E^A} \Delta E^A(x,t) + \xi \kappa M(x,t) V(x,t) + \mu E^L(x,t) - \delta E^A(x,t), \tag{5}$$

$$\frac{\partial V(x,t)}{\partial t} = D_V \Delta V(x,t) + \eta E^A(x,t) - \rho V(x,t) - \beta_N V(x,t) W^N(x,t) - \beta_S V(x,t) W^S(x,t), \tag{6}$$

$$\frac{\partial W^N(x,t)}{\partial t} = D_{W^N} \Delta W^N(x,t) + \gamma_N + \lambda_N V(x,t) W^N(x,t) - \psi_N W^N(x,t), \tag{7}$$

$$\frac{\partial W^S(x,t)}{\partial t} = D_{W^S} \Delta W^S(x,t) + \gamma_S + \lambda_S V(x,t) W^S(x,t) - \psi_S W^S(x,t). \tag{8}$$

The initial conditions (ICs) are specified as follows:

$$\begin{cases} M{=}\epsilon_1(x), E^L(x,0){=}\epsilon_2(x), E^A(x,0){=}\epsilon_3(x), \\ V{=}\epsilon_4(x), W^N(x,0){=}\epsilon_5(x), W^S(x,0){=}\epsilon_6(x), \\ \epsilon_i(x) \geq 0, i{=}1,2,\ldots,6, \quad x \in \bar{\Omega}. \end{cases} \tag{9}$$

Here, the $\epsilon_i(x)$ functions are considered to be continuous. In addition, homogeneous Neumann boundary conditions (NBCs) are imposed as specified below:

$$\frac{\partial M}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^L}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^A}{\partial \overrightarrow{\varsigma}} = \frac{\partial V}{\partial \overrightarrow{\varsigma}} = \frac{\partial W^N}{\partial \overrightarrow{\varsigma}} = \frac{\partial W^S}{\partial \overrightarrow{\varsigma}} = 0, \ t > 0, \ x \in \partial\Omega. \tag{10}$$

In this context, $\frac{\partial}{\partial \overrightarrow{\varsigma}}$ represents the outward normal derivative along the boundary $\partial\Omega$. The parameter definitions corresponding to the model (3)–(8) are provided in **Table 1**.

Table 1. Variables and parameters description for model (3)–(8).

Variables	**Justification**
M	Uninfected monocytes
E^L	Latently infected monocytes
E^A	Actively infected monocytes
V	Free DENV virus
W^N	Non–specific antibodies
W^T	Strain–specific antibodies
Parameter	**Justification**
ϕ	Source of uninfected monocytes
ϱ	Death rate of uninfected monocytes
κ	Infection rate of uninfected monocytes by DENV
ξ	A portion of newly DENV–infected monocytes that activate
μ	Activation rate of latently DENV–infected monocytes
φ	Death rate of latently DENV–infected monocytes
δ	Death rate of actively DENV–infected monocytes
η	Production rate of DENV by actively DENV–infected monocytes

Table 1. *Cont.*

Variables	Justification
ρ	Death rate of free DENV particles
β_N	Neutralization rate of DENV particles due to non–specific antibodies
β_S	Neutralization rate of DENV particles due to strain–specific antibodies
γ_N	Source of non–specific antibodies
γ_S	Source of strain–specific antibodies
λ_N	Stimulation rate of non–specific antibodies
λ_S	Stimulation rate of strain–specific antibodies
ψ_N	Death rate of non–specific antibodies
ψ_S	Death rate of strain–specific antibodies
D_ℓ	Diffusion coefficient of compartments

Remark 1. *In this study, we use the bilinear infection term, which is standard in mathematical virology because it is simple and reflects direct contact between target cells and viruses [32]. The expression assumes that new infections occur at a rate proportional to the product of these two populations.*

Several modified infection terms have appeared in dengue models, such as:

- Saturated incidence:
$$\frac{\kappa MV}{1+\upsilon V}, \quad \upsilon \geq 0,$$
used in the study of Dubey et al. [33]. This form limits the infection rate at high viral loads, with an upper bound $\frac{k}{\upsilon}M$.

- Michaelis–Menten incidence:
$$\frac{\kappa MV}{K_m+V}, \quad K_m > 0,$$
considered in Xu et al.'s study [34]. This term also produces a finite maximum infection rate, which approaches κM as $V \to \infty$.

- Beddington–DeAngelis incidence:
$$\frac{\kappa MV}{1+\upsilon V+\varpi M}, \quad \varpi \geq 0,$$
where υV represents interference among viruses and ϖM represents interactions among uninfected cells [12,35].

- General incidence:
$\Psi(M,\, V)$,
where Ψ is an arbitrary nonlinear function [36].

Because detailed experimental estimates for dengue infection rates are limited, the bilinear term is used here as a practical first approximation.

2.2. Well-posedness of solutions

This section is devoted to verifying the fundamental qualitative properties of the model system (3)–(8), specifically focusing on the existence, non–negativity, and

boundedness of its solutions. Additionally, we identify all equilibrium points and determine the conditions necessary for their existence.

Let $\mathbb{N} = \mathbb{C}_b(\bar{\Omega}, \mathbb{R}^6)$, denote the space of all bounded and continuous functions mapping into $\mathbb{R}^6$, and define $\mathbb{N}_+ = \mathbb{C}_b\left(\bar{\Omega}, \mathbb{R}^6_+\right) \subset \mathbb{N}$ as the corresponding positive cone. This cone $\mathbb{N}_+$ induces a partial ordering on $\mathbb{N}$. The norm on this space is defined by $\|\Psi\|_{\mathbb{N}} = \sup_{x\in\bar{\Omega}} |\Psi(x)|$, where $|\cdot|$ represents the Euclidean norm in $\mathbb{R}^6$. Equipped with this norm, the space $(\mathbb{N}, \|\cdot\|_{\mathbb{N}})$ forms a Banach lattice [37,38].

2.2.1. Non-negativity and boundedness

For model (3)–(8) to be biologically acceptable, all variables must stay non–negative for every $t \geq 0$. If the initial data are non–negative, the solution of (3)–(8) remains in the non–negative range for all $t \geq 0$ [39].

Lemma 1. *Assuming that $D_M = D_{E^L} = D_{E^A} = D_V = D_{W^N} = D_{W^S} = \widetilde{D}$, the system defined by Equations. (3)–(8) admits a unique, non-negative, and bounded solution on $\overline{\Omega} \times [0, +\infty)$ for all initial conditions that satisfy (9).*

Proof. For any $\epsilon = (\epsilon_1, \epsilon_2, \epsilon_3, \epsilon_4, \epsilon_5, \epsilon_6)^{\mathrm{T}} \in \mathbb{N}_+$, we define the mapping $B = (B_1, B_2, B_3, B_4, B_5, B_6)^{\mathrm{T}}$: as follows:

$$\begin{cases} B_1(\epsilon)(x) = \phi - \varrho\epsilon_1(x) - \kappa\epsilon_1(x)\epsilon_4(x), \\ B_2(\epsilon)(x) = (1-\xi)\kappa\epsilon_1(x)\epsilon_4(x) - (\mu+\varphi)\epsilon_2(x), \\ B_3(\epsilon)(x) = \xi\kappa\epsilon_1(x)\epsilon_4(x) + \mu\epsilon_2(x) - \delta\epsilon_3(x), \\ B_4(\epsilon)(x) = \eta\epsilon_3(x) - \rho\epsilon_4(x) - \beta_N\epsilon_4(x)\epsilon_5(x) - \beta_S\epsilon_4(x)\epsilon_6(x), \\ B_5(\epsilon)(x) = \gamma_N + \lambda_N\epsilon_4(x)\epsilon_5(x) - \psi_N\epsilon_5(x), \\ B_6(\epsilon)(x) = \gamma_S + \lambda_S\epsilon_4(x)\epsilon_6(x) - \psi_S\epsilon_6(x). \end{cases}$$

It can be observed that B is locally Lipschitz continuous on $\mathbb{N}_+$. Accordingly, the system described by Equations (3)–(8), along with the ICs (9) and NBCs (10), can be reformulated as an abstract differential equation of the form:

$$\begin{cases} \frac{d\widetilde{Q}}{dt} = D\widetilde{Q} + B(\widetilde{Q}), t > 0, \\ \widetilde{Q_0} = \epsilon \in \mathbb{N}_+, \end{cases}$$

where $\widetilde{Q} = (M, E^L, E^A, V, W^N, W^S)^T$and

$$D\widetilde{Q} = \left(D_M\Delta M, D_{E^L}\Delta E^L, D_{E^A}\Delta E^A, D_V\Delta V, D_{W^N}\Delta W^N, D_{W^S}\Delta W^S\right)^T.$$

It can be demonstrated that

$$\lim_{h\to 0^+} \frac{1}{h}\mathrm{dist}\left(\epsilon(0) + hB(\epsilon), \mathbb{N}_+\right) = 0, \quad \text{for any } \epsilon \in \mathbb{N}_+.$$

As established in studies [37, 38, 40], the system described by (3)–(8) admits a unique, non–negative solution on the interval $[0, \ \sigma_{max})$ for any $\epsilon \in \mathbb{N}_+$, where $[0, \ \sigma_{max})$ denotes the maximal time interval of existence for the solution.

We now proceed to demonstrate the boundedness of all state variables. To this end, define $\Gamma(x,\ t)$ as follows:

$$\Gamma(x,t) = M(x,t) + E^L(x,t) + E^A(x,t) + \frac{\delta}{2\eta}V(x,t) + \frac{\delta\beta_N}{2\eta\lambda_N}W^N(x,t) + \frac{\delta\beta_S}{2\eta\lambda_S}W^S(x,t).$$

Utilizing the system (3)–(8), we derive

$$\begin{aligned}
\tfrac{\partial\Gamma(x,t)}{\partial t} &= \tfrac{\partial M(x,t)}{\partial t} + \tfrac{\partial E^L(x,t)}{\partial t} + \tfrac{\partial E^A(x,t)}{\partial t} + \tfrac{\delta}{2\eta}\tfrac{\partial V(x,t)}{\partial t} + \tfrac{\delta\beta_N}{2\eta\lambda_N}\tfrac{\partial W^N(x,t)}{\partial t} + \tfrac{\delta\beta_S}{2\eta\lambda_S}\tfrac{\partial W^S(x,t)}{\partial t} \\
&= D_M\Delta M(x,t) + \phi - \varrho M(x,t) - \kappa M(x,t)V(x,t) + D_{E^L}\Delta E^L(x,t) + (1-\xi)\kappa M(x,t)V(x,t) \\
&-(\mu+\varphi)E^L(x,t) + D_{E^A}\Delta E^A(x,t) + \xi\kappa M(x,t)V(x,t) + \mu E^L(x,t) - \delta E^A(x,t) + \tfrac{\delta}{2\eta}[D_V\Delta V(x,t) \\
&+\eta E^A(x,t) - \rho V(x,t) - \beta_N V(x,t)W^N(x,t) - \beta_S V(x,t)W^S(x,t)] + \tfrac{\delta\beta_N}{2\eta\lambda_N}[D_{W^N}\Delta W^N(x,t) \\
&+\gamma_N + \lambda_N V(x,t)W^N(x,t) - \psi_N W^N(x,t)] + \tfrac{\delta\beta_S}{2\eta\lambda_S}[D_{W^S}\Delta W^S(x,t) + \gamma_S W(x,t) + \lambda_S W(x,t) \\
&-\psi_s W^S(x,t)].
\end{aligned}$$

Given that $D_M = D_{E^L} = D_{E^A} = D_V = D_{W^N} = D_{W^S} = \widetilde{D}$, it follows that the diffusion coefficients across all corresponding components are identical, allowing the system to be treated with a unified diffusion parameter $\widetilde{D}$.

$$\begin{aligned}
\tfrac{\partial\Gamma(x,t)}{\partial t} = \widetilde{D}\ \Delta\Gamma(x,t) + \phi + \tfrac{\delta\beta_N\gamma_N}{2\eta\lambda_N} + \tfrac{\delta\beta_S\gamma_S}{2\eta\lambda_S} - \varrho M(x,t) - \varphi E^L(x,t) - \tfrac{\delta}{2}E^A(x,t) - \tfrac{\delta\rho}{2\eta}V(x,t) \\
-\tfrac{\delta\beta_N\psi_N}{2\eta\lambda_N}W^N(x,t) - \tfrac{\delta\beta_S\psi_S}{2\eta\lambda_S}W^S(x,t).
\end{aligned}$$

As a result,

$$\begin{aligned}
\tfrac{\partial\Gamma(x,t)}{\partial t} - \widetilde{D}\ \Delta\Gamma(x,t) &= \phi + \tfrac{\delta\beta_N\gamma_N}{2\eta\lambda_N} + \tfrac{\delta\beta_S\gamma_S}{2\eta\lambda_S} - \varrho M(x,t) - \varphi E^L(x,t) - \tfrac{\delta}{2}E^A(x,t) - \tfrac{\delta\rho}{2\eta}V(x,t) \\
&-\tfrac{\delta\beta_N\psi_N}{2\eta\lambda_N}W^N(x,t) - \tfrac{\delta\beta_S\psi_S}{2\eta\lambda_S}W^S(x,t) \\
&\le \phi + \tfrac{\delta\beta_N\gamma_N}{2\eta\lambda_N} + \tfrac{\delta\beta_S\gamma_S}{2\eta\lambda_S} - \Lambda\Gamma(x,t),
\end{aligned}$$

$\Lambda = \min\{\rho, \varphi, \frac{\delta}{2}, \rho, \psi_N, \psi_S\}$. Thus, $\Gamma(x,\ t)$ is governed by the following system:

$$\begin{cases}
\frac{\partial\Gamma(x,t)}{\partial t} - \widetilde{D}\Delta\Gamma(x,t) \le \phi + \frac{\delta\beta_N\gamma_N}{2\eta\lambda_N} + \frac{\delta\beta_S\gamma_S}{2\eta\lambda_S} - \Lambda\Gamma(x,t), \\
\frac{\partial\Gamma}{\partial\overrightarrow{\varsigma}} = 0, \\
\Gamma(x,0) = \epsilon_1(x) + \epsilon_2(x) + \epsilon_3(x) + \frac{\delta}{2\eta}\epsilon_4(x) + \frac{\delta\beta_N}{2\eta\lambda_N}\epsilon_5(x) + \frac{\delta\beta_S}{2\eta\lambda_S}\epsilon_6(x) \ge 0.
\end{cases}$$

Define $\Gamma(t)$as a solution to the following ODE:

$$\begin{cases}
\frac{d\widetilde{\Gamma}(t)}{dt} = \phi + \frac{\delta\beta_N\gamma_N}{2\eta\lambda_N} + \frac{\delta\beta_S\gamma_S}{2\eta\lambda_S} - \Lambda\widetilde{\Gamma}(t), \\
\widetilde{\Gamma}(0) = \max\limits_{x\in\overline{\Omega}}\Gamma(x,0).
\end{cases}$$

Consequently, we have

$$\widetilde{\Gamma}(t) \le \max\left\{\frac{\phi}{\Lambda} + \frac{\delta\beta_N\gamma_N}{2\eta\lambda_N\Lambda} + \frac{\delta\beta_S\gamma_S}{2\eta\lambda_S\Lambda}, \max_{x\in\overline{\Omega}}\Gamma(x,0)\right\}.$$

By applying the comparison principle as established in Protter and

Weinberger [41], it follows that

$$\Gamma(x,t) \leq \widetilde{\Gamma}(t).$$

Therefore,

$$\Gamma(x,t) \leq \max\left\{\frac{\phi}{\Lambda} + \frac{\delta\beta_N Y_N}{2\eta\lambda_N\Lambda} + \frac{\delta\beta_S Y_S}{2\eta\lambda_S\Lambda},\ \max_{x\in\Omega}\Gamma(x,0)\right\}.$$

This result implies that the $M(x,t), E^L(x,t), E^A(x,t), V(x,t), W^N(x,t)$, and $W^S(x,t)$ remain bounded on the domain $\bar{\Omega}\times[0,\sigma_{\max})$. By invoking the standard theory for sem–ilinear parabolic systems [42], it follows that. Consequently, the solution

$$(M(x,t),\ E^L(x,t),\ E^A(x,t),\ V(x,t),\ W^N(x,t),\ W^S(x,t))$$

is defined for all $x \in \Omega$, $t > 0$, and it is both unique and nonnegative. □

2.2.2. Equilibria and basic reproduction number

This section explores the existence of equilibria for the system described by Equations (3)–(8). The basic reproduction number, $\mathcal{R}_0$, measures the expected number of secondary infections generated by a single infected cell over its infectious period, assuming all target cells are initially susceptible [43]. To $\mathcal{R}_0$ for determine this DENV model, we apply the next–generation matrix approach as presented in the study of Driessche and Watmough [44]. For the system in Equations (3)–(8), $\mathcal{R}_0$ is calculated at the disease–free equilibrium, defined by:

$$EP_0 = (M_0, 0, 0, 0, W_0^N, W_0^S)$$

where $M_0 = \frac{\phi}{\varrho}$, $W_0^N = \frac{\gamma_N}{\psi_N}$, and $W_0^S = \frac{\gamma_S}{\psi_S}$. $\mathcal{R}_0$ is defined as the spectral radius, that is, the largest eigenvalue of the next–generation matrix, denoted by $\rho\left(FV^{-1}\right)$. In this formulation, F represents the Jacobian matrix of new infection terms, while V corresponds to the Jacobian matrix of transition terms, both evaluated at the EP_0. The explicit forms of F and V are systematically derived from the model equations as follows:

$$F = \begin{pmatrix} 0 & 0 & \frac{(1-\xi)\kappa\phi}{\varrho} \\ 0 & 0 & \frac{\xi\kappa\phi}{\varrho} \\ 0 & 0 & 0 \end{pmatrix}, V = \begin{pmatrix} \mu+\varphi & 0 & 0 \\ -\mu & \delta & 0 \\ 0 & -\eta & \rho + \frac{\beta_N\gamma_N}{\psi_N} + \frac{\beta_S\gamma_S}{\psi_S} \end{pmatrix}.$$

Consequently,

$$\mathcal{R}_0 = \rho\left(FV^{-1}\right) = \frac{\eta\kappa\phi(\mu+\xi\varphi)}{\delta\varrho\rho(\mu+\varphi)\left(\frac{\beta_N\gamma_N}{\psi_N\rho} + \frac{\beta_S\gamma_S}{\psi_S\rho} + 1\right)}.$$

It should be noted that $\mathcal{R}_0$ represents the basic reproduction number for DENV infection accounting for the effects of the antibody response. As a result, we derive the following key result concerning the existence of equilibria for the system described

by Equations (3)–(8). The model specified in Equations (3)–(8) admits an endemic equilibrium denoted by $EP_1 = (M_1, E_1^L, E_1^A, V_1, W_1^N, W_1^S)$

$$\phi - \varrho M_1 - \kappa M_1 V_1 = 0,$$

$$(1-\xi)\kappa M_1 V_1 - (\mu+\varphi)E_1^L = 0,$$

$$\xi\kappa M_1 V_1 + \mu E_1^L - \delta E_1^A = 0,$$

$$\eta E_1^A - \rho V_1 - \beta_N V_1 W_1^N - \beta_S V_1 W_1^S = 0,$$

$$\gamma_N + \lambda_N V_1 W_1^N - \psi_N W_1^N = 0,$$

$$\gamma_S + \lambda_S V_1 W_1^S - \psi_S W_1^S = 0.$$

Lemma 2. *System (3)–(8) exhibits the following behavior [25]:*

(I) *When $\mathcal{R}_0 \leq 1$, the model possesses a unique disease-free equilibrium, denoted by EP_0.*

(II) *When $\mathcal{R}_0 > 1$, an endemic equilibrium EP_1 emerges in addition to the disease-free equilibrium EP_0.*

2.3. Global stability

In this section, we investigate the global asymptotic stability of all equilibrium points of the model defined by Equations (3)–(8) through the construction of Lyapunov functions. The methodology for constructing these Lyapunov functions is inspired by the frameworks presented in Hattaf et al.'s studies [45,46].

To verify the validity of Theorems 1–2, we introduce the auxiliary function and make use of the arithmetic–geometric mean inequality:

$$\frac{\sum_{\ell=1}^{n} S_\ell}{n} \geq \left(\prod_{\ell=1}^{n} S_\ell\right)^{\frac{1}{n}}, \; S_\ell \geq 0, \ell = 1, 2, \ldots, n$$

which leads to the following set of inequalities:

$$\begin{aligned} \frac{M_1}{M} - \frac{MVE_1^A}{M_1 V_1 E^A} - \frac{E^A V_1}{E_1^A V} &\geq 3, \\ \frac{M_1}{M} - \frac{MVE_1^L}{M_1 V_1 E^L} = \frac{E^A V_1}{E_1^A V} - \frac{E^L E_1^A}{E_1^L E^A} &\geq 4. \end{aligned} \tag{11}$$

Applying the Neumann boundary conditions specified in Equation (10) and utilizing the divergence theorem, we obtain:

$$0 = \int_{\partial\Omega} \nabla Q \cdot \overrightarrow{\varsigma}\, dx = \int_{\Omega} div(\nabla Q)\, \mathrm{d}x = \int_{\Omega} \Delta Q\, \mathrm{d}x,$$

$$0 = \int_{\partial\Omega} \frac{1}{Q}\nabla Q \cdot \overrightarrow{\varsigma}\, dx = \int_{\Omega} div\left(\frac{1}{Q}\nabla Q\right) \mathrm{d}x = \int_{\Omega} \left(\frac{\Delta Q}{Q} - \frac{\|\nabla Q\|^2}{Q^2}\right) dx.$$

Consequently, for each $Q \in \{M,\ E^L,\ E^A,\ V,\ W^N,\ W^S\}$, the following identities hold:

$$\begin{aligned} \int_\Omega \Delta Q \, \mathrm{d}x = 0, \\ \int_\Omega \frac{\Delta Q}{Q} \, \mathrm{d}x = \int_\Omega \frac{\|\nabla Q\|^2}{Q^2} \, \mathrm{d}x. \end{aligned} \tag{12}$$

For notational simplicity, we omit the dependence on space and time, denoting $(M, E^L, E^A, V, W^N, W^S) = (M(x,t), E^L(x,t), E^A(x,t), V(x,t), W^N(x,t), W^S(x,t))$. Let $\widehat{\Theta}_i$ denote a candidate

Lyapunov function defined by:

$$\widehat{\Theta}_i(t) = \int_\Omega \Theta_i(x,t) \, \mathrm{d}x, \quad i = 0, 1.$$

We define Φ'_i as the largest invariant set within:

$$\Phi_i = \left\{ (M, E^L, E^A, V, W^N, W^S) : \frac{d\widehat{\Theta}_i}{dt} = 0 \right\}, \ i = 0, 1.$$

Theorem 1. *Provided that $\mathcal{R}_0 \leq 1$, the disease-free equilibrium EP_0 of the model defined by Equations (3)–(8) is globally asymptotically stable (GAS).*

Proof. Define $\Theta_0(x,t)$ as:

$$\begin{aligned} \Theta_0(x,t) \ = M_0 \mathcal{L}\left(\tfrac{M}{M_0}\right) + \tfrac{\mu}{\mu+\xi\varphi} E^L + \tfrac{\mu+\varphi}{\mu+\xi\varphi} E^A + \tfrac{\delta(\mu+\varphi)}{\eta(\mu+\xi\varphi)} V + \tfrac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)} W_0^N \mathcal{L}\left(\tfrac{W^N}{W_0^N}\right) \\ + \tfrac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)} W_0^S \mathcal{L}\left(\tfrac{W^S}{W_0^S}\right). \end{aligned}$$

It is evident that for any $(M, E^L, E^A, V, W^N, W^S) > 0$, while satisfying the condition $\widehat{\Theta}_0(M_0, 0, 0, 0, W_0^N, W_0^S) = 0$. The time derivative $\frac{\partial \Theta_0}{\partial t}$ is computed along the trajectories of the system defined by Equations (3)–(8) as follows:

$$\begin{aligned} \tfrac{\partial \Theta_0}{\partial t} \ = \left(1 - \tfrac{M_0}{M}\right) \tfrac{\partial M}{\partial t} + \tfrac{\mu}{\mu+\xi\varphi} \tfrac{\partial E^L}{\partial t} + \tfrac{\mu+\varphi}{\mu+\xi\varphi} \tfrac{\partial E^A}{\partial t} + \tfrac{\delta(\mu+\varphi)}{\eta(\mu+\xi\varphi)} \tfrac{\partial V}{\partial t} + \tfrac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)} \left(1 - \tfrac{W_0^N}{W^N}\right) \tfrac{\partial W^N}{\partial t} \\ + \tfrac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)} \left(1 - \tfrac{W_0^S}{W^S}\right) \tfrac{\partial W^S}{\partial t}. \end{aligned}$$

By substituting the expressions from Equations (3)–(8) into the formulation, we arrive at the following expression:

$$\begin{aligned} \tfrac{\partial \Theta_0}{\partial t} = \left(1 - \tfrac{M_0}{M}\right) \left(D_M \Delta M + \phi - \varrho M - \kappa M V\right) + \tfrac{\mu}{\mu+\xi\varphi} \left(D_{E^L} \Delta E^L + (1-\xi)\kappa M V - (\mu+\varphi) E^L\right) \\ + \tfrac{\mu+\varphi}{\mu+\xi\varphi} \left(D_{E^A} \Delta E^A + \xi\kappa M V + \mu E^L - \delta E^A\right) + \tfrac{\delta(\mu+\varphi)}{\eta(\mu+\xi\varphi)} \left(D_V \Delta V + \eta E^A - \rho V - \beta_N V W^N - \beta_S V W^S\right) \\ + \tfrac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)} \left(1 - \tfrac{W_0^N}{W^N}\right) \left(D_{W^N} \Delta W^N + \gamma_N + \lambda_N V W^N - \psi_N W^N\right) \\ + \tfrac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)} \left(1 - \tfrac{W_0^S}{W^S}\right) \left(D_{W^S} \Delta W^S + \gamma_S + \lambda_S V W^S - \psi_S W^S\right). \end{aligned}$$

Upon consolidation of the relevant terms

$$\begin{aligned}\frac{\partial \Theta_0}{\partial t} &= \left(1-\tfrac{M_0}{M}\right)(\phi-\varrho M)+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_0^N}{W^N}\right)\left(\gamma_N-\psi_N W^N\right)\\ &+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_0^S}{W^S}\right)\left(\gamma_S-\psi_S W^S\right)+\kappa M_0 V-\tfrac{\delta\rho(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_0^N V\\ &-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_0^S V+D_M\left(1-\tfrac{M_0}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\Delta E^A+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\Delta V\\ &+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_0^N}{W^N}\right)\Delta W^N+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_0^S}{W^S}\right)\Delta W^S.\end{aligned}$$

Employing the substitutions $\phi=\varrho M_0,\ \gamma_N=\psi_N W_0^N$, and $\gamma_S=\psi_S W_0^S$, we derive

$$\begin{aligned}\frac{\partial \Theta_0}{\partial t} &= -\tfrac{\varrho(M-M_0)^2}{M}-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\tfrac{(W^N-W_0^N)^2}{W^N}-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\tfrac{(W^S-W_0^S)^2}{W^S}\\ &+\left(\kappa M_0-\tfrac{\delta\rho(\mu+\varphi)}{\eta(\mu+\xi\varphi)}-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_0^N-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_0^S\right)V\\ &+D_M\left(1-\tfrac{M_0}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\Delta E^A+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\Delta V\\ &+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_0^N}{W^N}\right)\Delta W^N+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_0^S}{W^S}\right)\Delta W^S.\end{aligned}$$

Then

$$\begin{aligned}\frac{\partial \Theta_0}{\partial t} &= -\tfrac{\varrho(M-M_0)^2}{M}-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\tfrac{(W^N-W_0^N)^2}{W^N}-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\tfrac{(W^S-W_0^S)^2}{W^S}\\ &+\tfrac{\delta\rho(\mu+\varphi)\left(\frac{\beta_N\gamma_N}{\psi_N\rho}+\frac{\beta_S\gamma_S}{\psi_S\rho}+1\right)}{\eta(\mu+\xi\varphi)}\left(\frac{\eta\kappa\varphi(\mu+\xi\varphi)}{\delta\varrho\rho(\mu+\varphi)\left(\frac{\beta_N\gamma^N}{\psi_N\rho}+\frac{\beta_S\gamma^S}{\psi_S\rho}+1\right)}-1\right)V+D_M\left(1-\tfrac{M_0}{M}\right)\Delta M\\ &+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\Delta E^\Lambda+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\Delta V+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_0^N}{W^N}\right)\Delta W^N\\ &+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_0^S}{W^S}\right)\Delta W^S.\end{aligned}$$

Upon computing the time derivative, expressed as $\frac{d\widehat{\Theta}_0}{dt}=\int_\Omega\frac{\partial\Theta_0}{\partial t}dx$, the following result is derived

$$\begin{aligned}\frac{d\widehat{\Theta}_0}{dt} &= -\varrho\int_\Omega\tfrac{(M-M_0)^2}{M}-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\int_\Omega\tfrac{(W^N-W_0^N)^2}{W^N}-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\int_\Omega\tfrac{(W^S-W_0^S)^2}{W^S}dx\\ &+\tfrac{\delta\rho(\mu+\varphi)\left(\frac{\beta_N\gamma_N}{\psi_N\rho}+\frac{\beta_S\gamma_S}{\psi_S\rho}+1\right)(\mathcal{R}_0-1)}{\eta(\mu+\xi\varphi)}\int_\Omega V dx+D_M\int_\Omega\left(1-\tfrac{M_0}{M}\right)\Delta M dx\\ &+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\int_\Omega\Delta E^L dx+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\int_\Omega\Delta E^A dx+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\int_\Omega\Delta V dx\\ &+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\int_\Omega\left(1-\tfrac{W_0^N}{W^N}\right)\Delta W^N dx+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\int_\Omega\left(1-\tfrac{W_0^S}{W^S}\right)\Delta W^S dx.\end{aligned}$$

Utilizing the relation given in (12), the above expression is transformed into the following form:

$$\begin{aligned}\frac{d\widehat{\Theta}_0}{dt} &= -\varrho\int_\Omega\tfrac{(M-M_0)^2}{M}dx-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\int_\Omega\tfrac{(W^N-W_0^N)^2}{W^N}dx-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\int_\Omega\tfrac{(W^S-W_0^S)^2}{W^S}dx\\ &+\tfrac{\delta\rho(\mu+\varphi)\left(\frac{\beta_N\gamma_N}{\psi_N\rho}+\frac{\beta_S\gamma_S}{\psi_S\rho}+1\right)(\mathcal{R}_0-1)}{\eta(\mu+\xi\varphi)}\int_\Omega V dx-D_M M_0\int_\Omega\tfrac{||\nabla M||^2}{M^2}dx\\ &-\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}W_0^N\int_\Omega\tfrac{||\nabla W^N||^2}{W^{N^2}}dx-\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}W_0^S\int_\Omega\tfrac{||\nabla W^S||^2}{W^{S^2}}dx.\end{aligned}$$

Given that $R_0\le 1$, it follows that $\frac{d\widehat{\Theta}_0}{dt}\le 0$. Equality holds, i.e., $\frac{d\widehat{\Theta}_0}{dt}=0$ when $M=M_0$, $W^N=W_0^N$, $W^S=W_0^S$, and $(\mathcal{R}_0-1)\int_\Omega V dx=0$. The solutions of

the system defined by Equations (3) through (8) asymptotically approach the set Φ'_0 as time progresses. Each element of Φ'_0 satisfies the conditions $M = M_0, W^N = W_0^N, W^S = W_0^S$, and

$$(R_0 - 1)\int_\Omega V dx = 0. \tag{13}$$

Thus, $\frac{\partial M}{\partial t} = \frac{\partial W^N}{\partial t} = \frac{\partial W^S}{\partial t} = \Delta M = \Delta W^N = \Delta W^S$ and then, the investigation can be structured around two distinct scenarios:

S-1. $\mathcal{R}_0 = 1$. From Equation (3), it follows that

$$0 = \frac{\partial M}{\partial t} = \phi - \varrho M_0 - \kappa M_0 V \quad \Rightarrow \quad V(x,t) = 0, \tag{14}$$

and then $\frac{dV}{dt} = \Delta V = 0$. Applying in Equation (6), we obtain

$$0 = \frac{\partial V}{\partial t} = \eta E^A \quad \Rightarrow \quad E^A(x,t) = 0. \tag{15}$$

Thus, $\frac{dV}{dt} = \Delta E^A = 0$. Similarly, Equation (5) implies that

$$0 = \frac{\partial EA}{\partial t} = \mu E^L \quad \Rightarrow \quad E^L(x,t) = 0. \tag{16}$$

Hence, the set Φ'_0 reduces to $\{EP_0\}$.

S-2. $\mathcal{R}_0 < 1$. According to Equation 13 we have $\int_\Omega V dx = 0 \Rightarrow V = 0$. Furthermore, from Equations 15 through 16 it directly follows that $E^A = E^L = 0$. Consequently, the set Φ'_0 reduce to the disease-free equilibrium, denoted by $\{EP_0\}$.

By virtue of LaSalle's invariance principle (LIP) [47], EP_0 is GAS. □

Theorem 2. *The endemic equilibrium EP_1 associated with the model given by Equations (3)–(8) exhibits GAS under the condition that $\mathcal{R}_0 > 1$.*

Proof. Construct $\Theta_1(x,t)$ as:

$$\Theta_1(x,t) = M_1\mathcal{L}\left(\frac{M}{M_1}\right) + \frac{\mu}{\mu+\xi\varphi}E_1^L\mathcal{L}\left(\frac{E^L}{E_1^L}\right) + \frac{\mu+\varphi}{\mu+\xi\varphi}E_1^A\mathcal{L}\left(\frac{E^A}{E_1^A}\right) + \frac{\delta(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1\mathcal{L}\left(\frac{V}{V_1}\right)$$
$$+\frac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}W_1^N\mathcal{L}\left(\frac{W^N}{W_1^N}\right) + \frac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}W_1^S\mathcal{L}\left(\frac{W^S}{W_1^S}\right).$$

Obviously, $\widehat{\Theta}_1(M, E^L, E^A, V, W^N, W^S) > 0$ for any $M, E^L, E^A, V, W^N, W^S > 0$ and $\widehat{\Theta}_1(M_1, E_1^L, E_1^A, V_1, W_1^N, W_1^S) = 0$. Evaluating $\frac{\partial\Theta_1}{\partial t}$ along the trajectories of system (3)–(8) yields:

$$\frac{\partial\Theta_1}{\partial t} = \left(1 - \frac{M_1}{M}\right)\frac{\partial M}{\partial t} + \frac{\mu}{\mu+\xi\varphi}\left(1 - \frac{E_1^L}{E^L}\right)\frac{\partial E^L}{\partial t} + \frac{\mu+\varphi}{\mu+\xi\varphi}\left(1 - \frac{E_1^A}{E^A}\right)\frac{\partial E^A}{\partial t} + \frac{\delta(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1 - \frac{V_1}{V}\right)\frac{\partial V}{\partial t}$$
$$+\frac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1 - \frac{W_1^N}{W^N}\right)\frac{\partial W^N}{\partial t} + \frac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1 - \frac{W_1^S}{W^S}\right)\frac{\partial W^S}{\partial t}.$$

Upon insertion of the equations from model (3)–(8), the following expression is derived

$$\begin{aligned}\frac{\partial\Theta_1}{\partial t} &= \left(1-\tfrac{M_1}{M}\right)\left(D_M\Delta M+\phi-\varrho M-\kappa MV\right)+\tfrac{\mu}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\left(D_{E^L}\Delta E^L+(1-\xi)\kappa MV-(\mu+\varphi)E^L\right)\\ &+\tfrac{\mu+\varphi}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\left(D_{E^A}\,\Delta E^A+\xi\kappa MV+\mu E^L-\delta E^A\right)\\ &+\tfrac{\delta(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{V_1}{V}\right)\left(D_V\Delta V+\eta E^A-\rho V-\beta_N VW^N-\beta_S VW^S\right)\\ &+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)\left(D_{W^N}\Delta W^N+\gamma_N+\lambda_N VW^N-\psi_N W^N\right)\\ &+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)\left(D_{W^S}\Delta W^S+\gamma_S+\lambda_S VW^S-\psi_S W^S\right).\end{aligned}$$

After combining the terms

$$\begin{aligned}\frac{\partial\Theta_1}{\partial t} &= \left(1-\tfrac{M_1}{M}\right)\left(\phi-\varrho M\right)+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)\left(\gamma_N-\psi_N W^N\right)\\ &+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)\left(\gamma_S-\psi_S W^S\right)+\kappa M_1V-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\tfrac{E_1^L}{E^L}\kappa MV+\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L\\ &-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\tfrac{E_1^A}{E^A}\kappa MV-\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}\tfrac{E_1^A}{E^A}E^L+\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A-\tfrac{\delta\rho(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V-\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}\tfrac{V_1}{V}E^A\\ &+\tfrac{\delta\rho(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W^N+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W^S-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_1^NV\\ &-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_1^SV+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A\\ &+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{V_1}{V}\right)\Delta V+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)\Delta W^N+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)\Delta W^S.\end{aligned}$$

With reference to the equilibrium conditions for EP_1 below

$$\begin{aligned}\phi &= \varrho M_1+\kappa M_1V_1,\\ (1-\xi)\kappa M_1V_1 &= (\mu+\varphi)E_1^L,\\ \xi\kappa M_1V_1+\mu E_1^L &= \delta E_1^A,\\ \gamma_N &= \psi_N W_1^N-\lambda_N V_1W_1^N,\\ \gamma_S &= \psi_S W_1^S-\lambda_S V_1W_1^S.\end{aligned}$$

We get

$$\begin{aligned}\frac{\partial_1}{\partial t} &= -\tfrac{\varrho(M-M_1)^2}{M}-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\tfrac{(W^N-W_1^N)^2}{W^N}-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\tfrac{(W^S-W_1^S)^2}{W^S}\\ &+\left(1-\tfrac{M_1}{M}\right)\kappa M_1V_1-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)V_1W_1^N-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)V_1W_1^S\\ &+\left(\kappa M_1V_1-\tfrac{\delta\rho(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_1^NV_1-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}W_1^SV_1\right)\tfrac{V}{V_1}\\ &-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}M_1V_1\tfrac{MVE_1^L}{M_1V_1E^L}+\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}M_1V_1\tfrac{MVE_1^A}{M_1V_1E^A}\\ &-\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L\tfrac{E^LE_1^A}{E_1^LE^A}+\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A-\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A\tfrac{E^AV_1}{E_1^AV}+\tfrac{\delta\rho(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1\\ &+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W^N+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W^S+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L\\ &+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{V_1}{V}\right)\Delta V\\ &+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)\Delta W^N+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)\Delta W^S.\end{aligned}\tag{17}$$

We have

$$\kappa M_1V_1=\frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1+\frac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1,$$

$$\frac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L = \frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1$$

and

$$\begin{aligned}\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A &= \tfrac{(\mu+\varphi)}{\mu+\xi\varphi}\left(\xi\kappa M_1V_1+\mu E_1^L\right)\\ &= \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1+\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L\\ &= \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1.\end{aligned}$$

Using the above relation, Equation (17) becomes

$$\begin{aligned}\tfrac{\partial\Theta_1}{\partial t} &= -\tfrac{\varrho(M-M_1)^2}{M}-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\tfrac{(W^N-W_1^N)^2}{W^N}-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\tfrac{(W^S-W_1^S)^2}{W^S}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1V_1+\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1V_1-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)V_1W_1^N\\
&-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)V_1W_1^S-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{MVE_1^L}{M_1V_1E^L}+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\\
&-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{MVE_1^A}{M_1V_1E^A}-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{E^LE_1^A}{E_1^LE^A}+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\\
&+\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1-\tfrac{\xi(\mu+\varphi)}{(\mu+\xi\varphi)}\kappa M_1V_1\tfrac{E^AV_1}{E_1^AV}-\tfrac{\mu(1-\xi)}{(\mu+\xi\varphi)}\kappa M_1V_1\tfrac{E^AV_1}{E_1^AV}\\
&+\tfrac{\delta\rho(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W^N+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W^S+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W_1^N\\
&-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W_1^N+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W_1^S-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1W_1^S+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M\\
&+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{V_1}{V}\right)\Delta V\\
&+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)\Delta W^N+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)\Delta W^S.\end{aligned}$$

It follows that

$$\begin{aligned}\tfrac{\partial\Theta_1}{\partial t} &= -\tfrac{\varrho(M-M_1)^2}{M}-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\tfrac{(W^N-W_1^N)^2}{W^N}-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\tfrac{(W^S-W_S^N)^2}{W^S}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1V_1+\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1V_1-\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(2-\tfrac{W_1^N}{W^N}-\tfrac{W^N}{W_1^N}\right)V_1W_1^N\\
&-\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(2-\tfrac{W_1^S}{W^S}-\tfrac{W^S}{W_1^S}\right)V_{_1}W_1^S-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{MVE_1^L}{M_1V_1E}+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\\
&-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{MVE_1^A}{M_1V_1E^A}-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{E^LE_1^A}{E_1^LE^A}+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1+\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\\
&-\tfrac{\xi(\mu+\varphi)}{(\mu+\xi\varphi)}\kappa M_1V_1\tfrac{E^AV_1}{E_1^AV}-\tfrac{\mu(1-\xi)}{(\mu+\xi\varphi)}\kappa M_1V_1\tfrac{E^AV_1}{E_1^AV}+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1+\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\\
&+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A\\
&+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{V_1}{V}\right)\Delta V+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)\Delta W^N+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)\Delta W^S.\end{aligned}$$

This leads to

$$\begin{aligned}\tfrac{\partial\Theta_1}{\partial t} &= -\tfrac{\varrho(M-M_1)^2}{M}-\tfrac{\delta\beta_N\psi_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\tfrac{(W^N-W_1^N)^2}{W^N}-\tfrac{\delta\beta_S\psi_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\tfrac{(W^S-W_1^S)^2}{W^S}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\left(4-\tfrac{M_1}{M}-\tfrac{MVE_1^L}{M_1V_1E^L}-\tfrac{E^AV_1}{E_1^AV}-\tfrac{E^LE_1^A}{E_1^LE^A}\right)\\
&+\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\left(3-\tfrac{M_1}{M}-\tfrac{MVE_1^A}{M_1V_1E^A}-\tfrac{E^AV_1}{E_1^AV}\right)+\tfrac{\delta\beta_N(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\tfrac{(W^N-W_1^N)^2}{W^NW_1^N}V_1W_1^N\\
&+\tfrac{\delta\beta_S(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\tfrac{(W^S-W_1^S)^2}{W^SW_1^S}V_1W_1^S+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L\\
&+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A+\tfrac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\left(1-\tfrac{V_1}{V}\right)\Delta V+\tfrac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\left(1-\tfrac{W_1^N}{W^N}\right)\Delta W^N\\
&+\tfrac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\left(1-\tfrac{W_1^S}{W^S}\right)\Delta W^S.\end{aligned}$$

In accordance with the above, is obtained as:

$$\begin{aligned}\frac{d\widehat{\Theta}_1}{dt} &= -\varrho\int_\Omega \frac{(M-M_1)^2}{M}\mathrm{d}x - \frac{\delta\beta_N\gamma_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\int_\Omega \frac{(W^N-W_1^N)^2}{W^N W_1^N}\mathrm{d}x - \frac{\delta\beta_S\gamma_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\int_\Omega \frac{(W^S-W_1^S)^2}{W^S W_1^S}\mathrm{d}x\\ &+\frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(4-\frac{M_1}{M}-\frac{MVE_1^L}{M_1V_1E^L}-\frac{E^AV_1}{E_1^AV}-\frac{E^LE_1^A}{E_1^LE^A}\right)\mathrm{d}x\\ &+\frac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(3-\frac{M_1}{M}-\frac{MVE_1^A}{M_1V_1E^A}-\frac{E^AV_1}{E_1^AV}\right)\mathrm{d}x + D_M\int_\Omega\left(1-\frac{M_1}{M}\right)\Delta M\mathrm{d}x\\ &+\frac{\mu D_{E^L}}{\mu+\xi\varphi}\int_\Omega\left(1-\frac{E_1^L}{E^L}\right)\Delta E^L\mathrm{d}x + \frac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\int_\Omega\left(1-\frac{E_1^A}{E^A}\right)\Delta E^A\mathrm{d}x + \frac{\delta D_V(\mu+\varphi)}{\eta(\mu+\xi\varphi)}\int_\Omega\left(1-\frac{V_1}{V}\right)\Delta V\mathrm{d}x\\ &+\frac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\int_\Omega\left(1-\frac{W_1^N}{W^N}\right)\Delta W^N\mathrm{d}x + \frac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\int_\Omega\left(1-\frac{W_1^S}{W^S}\right)\Delta W^S\mathrm{d}x.\end{aligned}$$

Ultimately, by applying the identity given in (12), we derive:

$$\begin{aligned}\frac{d\widehat{\Theta}_1}{dt} &= -\varrho\int_\Omega \frac{(M-M_1)^2}{M}\mathrm{d}x - \frac{\delta\beta_N\gamma_N(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}\int_\Omega \frac{(W^N-W_1^N)^2}{W^N W_1^N}\mathrm{d}x - \frac{\delta\beta_S\gamma_S(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}\int_\Omega \frac{(W^S-W_1^S)^2}{W^S W_1^S}\mathrm{d}x\\ &+\frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(4-\frac{M_1}{M}-\frac{MVE_1^L}{M_1V_1E^L}-\frac{E^AV_1}{E_1^AV}-\frac{E^LE_1^A}{E_1^LE^A}\right)\mathrm{d}x\\ &+\frac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(3-\frac{M_1}{M}-\frac{MVE_1^A}{M_1V_1E^A}+\frac{E^AV_1}{E_1^AV}\right)\mathrm{d}x - D_MM_1\int_\Omega\frac{\|\nabla M\|^2}{M^2}\mathrm{d}x\\ &-\frac{\mu D_{E^L}}{\mu+\xi\varphi}E_1^L\int_\Omega\frac{||\nabla E^L||^2}{E^{L2}}\mathrm{d}x - \frac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}E_1^A\int_\Omega\frac{||\nabla E^A||^2}{E^{A2}}\mathrm{d}x - \frac{\delta Dv(\mu+\varphi)}{\eta(\mu+\xi\varphi)}V_1\int_\Omega\frac{||\nabla V||^2}{V^2}\mathrm{d}x\\ &-\frac{\delta\beta_N D_{W^N}(\mu+\varphi)}{\eta\lambda_N(\mu+\xi\varphi)}W_1^N\int_\Omega\frac{\left|\left|\nabla W^N\right|\right|^2}{W^{N2}}\mathrm{d}x - \frac{\delta\beta_S D_{W^S}(\mu+\varphi)}{\eta\lambda_S(\mu+\xi\varphi)}W_1^S\int_\Omega\frac{||\nabla W^S||^2}{W^{S2}}\mathrm{d}x.\end{aligned}$$

Table 2 presents a summary of the global stability conditions corresponding to the equilibria of the model defined by Equations (3)–(8).

Table 2. Criteria for the existence and global stability of equilibria in the model (3)–(8).

Equilibrium	Existence condition	Stability condition
$EP_0 = (M_0, 0, 0, 0, W^N, W^S)$	–	$\mathcal{R}_0 \leq 1$
$EP_1 = (M_1, E_1^L, E_1^A, V_1, W_1^N, W_1^S)$	$\mathcal{R}_0 > 1$	$\mathcal{R}_0 > 1$

Hence, it follows that $\frac{d\widehat{\Theta}_1}{dt} \leq 0$ for any $(M, E^L, E^A, V, W^N, W^S) > 0$. Furthermore, the derivative $\frac{d\widehat{\Theta}_1}{dt} = 0$,when $(M, E^L, E^A, V, W^N, W^S) = (M_1, E_1^L, E_1^A, V_1, W_1^N, W_1^S)$. Solution of the system tend to $\Phi_1' = \{EP_1\}$, and by LIP the equilibrium point EP_1 is GAS. □

3. Model with CTL response

In the previous section, we posited that DENV particles are cleared from the host through immune mechanisms involving both non–specific and strain–specific antibodies, which help prevent further infections.

In this section, we underscore the pivotal role of T cell–mediated immunity in the rational design of effective dengue vaccines, especially in light of the current lack of approved vaccines or antiviral therapies. According to a recent study [48], both $CD4^+$ and $CD8^+$ T cells are implicated in the immune response to DENV, contributing to both protective and pathogenic immune responses. Among these, $CD4^+$ T cells (CTLs) exhibit a protective function by identifying and eliminating infected host cells.

3.1. Model formulation

The previously discussed DENV dynamic model emphasized the role of antibodies in mediating viral clearance. In this section, rather than focusing on antibody effects, we analyze the influence of CTLs on the DENV dynamic system, as detailed below:

H1. *CTLs directed against the primary DENV infection are postulated to be elicited through the engagement of immunological memory pathways*.

H2. *Two immunologically distinct populations of CTLs have been characterized: non–specific CTLs (T^N), which are elicited during the primary DENV infection in response to a single serotype, and strain-specific CTLs (T^S), which are selectively activated upon exposure to a heterologous DENV serotype during secondary infection.*

H3. Actively infected monocytes are subject to cytolytic clearance mediated by both non–specific and strain–specific CTLs, occurring at rates denoted by $\zeta_N E^A T^N$ *and* $\zeta_S E^A T^S$, respectively. Experimental studies have demonstrated that during secondary heterologous DENV infections, non–specific CTLs exhibit reduced efficacy in targeting and eliminating infected cells relative to their strain–specific counterparts, as indicated by the inequality [18,49].

H4. *The induction of CTLs is governed by both self–regulatory mechanisms and interaction dynamics resembling a predator–prey framework. Non–specific and strain–specific CTLs are generated at constant rates, denoted by α_N and α_S, respectively. Their antigen–driven expansion is further characterized by the interaction terms $\vartheta_N E^A T^N$ and $\vartheta_S E^A T^S$, as detailed in Equations (23)–(24)*.

H5. *Analogous to the preceding model, the compartments and diffuse in accordance with Fick's law, characterized by diffusion terms $D_{T^N}\Delta T^N$ and $D_{T^S}\Delta T^S$, respectively. Additionally, these compartments undergo natural decay, clearance, or cell death at rates proportional to their densities, specifically $\nu_N T^N$ and $\nu_S T^S$, respectively. Each model component $\mathcal{K}(x,t)$undergoes diffusion within the domain at a rate governed by its corresponding diffusion coefficient $D_{\mathcal{K}}$ [27,28]*.

Given the aforementioned hypothesis, the dynamics of the diffusion–based DENV model that includes CTL response are represented by a system of six PDEs:

$$\frac{\partial M(x,t)}{\partial t} = D_M \Delta M(x,t) + \phi - \varrho M(x,t) - \kappa M(x,t) V(x,t), \tag{18}$$

$$\frac{\partial E^L(x,t)}{\partial t} = D_{E^L}\Delta E^L(x,t) + (1-\xi)\kappa M(x,t)V(x,t) - (\mu+\varphi)E^L(x,t), \tag{19}$$

$$\frac{\partial E^A(x,t)}{\partial t} = D_{E^A}\Delta E^A(x,t) + \xi\kappa M(x,t)V(x,t) + \mu E^L(x,t) - \delta E^A(x,t) - \zeta_N E^A(x,t)T^N(x,t) \tag{20}$$

$$-\zeta_S E^A(x,t)T^S(x,t), \tag{21}$$

$$\frac{\partial V(x,t)}{\partial t} = D_V \Delta V(x,t) + \eta E^A(x,t) - \rho V(x,t), \tag{22}$$

$$\frac{\partial T^N(x,t)}{\partial t} = D_{T^N}\Delta T^N(x,t) + \alpha_N + \vartheta_N E^A(x,t)T^N(x,t) - v_N T^N(x,t), \tag{23}$$

$$\frac{\partial T^S(x,t)}{\partial t} = D_{T^S}\Delta T^S(x,t) + \alpha_S + \vartheta_S E^A(x,t)T^S(x,t) - v_S T^S(x,t) \tag{24}$$

The parameters corresponding to the model described by Equations (18)–(24) are defined as follows. The terms and represent the killing rates of actively infected monocytes by non–specific CTLs and strain–specific CTLs, respectively. The parameters and α_S denote the source of non–specific and strain–specific CTLs. The stimulation rates of these CTL populations are given by ϑ_N (non–specific CTLs) and ϑ_S (strain–specific CTLs). Lastly, ν_N and ν_S represent the death rates of non–specific and strain–specific CTLs, respectively.

The corresponding ICs are specified as follows:

$$\begin{cases} M(x,0) = \varepsilon_1(x),\ E^L(x,0) = \varepsilon_2(x),\ E^A(x,0) = \varepsilon_3(x), \\ V(x,0) = \varepsilon_4(x),\ T^N(x,0) = \varepsilon_5(x),\ T^S(x,0) = \varepsilon_6(x), \\ \varepsilon_i(x) \geq 0,\ i = 1,2,\cdots,6,\ x \in \overline{\Omega}. \end{cases} \tag{25}$$

Similarly with $\epsilon_i(x)$, the functions $\varepsilon_i(x)$, are considered to be continuous. In addition, the NBCs corresponding to model (18)–(24) are imposed as outlined below:

$$\frac{\partial M}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^L}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^A}{\partial \overrightarrow{\varsigma}} = \frac{\partial V}{\partial \overrightarrow{\varsigma}} = \frac{\partial T^N}{\partial \overrightarrow{\varsigma}} = \frac{\partial T^S}{\partial \overrightarrow{\varsigma}} = 0,\ t > 0,\ x \in \partial\Omega. \tag{26}$$

3.2. Well-posedness of solutions

3.2.1. Non-negativity and boundedness

Lemma 3. *Assuming that $D_M = D_{E^L} = D_{E^A} = D_V = D_{T^N} = D_{T^S} = \widetilde{D}$, the system governed by Equations (18)–(24) possesses a unique, non-negative, and bounded solution on $\overline{\Omega} \times [0,+\infty)$ for any initial conditions satisfying (25).*

Proof. Let $\varepsilon = (\varepsilon_1,\varepsilon_2,\varepsilon_3,\varepsilon_4,\varepsilon_5,\varepsilon_6)^T \in \mathbb{N}_+$be given. We define the mapping $U = (U_1,U_2,U_3,U_4,U_5,U_6)^T : \mathbb{N}_+ \to \mathbb{N}$ as follows:

$$\begin{cases} U_1(\varepsilon)(x) = \phi - \varrho\varepsilon_1(x) - \kappa\varepsilon_1(x)\varepsilon_4(x), \\ U_2(\varepsilon)(x) = (1-\xi)\kappa\varepsilon_1(x)\varepsilon_4(x) - (\mu+\varphi)\varepsilon_2(x), \\ U_3(\varepsilon)(x) = \xi\kappa\varepsilon_1(x)\varepsilon_4(x) + \mu\varepsilon_2(x) - \delta\varepsilon_3(x) - \zeta_N\varepsilon_3(x)\varepsilon_5(x) - \zeta_S\varepsilon_3(x)\varepsilon_6(x), \\ U_4(\varepsilon)(x) = \eta\varepsilon_3(x) - \rho\varepsilon_4(x), \\ U_5(\varepsilon)(x) = \alpha_N + \vartheta_N\varepsilon_3(x)\varepsilon_5(x) - \nu_N\varepsilon_5(x), \\ U_6(\varepsilon)(x) = \alpha_S + \vartheta_S\varepsilon_3(x)\varepsilon_6(x) - \nu_S\varepsilon_6(x). \end{cases}$$

It can be verified that the mapping U is locally Lipschitz continuous on $\mathbb{N}_+$. Consequently, the system defined by Equations (18)–(24), together with the ICs (25) and NBCs (26), can be reformulated as DE of the form:

$$\begin{cases} \frac{d\widetilde{\mathcal{K}}}{dt} = D\widetilde{\mathcal{K}} + U(\widetilde{\mathcal{K}}),\ t > 0, \\ \widetilde{\mathcal{K}_0} = \varepsilon \in \mathbb{N}_+, \end{cases}$$

where $\widetilde{\mathcal{K}} = \left(M, E^L,\ E^A, V, T^N, T^S\right)^T$ and

$$D\widetilde{\mathcal{K}} = \left(D_M\Delta M, D_{E^L}\Delta E^L, D_{E^A}\Delta E^A, D_V\Delta V, D_{T^N}\Delta T^N, D_{T^S}\Delta T^S\right)^T.$$

It can be demonstrated that

$$\lim_{h\to 0^+}\frac{1}{h}\text{dist}\left(\varepsilon(0)+hU(\varepsilon), \mathbb{N}_+\right) = 0, \text{ for any } \varepsilon \in \mathbb{N}_+.$$

As demonstrated in studies of Zhang, Xu, and Smith et al. [37,38,40], the system defined by Equations (18)–(24) possesses a unique, non–negative solution over the interval for every $\varepsilon \in \mathbb{N}_+$, where $[0, \sigma_{\max})$ represents the maximal interval $[0, \sigma_{\max})$ over which the solution exists.

We now aim to establish that all state variables remain bounded. To facilitate this analysis, we introduce the function $\Psi(t)$, defined as follows:

$$\Psi(x,t) = M(x,t) + E^L(x,t) + E^A(x,t) + \frac{\delta}{2\eta}V(x,t) + \frac{\zeta_N}{\vartheta_N}T^N(x,t) + \frac{\zeta_S}{\vartheta_S}T^S(x,t).$$

By applying the system of Equations (18)–(24), we obtain the following derivation:

$$\begin{aligned}
\frac{\partial\Psi(x,t)}{\partial t} &= \frac{\partial M(x,t)}{\partial t} + \frac{\partial E^L(x,t)}{\partial t} + \frac{\partial E^A(x,t)}{\partial t} + \frac{\delta}{2\eta}\frac{\partial V(x,t)}{\partial t} + \frac{\zeta_N}{\vartheta_N}\frac{\partial T^N(x,t)}{\partial t} + \frac{\zeta_S}{\vartheta_S}\frac{\partial T^S(x,t)}{\partial t}\\
&= D_M\Delta M(x,t) + \phi - \varrho M(x,t) - \kappa M(x,t)V(x,t) + D_{E^L}\Delta E^L(x,t) + (1-\xi)\kappa M(x,t)V(x,t)\\
&-(\mu+\varphi)E^L(x,t) + D_{E^A}\Delta E^A(x,t) + \xi\kappa M(x,t)V(x,t) + \mu E^L(x,t) - \delta E^A(x,t) - \zeta_N E^A(x,t)T^N(x,t)\\
&-\zeta_S E^A(x,t)T^S(x,t) + \frac{\delta}{2\eta}\left[D_V\Delta V(x,t) + \eta E^A(x,t) - \rho V(x,t)\right] + \frac{\zeta_N}{\vartheta_N}[D_{T^N}\Delta T^N(x,t)\\
&+\alpha_N + \vartheta_N E^A(x,t)T^N(x,t) - v_N T^N(x,t)] + \frac{\zeta_S}{\vartheta_S}\left[D_{T^S}\Delta T^S(x,t) + \alpha_S + \vartheta_S E^A(x,t)T^S(x,t) - v_S T^S(x,t)\right].
\end{aligned}$$

Under the assumption that $D_M = D_{E^L} = D_{E^A} = D_V = D_{T^N} = D_{T^S} = \widetilde{D}$, it follows that

$$\begin{aligned}
\frac{\partial\Psi(x,t)}{\partial t} &= \widetilde{D}\Delta\Psi(x,t) + \phi + \frac{\zeta_N\alpha_N}{\vartheta_N} + \frac{\zeta_S\alpha_S}{\vartheta_S} - \varrho M(x,t) - \varphi E^L(x,t) - \frac{\delta}{2}E^A(x,t) - \frac{\delta\rho}{2\eta}V(x,t)\\
&-\frac{\zeta_N v_N}{\vartheta_N}T^N(x,t) - \frac{\zeta_S v_S}{\vartheta_S}T^S(x,t).
\end{aligned}$$

As a result,

$$\begin{aligned}
\frac{\partial\Psi(x,t)}{\partial t} - \widetilde{D}\Delta\Psi(x,t) &= \phi + \frac{\zeta_N\alpha_N}{\partial_N} + \frac{\zeta_S\alpha_S}{\partial_S} - \varrho M(x,t) - qE^L(x,t) - \frac{\delta}{2}E^A(x,t) - \frac{\delta\rho}{2\eta}V(x,t)\\
&-\frac{\zeta_N v_N}{\vartheta_N}T^N(x,t) - \frac{\zeta_S v_S}{\vartheta_S}T^S(x,t)\\
&\le \phi + \frac{\zeta_N\alpha_N}{\vartheta_N} + \frac{\zeta_S\alpha_S}{\vartheta_S} - \bar{\Lambda}\Psi(x,t),
\end{aligned}$$

where $\bar{\Lambda} = \min\{\varrho, \varphi, \frac{\delta}{2}, \rho, v_N, v_S\}$, Consequently, $\Psi(x,t)$ satisfies the following system:

$$\begin{cases}
\frac{\partial\Psi(x,t)}{\partial t} - \widetilde{D}\Delta\Psi(x,t) \le \phi + \frac{\zeta_N\alpha_N}{\vartheta_N} + \frac{\zeta s\alpha_S}{\vartheta_S} - \bar{\Lambda}\Psi(x,t),\\
\frac{\partial\Psi}{\partial\overrightarrow{\varsigma}} = 0,\\
\Psi(x,0) = \varepsilon_1(x) + \varepsilon_2(x) + \varepsilon_3(x) + \frac{\delta}{2\eta}\varepsilon_4(x) + \frac{\zeta_N}{\vartheta_N}\varepsilon_5(x) + \frac{\zeta_S}{\vartheta_S}\varepsilon_6(x) \ge 0.
\end{cases}$$

Define $\widetilde{\Psi}(t)$ as a solution to the following ODE:

$$\begin{cases} \frac{d\widetilde{\Psi}(t)}{dt} = \phi + \frac{\zeta_N \alpha_N}{\vartheta_N} + \frac{\zeta_S \alpha_S}{\vartheta_S} - \Lambda \widetilde{\Psi}(t), \\ \widetilde{\Psi}(0) = \max_{x \in \overline{\Omega}} \Psi(x, 0). \end{cases}$$

Hence, it follows that

$$\overline{\psi}(t) \leq \max \left\{ \frac{\phi}{\overline{\Lambda}} + \frac{\zeta_N \alpha_N}{\vartheta_N \overline{\Lambda}} + \frac{\zeta_S \alpha_S}{\vartheta_S \overline{\Lambda}}, \max_{x \in \overline{\Omega}} \Psi(x, 0) \right\}.$$

Employing the comparison principle as formulated by Protter and Weinberger [41], we deduce that $\Psi(x,\ t)\ \leq\ \widetilde{\Psi}(t)$.

Therefore,

$$\Psi(x,t) \leq \max \left\{ \frac{\phi}{\overline{\Lambda}} + \frac{\zeta_N \alpha_N}{\vartheta_N \overline{\Lambda}} + \frac{\zeta_S \alpha_S}{\vartheta_S \overline{\Lambda}}, \max_{x \in \overline{\Omega}} \Psi(x, 0) \right\}.$$

This result indicates that $M(x,t),\ E^L(x,t),\ E^A(x,t),\ V(x,t),\ T^N(x,t)$ and $T^S(x,t)$ remain bounded on the domain $\bar{\Omega} \times [0, \sigma_{\max})$. By applying the standard theory of semilinear parabolic systems [42], it follows that $\sigma_{\max} = +\infty$. Hence, the solution

$$(M(x,t), E^L(x,t), E^A(x,t), V(x,t), T^N(x,t), T^S(x,t))$$

exists for all $x \in \Omega, t > 0$, and is unique and nonnegative. □

3.2.2. Equilibria and basic reproduction number

Utilizing the next–generation matrix approach as presented in the study of Driessche and Watmough [44], we derive the basic reproduction number, $\widetilde{\mathcal{R}}_0$, for the DENV model described by Equations (18)–(24). The value of is computed at the disease–free equilibrium EP_0, which is defined as follows:

$$EP_0 = \left(M_0, 0, 0, 0, T_0^N, T_0^S\right).$$

where $M_0 = \frac{\phi}{\varrho}$, $T_0^N = \frac{\alpha_N}{v_N}$, and $\mathrm{T_0^S} = \frac{\alpha_S}{v_S}$. Following a procedure analogous to that used for model (3)–(8), we proceed to compute for model (18)–(24). To initiate this process, we define the following matrices:

$$\bar{F} = \begin{pmatrix} 0 & 0 & \frac{(1-\xi)\kappa\phi}{\varrho} \\ 0 & 0 & \frac{\xi\kappa\phi}{\varrho} \\ 0 & 0 & 0 \end{pmatrix}, \ \overline{V} = \begin{pmatrix} \mu + \varphi & 0 & 0 \\ -\mu & \delta + \frac{\alpha_N \zeta_N}{v_N} + \frac{\alpha_S \zeta_S}{v_S} & 0 \\ 0 & -\eta & \rho \end{pmatrix}.$$

Hence,

$$\widetilde{\mathcal{R}}_0 = \rho\left(\bar{F}\bar{V}^{-1}\right) = \frac{\eta\kappa\phi(\mu + \xi\varphi)}{\delta\varrho\rho(\mu + \varphi)\left(\frac{\alpha_N\zeta_N}{\delta v_N} + \frac{\alpha_S\zeta_S}{\delta v_S} + 1\right)}.$$

It is essential to highlight that represents the basic reproduction number corresponding to DENV infection in the presence of CTLs response. Consequently, we establish the following fundamental result regarding the existence of equilibrium

points for the system defined by Equations (18)–(24).

The system described by Equations (3)–(8) admits the existence of an endemic equilibrium, represented by $EP_1 = \left(M_1, E_1^L, E_1^A, V_1, T_1^N, T_1^S\right)$

$$\begin{aligned}
\phi + \varrho M_1 + \kappa M_1 V_1 = 0,\\
(1-\xi)\kappa M_1 V_1 - (\mu+\varphi)E_1^L = 0,\\
\xi\kappa M_1 V_1 + \mu E_1^L - \delta E_1^A - \zeta_N E_1^A T_1^N - \zeta_S E_1^A T_1^S = 0,\\
\eta E_1^A - \rho V_1 = 0,\\
\alpha_N + \vartheta_N E_1^A T_1^N - \nu_N T_1^N = 0,\\
a_S + \vartheta_S E_1^A T_1^S - v_S T_1^S = 0.
\end{aligned}$$

Lemma 4. *Let $\overline{\mathcal{R}}_0$ be the basic reproduction number corresponding to system (18)–(24) [26]. Then the system exhibits the following behavior:*

(I) *When $\overline{\mathcal{R}}_0 \leq 1$, the model possesses a unique disease-free equilibrium, denoted by EP_0.*

(II) *When $\overline{\mathcal{R}}_0 > 1$, an endemic equilibrium EP_1 emerges in addition to the disease-free equilibrium EP_0.*

3.3. Global stability

Let Ξ be the potential Lyapunov function and χ' be the largest invariant set of

$$\chi_i = \left\{(M, E^L, E^A, V, T^N, T^S) : \frac{d\bar{\Xi}_i}{dt} = 0\right\}, \quad i = 0, 1.$$

Theorem 3. *Assuming that the basic reproduction number satisfies $\overline{\mathcal{R}}_0 \leq 1$, the disease-free equilibrium EP_0 of the model given by Equations (18)–(24) is GAS.*

Proof. Define $\Xi_0(x,t)$ as:

$$\begin{aligned}
\Xi_0(x,t) \;&= M_0\mathcal{L}\left(\tfrac{M}{M_0}\right) + \tfrac{\mu}{\mu+\xi\varphi}E^L + \tfrac{\mu+\varphi}{\mu+\xi\varphi}E^A + \tfrac{\kappa M_0}{\rho}V + \tfrac{\zeta_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}T_0^N\mathcal{L}\left(\tfrac{T^N}{T_0^N}\right)\\
&\quad + \tfrac{\zeta_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}T_0^S\mathcal{L}\left(\tfrac{T^S}{T_0^S}\right).
\end{aligned}$$

It is evident $\overline{\Xi}_0(M, E^L, E^A, V, T^N, T^S) > 0$ that for any $M, E^L, E^A, V, T^N, T^S > 0$, while satisfying the condition $\overline{\Xi}_0(M_0, 0, 0, 0, T_0^N, T_0^S) = 0$. The time derivative $\frac{\partial\Xi_0}{\partial t}$ is computed along the trajectories of the system defined by Equations (18)–(24) as follows:

$$\begin{aligned}
\tfrac{\partial\Xi_0}{\partial t} \;&= \left(1 - \tfrac{M_0}{M}\right)\tfrac{\partial M}{\partial t} + \tfrac{\mu}{\mu+\xi\varphi}\tfrac{\partial E^L}{\partial t} + \tfrac{\mu+\varphi}{\mu+\xi\varphi}\tfrac{\partial E^A}{\partial t} + \tfrac{\kappa M_0}{\rho}\tfrac{\partial V}{\partial t} + \tfrac{\zeta_N(\mu+\varphi)}{\delta_N(\mu+\xi\varphi)}\left(1 - \tfrac{T_0^N}{T^N}\right)\tfrac{\partial T^N}{\partial t}\\
&\quad + \tfrac{\zeta_S(\mu+\varphi)}{\delta_S(\mu+\xi\varrho)}\left(1 - \tfrac{T_0^S}{T^S}\right)\tfrac{\partial T^S}{\partial t}.
\end{aligned}$$

By substituting the expressions from Equations (18)–(24) into the formulation, we

obtain:

$$\begin{aligned}
&\tfrac{\partial \Xi_0}{\partial t} = \left(1-\tfrac{M_0}{M}\right)\left(D_M\Delta M+\phi-\varrho M-\kappa MV\right)+\tfrac{\mu}{\mu+\xi\varphi}\left(D_{E^L}\Delta E^L+(1-\xi)\kappa MV-(\mu+\varphi)E^L\right)\\
&+\tfrac{\mu+\varphi}{\mu+\xi\varphi}\left(D_{E^A}\Delta E^A+\xi\kappa MV+\mu E^L-\delta E^A-\zeta_N E^A T^N-\zeta_S E^A T^S\right)+\tfrac{\kappa M_0}{\rho}\left(D_V\Delta V+\eta E^A-\rho V\right)\\
&+\tfrac{\zeta_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_0^N}{T^N}\right)\left(D_{T^N}\Delta T^N+\alpha_N+\vartheta_N E^A T^N-\nu_N T^N\right)\\
&+\tfrac{\zeta_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_0^S}{T^S}\right)\left(D_{T^S}\Delta T^S+\alpha_S+\vartheta_S T^S-\nu_S T^S\right).
\end{aligned}$$

Upon collecting and simplifying the relevant terms, we obtain:

$$\begin{aligned}
\tfrac{\partial \Xi_0}{\partial t} &= \left(1-\tfrac{M_0}{M}\right)(\phi-\varrho M)+\tfrac{\zeta_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_0^N}{T^N}\right)(\alpha_N-\nu_N T^N)+\tfrac{\zeta_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_0^S}{T^S}\right)(\alpha_S-\nu_S T^S)\\
&-\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E^A+\tfrac{\kappa\eta M_0}{\rho}E^A-\tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}T_0^N E^A-\tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}T_0^S E^A+D_M\left(1-\tfrac{M_0}{M}\right)\Delta M\\
&+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\Delta E^A+\tfrac{\kappa M_0 DV}{\rho}\Delta V+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\partial_N(\mu+\xi\varphi)}\left(1-\tfrac{T_0^N}{T^N}\right)\Delta T^N\\
&+\tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_0^S}{T^S}\right)\Delta T^S.
\end{aligned}$$

Utilizing the substitutions $\phi=\varrho M_0,\ \alpha_N=v_N T_0^N$, and $\alpha_S=v_S T_0^S$, we obtain:

$$\begin{aligned}
\tfrac{\partial \Xi_0}{\partial t} &= -\tfrac{\varrho(M-M_0)^2}{M}-\tfrac{\zeta_N v_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\tfrac{(T^N-T_0^N)}{T^N}-\tfrac{\zeta_S v_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\tfrac{\left(T^S-T_0^S\right)^2}{T^S}\\
&+\left(\tfrac{\kappa\eta M_0}{\rho}-\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}-\tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}T_0^N-\tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}T_0^S\right)E^A+D_M\left(1-\tfrac{M_0}{M}\right)\Delta M\\
&+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\Delta E^A+\tfrac{\kappa M_0 D_V}{\rho}\Delta V+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_0^N}{T^N}\right)\Delta T^N\\
&+\tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_0^S}{T^S}\right)\Delta T^S.
\end{aligned}$$

Then

$$\begin{aligned}
\tfrac{\partial \Xi_0}{\partial t} &= -\tfrac{\varrho(M-M_0)^2}{M}-\tfrac{\zeta_N v_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\tfrac{(T^N-T_0^N)^2}{T^N}-\tfrac{\zeta_S v_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\tfrac{(T^S-T_0^S)^2}{T^S}\\
&+\tfrac{\delta(\mu+\varphi)\left(\frac{\alpha_N\zeta_N}{\delta v_N}+\frac{\alpha_S\zeta_S}{\delta v_S}+1\right)}{(\mu+\xi\varphi)}\left(\tfrac{\eta\kappa\phi(\mu+\xi\varphi)}{\delta\varrho\rho(\mu+\varphi)\left(\frac{\alpha_N\zeta_N}{\delta v_N}+\frac{\alpha_S\zeta_S}{\delta v_S}+1\right)}-1\right)E^A+D_M\left(1-\tfrac{M_0}{M}\right)\Delta M\\
&+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\Delta E^L+\tfrac{D_{E^A}\ (\mu+\varphi)}{\mu+\xi\varphi}\Delta E^A+\tfrac{\kappa M_0 D_V}{\rho}\Delta V+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_0^N}{T_N}\right)\Delta T^N\\
&+\tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_0^S}{T^S}\right)\Delta T^S.
\end{aligned}$$

By computing the time derivative, given by $\frac{d\bar{\Xi}_0}{dt}=\int_\Omega\frac{\partial\Xi_0}{\partial t}dx$, we derive the following result:

$$\begin{aligned}
\frac{d\bar{\Xi}_0}{dt} &= -\varrho\int_\Omega\frac{(M-M_0)^2}{M}dx-\frac{\zeta_N\nu_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\int_\Omega\frac{(T^N-T_0^N)^2}{T^N}dx-\frac{\zeta_S\nu_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\int_\Omega\frac{\left(T^S-T_0^S\right)^2}{T^S}dx\\
&+\tfrac{\delta(\mu+\varphi)\left(\frac{a_N\zeta_N}{\delta v_N}+\frac{a_S\zeta_S}{\delta v_S}+1\right)(\bar{\mathcal{R}}_0-1)}{(\mu+\xi\varphi)}\int_\Omega E^A dx+D_M\int_\Omega\left(1-\tfrac{M_0}{M}\right)\Delta M dx\\
&+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\int_\Omega\Delta E^L dx+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\int_\Omega\Delta E^A dx+\tfrac{\kappa M_0 D_V}{\rho}\int_\Omega\Delta V dx\\
&+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\int_\Omega\left(1-\tfrac{T_0^N}{T^N}\right)\Delta T^N dx+\tfrac{\zeta_S D_{T^S}(\mu+\xi\varphi)}{\vartheta_S(\mu+\xi\varphi)}\int_\Omega\left(1-\tfrac{T_0^S}{T^S}\right)\Delta T^S dx.
\end{aligned}$$

Utilizing the relation given in (12), the above expression is transformed into the following form:

$$\begin{aligned}\frac{d\bar{\Xi}_0}{dt} &= -\varrho\int_\Omega \frac{(M-M_0)^2}{M}dx - \frac{\zeta_N\nu_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\int_\Omega \frac{(T^N-T_0^N)^2}{T^N}dx - \frac{\zeta_S\nu_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\int_\Omega \frac{\left(T^S-T_0^S\right)^2}{T^S}dx\\ &+\frac{\delta(\mu+\varphi)\left(\frac{a_N\zeta_N}{\delta v_N}+\frac{a_S\zeta_S}{\delta v_S}+1\right)\left(\widetilde{\mathcal{R}}_0-1\right)}{(\mu+\xi\varphi)}\int_\Omega E^A dx - D_M M_0\int_\Omega \frac{\|\nabla M\|^2}{M^2}dx\\ &-\frac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}T_0^N\int_\Omega \frac{\left\|\nabla T^N\right\|^2}{T^{N^2}}dx - \frac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}T_0^S\int_\Omega \frac{\left\|\nabla T^S\right\|^2}{T^{S^2}}dx.\end{aligned}$$

Given that $\widetilde{\mathcal{R}}_0 \leq 1$, it follows that $\frac{d\bar{\Xi}_0}{dt} \leq 0$. Equality, i.e., $\frac{d\bar{\Xi}_0}{dt} = 0$, holds precisely when the following conditions are met: $M = M_0,\ T^N = T_0^N,\ T^S = T_0^S, and\ \left(\widetilde{\mathcal{R}}_0 - 1\right)\int_\Omega E^A dx = 0$. The solutions of the system defined by Equations (18)–(24) converge asymptotically to the set χ'_0 as $t \to \infty$. Each element of χ'_0 satisfies the conditions $M = M_0,\ T^N = T_0^N,\ T^S = T_0^S$, and

$$\left(\bar{\mathcal{R}}_0 - 1\right)\int_\Omega E^A dx = 0. \tag{27}$$

The study may be conducted by considering the following two separate cases:

F-1. $\widetilde{\mathcal{R}}_0 = 1$. Equation (18) implies that

$$0 = \frac{\partial M}{\partial t} = \phi - \varrho M_0 - \kappa M_0 V \qquad \Rightarrow \qquad V(x,t) = 0. \tag{28}$$

By utilizing Equation (22), we derive the following result:

$$0 = \frac{\partial V}{\partial t} = \eta E^A \qquad \Rightarrow \qquad E^A(x,t) = 0. \tag{29}$$

In a similar manner, Equation (21) indicates that

$$0 = \frac{\partial E^A}{\partial t} = \mu E^L \qquad \Rightarrow \qquad E^L(x,t) = 0 \tag{30}$$

Hence, the set χ'_0 reduces to $\{EP_0\}$.

F-2. When n $\overline{\mathcal{R}}_0 < 1$. Equation (27) implies that $\int_\Omega E^A dx = 0$, then , $E^A = 0$. Moreover, from Equations (28) to (30), it immediately follows that

$$V = E^L = 0.$$

Hence, the set χ'_0 reduces to the disease–free equilibrium, denoted by $\{EP_0\}$.

By applying LIP [47], it follows that the equilibrium point EP_0 is GAS.□

Theorem 4. *The endemic equilibrium of the model defined by Equations (18)–(24) is GAS provided that* $\overline{\mathcal{R}}_0 > 1$.

Proof. Construct $\Xi_1(x,t)$ as:

$$\begin{aligned}\Xi_1(x,t) &= M_1\mathcal{L}\left(\frac{M}{M_1}\right) + \frac{\mu}{\mu+\xi\varphi}E_1^L\mathcal{L}\left(\frac{E^L}{E_1^L}\right) + \frac{\mu+\varphi}{\mu+\xi\varphi}E_1^A\mathcal{L}\left(\frac{E^A}{E_1^A}\right) + \frac{\kappa M_1}{\rho}V_1\mathcal{L}\left(\frac{V}{V_1}\right)\\ &+\frac{\zeta_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}T_1^N\mathcal{L}\left(\frac{T^N}{T_1^N}\right) + \frac{\zeta_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}T_1^S\mathcal{L}\left(\frac{T^S}{T_1^S}\right).\end{aligned}$$

Obviously, for any and $\Xi_1(M_1, E_1^L, E_1^A, V_1, T_1^N, T_1^S) = 0$

Substituting the expressions from model (18)–(24), into the derivative, $\frac{\partial\Xi_1}{\partial t}$ we

obtain the following result:

$$\begin{aligned}\frac{\partial \Xi_1}{\partial t} &= \left(1-\tfrac{M_1}{M}\right)\left(D_M\Delta M+\phi-\varrho M-\kappa MV\right)+\tfrac{\mu}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\left(D_{E^L}\Delta E^L+(1-\xi)\kappa MV-(\mu+\varphi)E^L\right)\\ &+\tfrac{\mu+\varphi}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\left(D_{E^A}\Delta E^A+\xi\kappa MV+\mu E^L-\delta E^A-\zeta_N E^A T^N-\zeta_S E^A T^S\right)\\ &+\tfrac{\kappa M_1}{\rho}\left(1-\tfrac{V_1}{V}\right)\left(D_V\Delta V+\eta E^A-\rho V\right)\\ &+\tfrac{\zeta_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)\left(D_{T^N}\Delta T^N+\alpha_N+\vartheta_N E^A T^N-\nu_N T^N\right)\\ &+\tfrac{\zeta_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)\left(D_{T^S}\Delta T^S+\alpha_S+\vartheta_S T^A T^S-\nu_S T^S\right).\end{aligned}$$

After aggregating the terms, we obtain:

$$\begin{aligned}\frac{\partial \Xi_1}{\partial t} &= \left(1-\tfrac{M_1}{M}\right)(\phi-\varrho M)+\tfrac{\zeta_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T^N}{T^N}\right)(\alpha_N-\nu_N T^N)\\ &+\tfrac{\zeta_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)(\alpha_S-v_S T^S)-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\tfrac{E_1^L}{E^L}\kappa MV+\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L\\ &-\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E^A-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\tfrac{E_1^A}{E^A}KMV-\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}\tfrac{E_1^A}{E^A}E^L+\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A+\tfrac{\zeta_N(\mu+\varphi)}{\mu+\xi\varphi}E_1^A T^N\\ &+\tfrac{\zeta_S(\mu+\varphi)}{\mu+\xi\varphi}E_1^A T^S+\tfrac{\kappa\eta M_1}{\rho}E^A-\tfrac{\kappa\eta M_1}{\rho}\tfrac{V_1}{V}E^A+\kappa M_1V_1-\tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}T_1^N E^A-\tfrac{\zeta_S(\mu+\varphi)}{\mu+\xi\varphi}T_1^S E^A\\ &+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A\\ &+\tfrac{\kappa M_1 D_V}{\rho}\left(1-\tfrac{V_1}{V}\right)\Delta V+\tfrac{\zeta_N D_{T^N}\,(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)\Delta T^N+\tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)\Delta T^S.\end{aligned}$$

With reference to the equilibrium conditions stated below

$$\begin{cases}\phi=\varrho M_1+\kappa M_1V_1,\\ (1-\xi)\kappa M_1V_1=(\mu+\varphi)E_1^L,\\ \xi\kappa M_1V_1+\mu E_1^L=\delta E_1^A+\zeta_N E_1^A T_1^N+\zeta_S E_1^A T_1^S,\\ \eta E_1^A=\rho V_1,\\ \alpha_N=\nu_N T_1^N-\vartheta_N E_1^A T_1^N,\\ \alpha_S=\nu_S T_1^S-\vartheta_S E_1^A T_1^S.\end{cases}$$

We derive

$$\begin{aligned}\frac{\partial \Xi_1}{\partial t} &= -\tfrac{\varrho(M-M_1)^2}{M}-\tfrac{\zeta_N v_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\tfrac{(T^N-T_1^N)^2}{T^N}-\tfrac{\zeta_S v_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\tfrac{(T^S-T_1^S)^2}{T^S}\\ &+\left(1-\tfrac{M_1}{M}\right)\kappa M_1V_1-\tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)E_1^A T_1^N-\tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)E_1^A T_1^S\\ &+\left(\tfrac{\kappa\eta M_1}{\rho}E_1^A-\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A-\tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}T_1^N E_1^A-\tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}T_1^S E_1^A\right)E_1^A\\ &-\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{MVE_1^L}{M_1V_1E^L}+\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\tfrac{MVE_1^A}{M_1V_1E^A}\\ &-\tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L\tfrac{E^LE_1^A}{E^LE^A}+\tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A-\tfrac{\kappa\eta M_1}{\rho}E_1^A\tfrac{E^AV_1}{E_1^AV}+\kappa M_1V_1+\tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T^N\\ &+\tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T^S+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A\\ &+\tfrac{\kappa M_1D_V}{\rho}\left(1-\tfrac{V_1}{V}\right)\Delta V+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)\Delta T^N+\tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)\Delta T^S.\end{aligned}\tag{31}$$

We have

$$\kappa M_1V_1=\frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1+\frac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1,$$

$$\frac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L = \frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1,$$

and

$$\begin{aligned}\tfrac{(\mu+\varphi)}{\mu+\xi\varphi}\left(\delta E_1^A + \zeta_N E_1^A T_1^N + \zeta_S E_1^A T_1^S\right) &= \tfrac{(\mu+\varphi)}{\mu+\xi\varphi}\left(\xi\kappa M_1 V_1 + \mu E_1^L\right)\\ &= \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1 + \tfrac{\mu(\mu+\varphi)}{\mu+\xi\varphi}E_1^L\\ &= \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1 + \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1.\end{aligned}$$

Utilizing the above relations, Equation (31) can be rewritten as:

$$\begin{aligned}\frac{\partial \Xi_1}{\partial t} &= -\frac{\varrho(M-M_1)^2}{M} - \frac{\zeta_N v_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\frac{(T^N-T_1^N)^2}{T^N} - \frac{\zeta_S v_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\frac{(T^S-T_1^S)^2}{T^S}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1 V_1 + \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1 V_1 - \tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)E_1^A V_1^N\\
&-\tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)E_1^A T_1^S - \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{MVE_1^L}{M_1V_1E^L} + \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1\\
&-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{MVE_1^A}{M_1V_1E^A} - \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{E^L E_1^A}{E_1^L E^A} + \tfrac{\delta(\mu+\varphi)}{\mu+\xi\varphi}E_1^A - \kappa M_1 V_1\tfrac{E^A V_1}{E_1^A V}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1 + \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1 + \tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T^N + \tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T^S + \tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T_1^N\\
&-\tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T_1^N + \tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T_1^S - \tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}E_1^A T_1^S + D_M\left(1-\tfrac{M_1}{M}\right)\Delta M\\
&+\tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L + \tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A + \tfrac{\kappa M_1 D_V}{\rho}\left(1-\tfrac{V_1}{V}\right)\Delta V\\
&+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)\Delta T^N + \tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)\Delta T^S.\end{aligned}$$

It follows that

$$\begin{aligned}\tfrac{\partial \Xi_1}{\partial t} &= -\tfrac{\varrho(M-M_1)^2}{M} - \tfrac{\zeta_N v_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\tfrac{(T^N-T_1^N)^2}{T^N} - \tfrac{\zeta_S v_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\tfrac{(T^S-T_1^S)^2}{T^S}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1 V_1 + \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{M_1}{M}\right)\kappa M_1 V_1 - \tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}\left(2-\tfrac{T_1^N}{T^N}-\tfrac{T^N}{T_1^N}\right)E_1^A T_1^N\\
&-\tfrac{\zeta_S(\mu+\varrho)}{(\mu+\xi\varphi)}\left(2-\tfrac{T_1^S}{T^S}-\tfrac{T^S}{T_1^S}\right)E_1^A T_1^S - \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{MVE_1^L}{M_1V_1E^L} + \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1\\
&-\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{MVE_1^A}{M_1V_1E^A} - \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{E^L E_1^A}{E_1^L E^A} - \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{E^A V_1}{E_1^A V} - \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1\tfrac{E^A V_1}{E_1^A V}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1 + \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1 + \tfrac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1 V_1 + \tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1\\
&+D_M\left(1-\tfrac{M_1}{M}\right)\Delta M + \tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L + \tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A + \tfrac{\kappa M_1 D_V}{\rho}\left(1-\tfrac{V_1}{V}\right)\Delta V\\
&+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)\Delta T^N + \tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)\Delta T^S.\end{aligned}$$

Then

$$\begin{aligned}\tfrac{\partial \Xi_1}{\partial t} &= -\tfrac{\varrho(M-M_1)^2}{M} - \tfrac{\zeta_N v_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\tfrac{(T^N-T_1^N)^2}{T^N} - \tfrac{\zeta_S v_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\tfrac{(T^S-T_1^S)^2}{T^S}\\
&+\tfrac{\mu(1-\xi)}{\mu+\xi\rho}\kappa M_1 V_1\left(4-\tfrac{M_1}{M}-\tfrac{MVE_1^L}{M_1V_1E^L}-\tfrac{E^A V_1}{E_1^A V}-\tfrac{E^L E_1^A}{E_1^L E^A}\right)\\
&+\tfrac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1 V_1\left(3-\tfrac{M_1}{M}-\tfrac{MVE_1^A}{M_1V_1E_A}-\tfrac{E^A V_1}{E_1^A V}\right) + \tfrac{\zeta_N(\mu+\varphi)}{(\mu+\xi\varphi)}\tfrac{(T^N-T_1^N)^2}{T^N T_1^N}E_1^A T_1^N\\
&+\tfrac{\zeta_S(\mu+\varphi)}{(\mu+\xi\varphi)}\tfrac{(T^S-T_1^S)^2}{T^S T_1^S}E_1^A T_1^S + D_M\left(1-\tfrac{M_1}{M}\right)\Delta M + \tfrac{\mu D_{E^L}}{\mu+\xi\varphi}\left(1-\tfrac{E_1^L}{E^L}\right)\Delta E^L\\
&+\tfrac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\tfrac{E_1^A}{E^A}\right)\Delta E^A + \tfrac{\kappa M_1 D_V}{\rho}\left(1-\tfrac{V_1}{V}\right)\Delta V\\
&+\tfrac{\zeta_N D_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\tfrac{T_1^N}{T^N}\right)\Delta T^N + \tfrac{\zeta_S D_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\left(1-\tfrac{T_1^S}{T^S}\right)\Delta T^S.\end{aligned}$$

This leads to

$$\begin{aligned}\frac{\partial \Xi_1}{dt} &= -\frac{\varrho(M-M_1)^2}{M} - \frac{\zeta_N\alpha_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\frac{(T^N-T_1^N)^2}{T^NT_1^N} - \frac{\zeta_S\alpha_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\frac{(T^S-T_1^S)^2}{T^ST_1^S}\\ &+\frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\left(4-\frac{M_1}{M}-\frac{MVE_1^L}{M_1V_1E^L}-\frac{E^AV_1}{E_1^AV}-\frac{E^LE_1^A}{E_1^LE^A}\right)\\ &+\frac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\left(3-\frac{M_1}{M}-\frac{MVE_1^A}{M_1V_1E^A}-\frac{E^AV_1}{E_1^AV}\right)+D_M\left(1-\frac{M_1}{M}\right)\Delta M+\frac{\mu D_{EL}}{\mu+\xi\varphi}\left(1-\frac{E_1^L}{E^L}\right)\Delta E^L\\ &+\frac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\left(1-\frac{E_1^A}{E^A}\right)\Delta E^A+\frac{\kappa M_1D_V}{\rho}\left(1-\frac{V_1}{V}\right)\Delta V+\frac{\zeta_ND_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\left(1-\frac{T_1^N}{T^N}\right)\Delta T^N\\ &+\frac{\zeta_SD_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\zeta\varphi)}\left(1-\frac{T_1^5}{T^5}\right)\Delta T^S.\end{aligned}$$

In accordance with the above, the time derivative is given by

$$\begin{aligned}\frac{d\bar{\Xi}_1}{dt} &= -\varrho\int_\Omega\frac{(M-M_1)^2}{M}\mathrm{d}x-\frac{\zeta_N\alpha_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\int_\Omega\frac{(T^N-T_1^N)^2}{T^NT_1^N}\mathrm{d}x-\frac{\zeta_S\alpha_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\int_\Omega\frac{(T^S-T_1^S)^2}{T^ST_1^S}\mathrm{d}x\\ &+\frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(4-\frac{M_1}{M}-\frac{MVE_1^L}{M_1V_1E^L}-\frac{E^AV_1}{E_1^AV}-\frac{E^LE_1^A}{E_1^LE_1^A}\right)\mathrm{d}x\\ &+\frac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(3-\frac{M_1}{M}-\frac{MVE_1^A}{M_1V_1E^A}+\frac{E^AV_1}{E_1^AV}\right)\mathrm{d}x+D_M\int_\Omega\left(1-\frac{M_1}{M}\right)\Delta M\mathrm{d}x\\ &+\frac{\mu D_{EL}}{\mu+\xi\varphi}\int_\Omega\left(1-\frac{E_L^L}{E^L}\right)\Delta E^L\mathrm{d}x+\frac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}\int_\Omega\left(1-\frac{E_1^A}{E^A}\right)\Delta E^A\mathrm{d}x+\frac{\kappa M_1D_V}{\rho}\int_\Omega\left(1-\frac{V_1}{V}\right)\Delta V\mathrm{d}x\\ &+\frac{\zeta_ND_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\int_\Omega\left(1-\frac{T_1^N}{T^N}\right)\Delta T^N\mathrm{d}x+\frac{\zeta_SD_{T^S}(\mu+\xi\varphi)}{\vartheta_S(\mu+\xi\varphi)}\int_\Omega\left(1-\frac{T_1^S}{T^S}\right)\Delta T^S\mathrm{d}x.\end{aligned}$$

Ultimately, by applying the identity given in (12), we derive:

$$\begin{aligned}\frac{d\bar{\Xi}_1}{dt} &= -\varrho\int_\Omega\frac{(M-M_1)^2}{M}\mathrm{d}x-\frac{\zeta_N\alpha_N(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}\int_\Omega\frac{(T^N-T_1^N)^2}{T^NT_1^N}\mathrm{d}x-\frac{\zeta_S\alpha_S(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}\int_\Omega\frac{(T^S-T_1^S)^2}{T^ST_1^S}\mathrm{d}x\\ &+\frac{\mu(1-\xi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(4-\frac{M_1}{M}-\frac{MVE_1^L}{M_1V_1E^L}-\frac{E^AV_1}{E_1^AV}-\frac{E^LE_1^A}{E_1^LE_1^A}\right)\mathrm{d}x\\ &+\frac{\xi(\mu+\varphi)}{\mu+\xi\varphi}\kappa M_1V_1\int_\Omega\left(3-\frac{M_1}{M}-\frac{MVE_1^A}{M_1V_1E^A}-\frac{E^AV_1}{E_1^AV}\right)\mathrm{d}x-D_MM_1\int_\Omega\frac{\|\nabla M\|^2}{M^2}\mathrm{d}x\\ &-\frac{\mu D_{E^L}}{\mu+\xi\varphi}E_1^L\int_\Omega\frac{||\nabla E^L||^2}{{E^L}^2}\mathrm{d}x-\frac{D_{E^A}(\mu+\varphi)}{\mu+\xi\varphi}E_1^A\int_\Omega\frac{||\nabla E^A||^2}{{E^A}^2}\mathrm{d}x-\frac{\kappa M_1D_V}{\rho}V_1\int_\Omega\frac{||\nabla V||^2}{V^2}\mathrm{d}x\\ &-\frac{\zeta_ND_{T^N}(\mu+\varphi)}{\vartheta_N(\mu+\xi\varphi)}T_1^N\int_\Omega\frac{||\nabla T^N||^2}{{T^N}^2}\mathrm{d}x-\frac{\zeta_SD_{T^S}(\mu+\varphi)}{\vartheta_S(\mu+\xi\varphi)}T_1^S\int_\Omega\frac{||\nabla T^S||^2}{{T^S}^2}\mathrm{d}x.\end{aligned}$$

Therefore, it follows that for any $(M, E^L, E^A, V, T^N, T^S) > 0$. Moreover, the equality $\frac{\partial \Xi_1}{\partial t} = 0$ holds if and only if $(M, E^L, E^A, V, T^N, T^S) = (M_1, E_1^L, E_1^A, V_1, T_1^N, T_1^S)$. Solution of the system tend to **Table 3** gives an overview of when the model's equilibrium points stay stable, based on Equations (18)–(24).

Table 3. Criteria for the existence and global stability of equilibria in the model (18)–(24).

Equilibrium	Existence Condition	Stability Condition
$EP_0 = (M_0, 0, 0, 0, T^N, T^S)$	–	$\overline{\mathcal{R}}_0 \leq 1$
$EP_1 = (M_1, E_1^L, E_1^A, V_1, T_1^N, T_1^S)$	$\overline{\mathcal{R}}_0 > 1$	$\overline{\mathcal{R}}_0 > 1$

$\chi_1' = \{EP_1\}$. Therefore, by LIP, EP_1 is GAS. □

Remark 2. *Incorporating memory effects into our DENV dynamics model through fractional differential equations (FDEs) offers a promising direction for future research. Fractional derivatives naturally capture memory and long-range interactions, making them particularly suitable for modeling biological and epidemiological systems where past states influence current dynamics [50]. Recent work has shown that Lyapunov-based methods provide a powerful framework for analyzing the global*

stability of fractional-order systems [51–53]. The Lyapunov functions introduced in this study serve as a foundational tool, enabling future investigations into the stability and long-term behavior of DENV infection models formulated with fractional dynamics. Furthermore, extending the current model to a fractional-order setting could offer deeper insight into immune memory effects, viral persistence, and the temporal evolution of host-pathogen interactions over multiple time scales.

4. Numerical simulations

This section provides a series of numerical simulations intended to illustrate the characteristics derived from our theoretical findings regarding the stability of the reaction–diffusion system. To achieve a more thorough understanding of the system's behavior, we analyze the effects of varying system parameters on its dynamics. By employing the PDEPE solver in MATLAB, numerical simulations for the DENV model incorporating antibodies (Equations (3)–(8)) and the DENV model incorporating CTLs (Equations (18)–(24)) are carried out. To do so, it is important to note the discretization of the entire spatial domain x and temporal domain t. The grid points (x_d, t_e) are defined as follows:

$$x_d = x_0 + d\bar{\Delta}x, \quad for \quad d = 0, 1, 2, \ldots, N_x$$
$$t_e = t_0 + e\bar{\Delta}t, \quad for \quad e = 0, 1, 2, \ldots, N_t$$

where:

$$x_0 = 0,\ \bar{\Delta}x = 0.02,\ x_{N_x} = 2,\ so\ N_x = \frac{2-0}{0.02} = 100,$$

$$t_0 = 0,\ \ \bar{\Delta}t = 0.1,\ t_{N_t} = 1000,\ so\ N_t = \frac{1000-0}{0.1} = 10,000.$$

Thus, the grid points are defined as:

$$x_d \in \{0, 0.02, 0.04, \ldots, 2\}, \quad t_e \in \{0, 0.1, 0.2, \ldots, 1000\}.$$

4.1. Numerical simulations for system (3)–(8)

This subsection is devoted to analyzing the dynamic behavior of system (3)–(8). The simulations are conducted using the following initial conditions:

$$M(x,0) = 450\left[1 + 0.4\cos^2(\pi x)\right], \quad E^L(x,0) = 50\left[1 + 0.5\cos^2(\pi x)\right], \tag{32}$$

$$E^A(x,0) = 5\left[1 + 0.5\cos^2(\pi x)\right], \quad V(x,0) = 2\left[1 + 0.5\cos^2(\pi x)\right], \tag{33}$$

$$W^N(x,0) = 200\left[1 + 0.5\cos^2(\pi x)\right], \quad W^S(x,0) = 150\left[1 + 0.5\cos^2(\pi x)\right],\ x \in [0,2]. \tag{34}$$

Furthermore, homogeneous Neumann boundary conditions are imposed, expressed as:

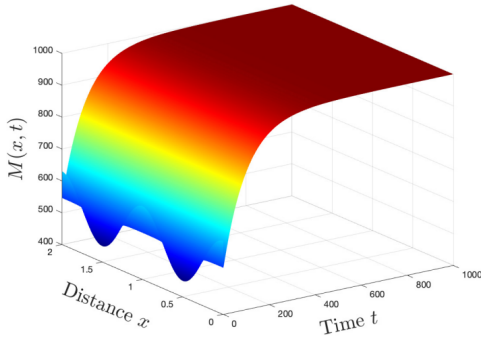
$$\frac{\partial M}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^L}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^A}{\partial \overrightarrow{\varsigma}} = \frac{\partial V}{\partial \overrightarrow{\varsigma}} = \frac{\partial W^N}{\partial \overrightarrow{\varsigma}} = \frac{\partial W^S}{\partial \overrightarrow{\varsigma}} = 0, \quad t > 0, \quad x = 0, 2.$$

We examine the system under varying values of κ, employing the parameter set summarized in **Table 4**, together with the initial conditions specified above. This leads to the emergence of two distinct scenarios:

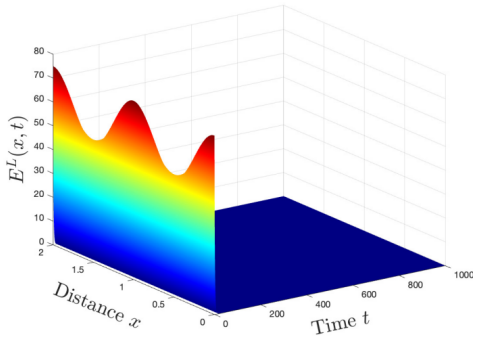
Table 4. Parameters for model (3)–(8).

Parameter	Value	Parameter	Value	Parameter	Value
ϕ	10	δ	0.5	λ_S	0.002
ϱ	0.01	β_N	0.3	γ_N	5
κ	varied	β_S	0.8	γ_S	3
ξ	0.3	ρ	3	ψ_N	0.1
μ	0.4	η	20	ψ_S	0.1
φ	0.1	λ_N	0.01	D_ℓ	0.1

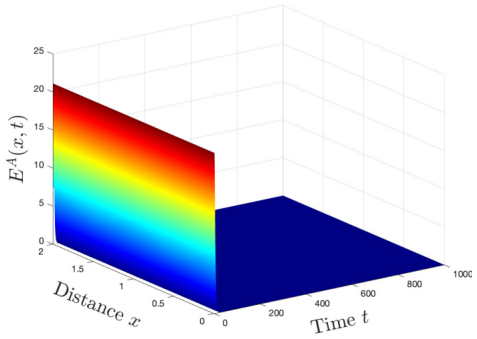
Scenario-1: The parameter κ is set to 0.0005. Based on this value, the basic reproduction number is computed as $\mathcal{R}_0 = 0.41 < 1$. This satisfies the stability conditions presented in **Table 2**. Numerical simulations reveal that, over time, all solution trajectories asymptotically approach the disease–free equilibrium, denoted by $EP_0 = (1000,\ 0,\ 0,\ 0,\ 50,\ 30)$. This equilibrium is shown to be GAS as stated in Theorem 1 and are illustrated in **Figure 1**. In this specific scenario, it is confirmed that the individual is cleared from by DENV.



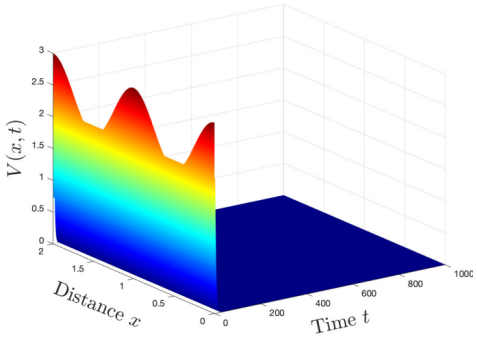
(a) Uninfected monocytes.



(b) Latently DENV–infected monocytes.

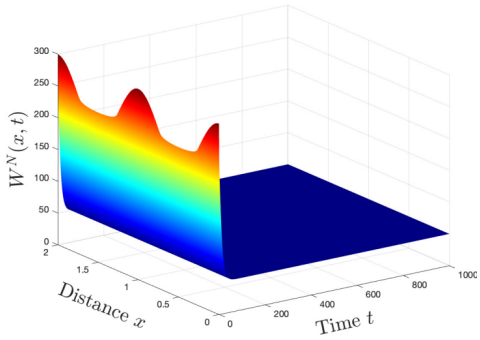


(c) Actively DENV–infected monocytes.

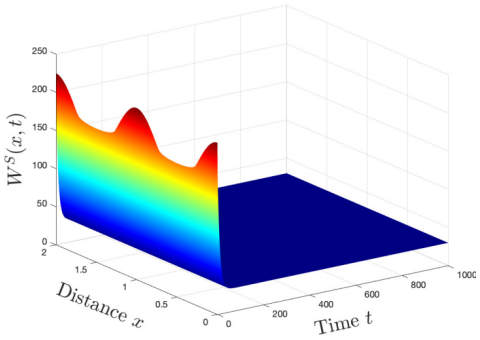


(d) Free DENV virus.

Figure 1. *Cont.*



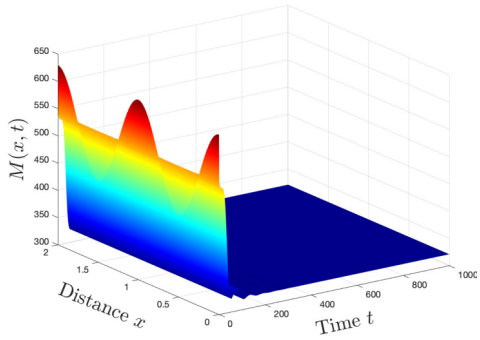
(e) Non–specific antibodies.



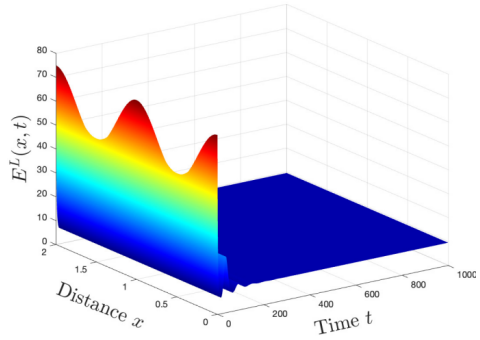
(f) Strain–specific antibodies.

Figure 1. Numerical simulations indicate that the solutions of the system defined by Equations (3)–(8) eventually converge to the disease–free equilibrium point, given by EP0 = (1000, 0, 0, 0, 50, 30) (Scenario-1).

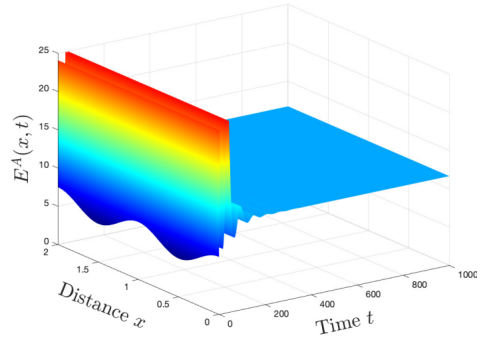
Scenario-2: Given the parameter choice $\kappa = 0.005$, the corresponding basic reproduction number is determined to be $\mathcal{R}_0 = 0.41 > 1$, indicating that the stability criteria specified in **Table 2** are fulfilled. Theorem 2 establishes that the equilibrium point EP1 is GAS. As depicted in **Figure 2**, the system's dynamic behavior demonstrates that the solutions eventually converge to the endemic equilibrium $EP_1 = (321.02,\ 9.51,\ 11.68,\ 4.23,\ 86.66,\ 32.77)$. This case corresponds to a scenario in which the individual is infected with DENV.



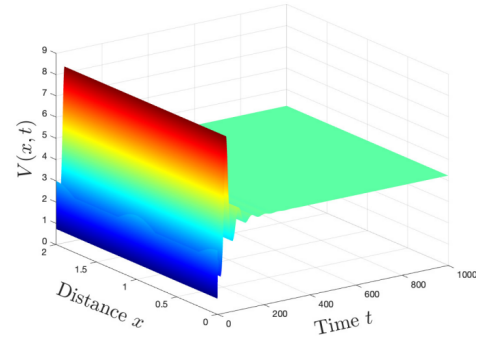
(a) Uninfected monocytes.



(b) Latently DENV–infected monocytes.

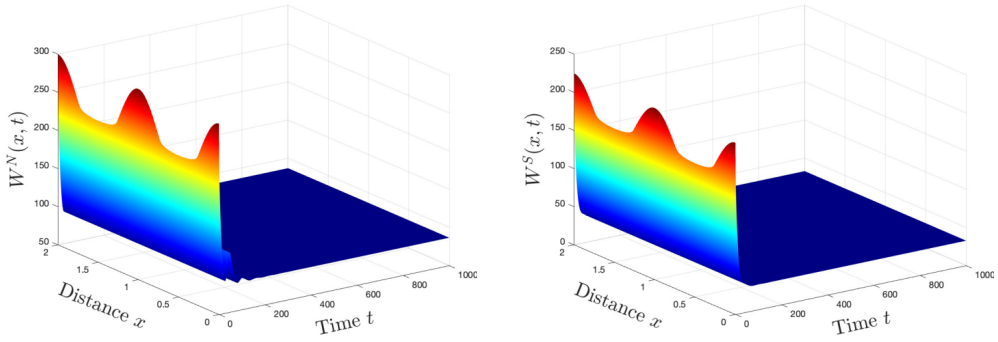


(c) Actively DENV–infected monocytes.



(d) Free DENV virus.

Figure 2. *Cont.*



(e) Non–specific antibodies. **(f)** Strain–specific antibodies.

Figure 2. Numerical simulations indicate that the solutions of the system defined by Equations (3)–(8) eventually converge to the endemic equilibrium point, given by EP_1 = (321.02, 9.51, 11.68, 4.23, 86.66, 32.77) (Scenario-2).

4.2. Numerical simulations for system (18)–(24)

The initial conditions for M, E^L, E^A, and V are adopted in accordance with Equations (32) and (33), whereas the initial values for T^N, and T^S are specified as follows:

$$T^N(x,0) = 200\left[1 + 0.5\cos^2(\pi x)\right], \quad T^S(x,0) = 150\left[1 + 0.5\cos^2(\pi x)\right], x \in [0,2].$$

Furthermore, homogeneous Neumann boundary conditions are imposed, expressed as:

$$\frac{\partial M}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^L}{\partial \overrightarrow{\varsigma}} = \frac{\partial E^A}{\partial \overrightarrow{\varsigma}} = \frac{\partial V}{\partial \overrightarrow{\varsigma}} = \frac{\partial T^N}{\partial \overrightarrow{\varsigma}} = \frac{\partial T^S}{\partial \overrightarrow{\varsigma}} = 0, \ t > 0, \ x = 0, 2.$$

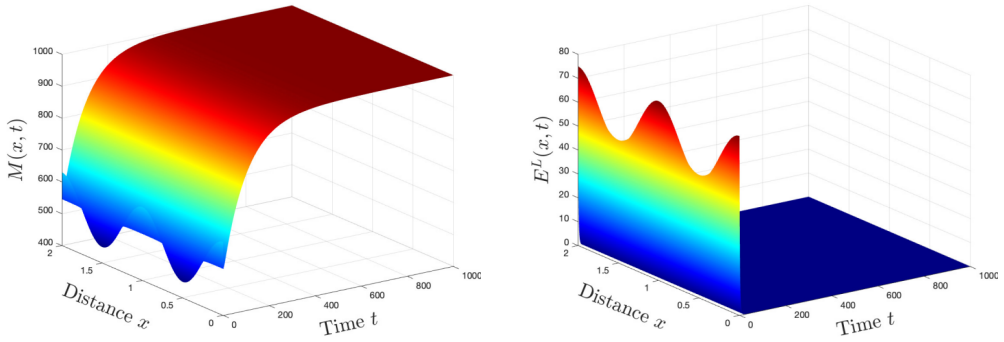
The system (18)–(24) is analyzed under varying values of κ, using the parameter set outlined in **Table 5** alongside the initial conditions previously specified.

Table 5. Parameters for model (18)–(24).

Parameter	Value	Parameter	Value	Parameter	Value
ϕ	10	δ	0.5	α_S	30
ϱ	0.01	ζ_N	0.00000277	ϑ_N	0.000444
κ	varied	ζ_S	0.0000104	ϑ_s	0.00153
ξ	0.3	η	10	ν_N	0.5
μ	0.4	ρ	3	ν_S	0.5
φ	0.1	α_N	30	$\widetilde{D}$	0.1

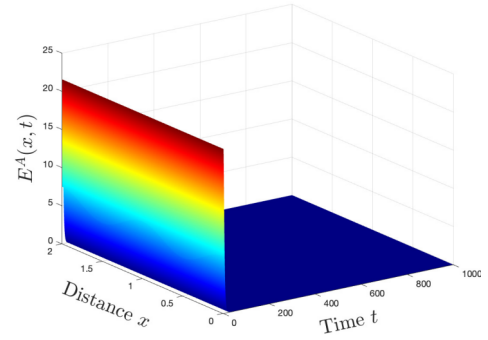
Scenario-3: Given the parameter value $\kappa = 0.00005$, the corresponding basic reproduction number is calculated to be $\overline{\mathcal{R}}_0 = 0.29$, which is less than unity. This satisfies the stability criteria outlined in **Table 2**. Numerical simulations demonstrate that, over time, all solution trajectories converge asymptotically to the disease–free equilibrium point, denoted by $EP_0 = (1000,\ 0,\ 0,\ 0,\ 60,\ 60)$. This equilibrium is shown to be GAS, indicating that the system stabilizes at this state for a wide range of initial conditions. These results are consistent with the theoretical findings presented in Theorem 3 and are visually supported by **Figure 3**. Under this specific parameter

setting, it is concluded that the individual does not contract DENV.

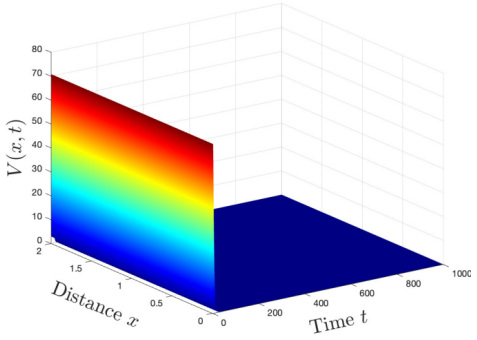


(a) Uninfected monocytes.

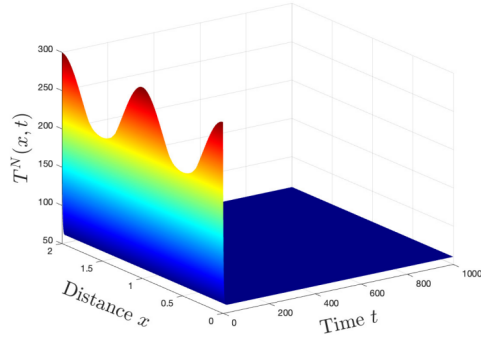
(b) Latently DENV–infected monocytes.



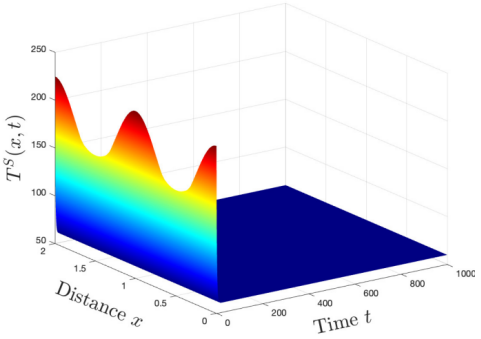
(c) Actively DENV–infected monocytes.



(d) Free DENV virus.



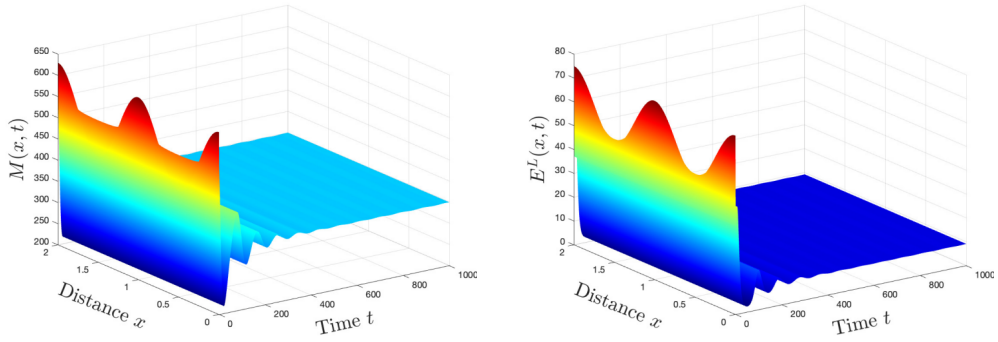
(e) Non–specific CTLs.



(f) Strain–specific CTLs.

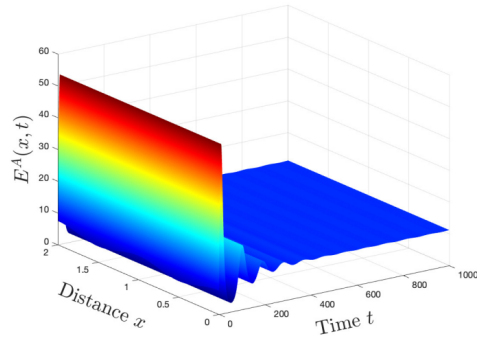
Figure 3. Numerical simulations indicate that the solutions of the system defined by Equations (18)–(24) eventually converge to the disease–free equilibrium point, given by (Scenario-3).

Scenario-4: With the parameter set to $\kappa = 0.0005$, the resulting basic reproduction number is calculated as $\overline{\mathcal{R}}_0 = 2.86$, which exceeds unity. This confirms that the stability conditions outlined in **Table 2** are satisfied. According to Theorem 4, the endemic equilibrium point EP1 is GAS. As illustrated in **Figure 4**, the system's dynamics show that all solution trajectories ultimately converge to the endemic equilibrium state, given by $EP_1 = (349.41,\ 9.11,\ 11.17,\ 37.24,\ 60.60,\ 62.12)$. This scenario represents a case in which the individual becomes infected with DENV.

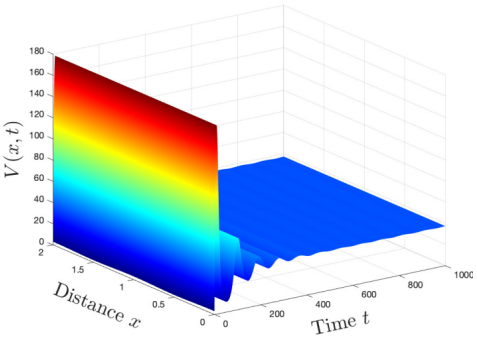


(a) Uninfected monocytes.

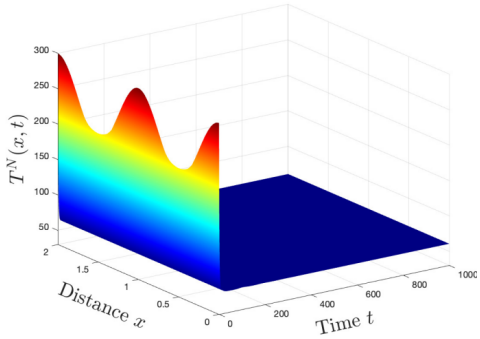
(b) Latently DENV–infected monocytes.



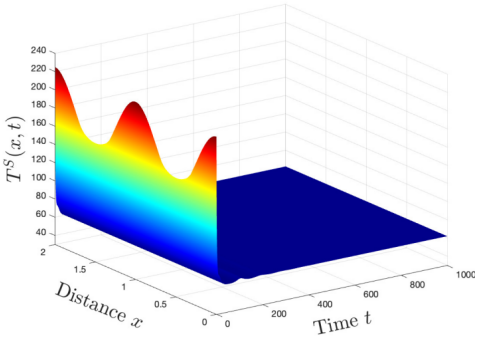
(c) Actively DENV–infected monocytes.



(d) Free DENV virus.



(e) Non–specific CTLs.



(f) Strain–specific CTLs.

Figure 4. Numerical simulations indicate that the solutions of the system defined by Equations (18)–(24) eventually converge to the endemic equilibrium point, given by $EP_1 = (349.41,\ 9.11,\ 11.17,\ 37.24,\ 60.60,\ 62.12)$ (Scenario-4).

These numerical simulations confirm the theoretical stability results and illustrate the biological role of immune responses. The antibody response influences whether the infection is cleared or persists, while the CTL response helps control viral replication and guides the system toward equilibrium. Changes in the strength or timing of these responses can affect clinical outcomes during secondary DENV infection, emphasizing the importance of both antibody- and CTL-mediated mechanisms in disease progression.

The Lyapunov-based stability results can be interpreted biologically as follows: when the basic reproduction number $\overline{\mathcal{R}}_0 < 1$, the combined effects of immune responses and viral clearance mechanisms dominate, driving the system toward the disease-free equilibrium. Conversely, if $\overline{\mathcal{R}}_0 > 1$, viral replication outpaces immune control, and the system settles at an endemic equilibrium where both virus and immune

responses coexist in a balanced state. Graphically, this behavior is illustrated by the numerical simulations, which show solution trajectories gradually approaching the corresponding equilibrium, providing a visual representation of how infection is cleared or persists over time.

For comparison, previous PDE-based models [30, 31] considered antibody dynamics solely through virus-induced proliferation, without baseline production. In contrast, our formulation includes self-regulated antibody generation, allowing both non-specific and strain-specific antibodies to coexist. This inclusion enhances infection control and shapes the convergence to disease-free or endemic equilibria, providing a more realistic representation of immune dynamics and highlighting the complementary roles of humoral and cellular responses in controlling DENV infection.

4.3. Sensitivity analysis for system (18)–(24)

Sensitivity analysis plays a crucial role in disciplines such as pathology and epidemiology, as it enables the evaluation of intricate interactions within mathematical models. With respect to the system of Equations (18)–(24), this method provides a means to quantify the relative impact of individual parameters. Parameters associated with the highest sensitivity indices are deemed most influential, underscoring their significant role in governing the model's dynamics and informing the development of targeted antiviral therapies. The normalized forward sensitivity index of the basic reproduction number, $\overline{\mathcal{R}}_0$, is given by Zeb et al. [54]:

$$S_{\omega}^{\bar{R}_0} = \frac{\partial \overline{\mathcal{R}}0}{\partial \omega} \times \frac{\omega}{\bar{R}_0} \tag{35}$$

where the variable $\omega = \eta, \kappa, \phi, v_N, v_S, \mu, \xi, \varphi, \rho, \zeta_S, \alpha_S, \zeta_N, \alpha_N, \delta \ and \ \varrho$ depends differentially on $\overline{\mathcal{R}}_0$.

The sensitivity indices of $\overline{\mathcal{R}}_0$ with respect to each model parameter are computed using Equation (35), with fixed at 0.0005, and the results are presented in **Table 6** and **Figure 5**. The signs of the indices, as shown in **Table 6**, offer valuable insight into the direction and extent of each parameter's influence within the sensitivity analysis.

- Parameters and ν_N exhibit a positive influence on $\overline{\mathcal{R}}_0$. For instance, the sensitivity index for μ is 0.1302, indicating that a 10% increase (or decrease) in this parameter leads to a corresponding 1.30% increase (or decrease) in $\overline{\mathcal{R}}_0$.
- In contrast, the remaining parameters possess negative sensitivity indices, signifying a diminishing effect on $\overline{\mathcal{R}}_0$ when their values increase.

Parameters with high sensitivity demand accurate estimation, as minor deviations in their values can induce substantial quantitative changes in the system's behavior. Analyzing the sensitivity indices of $\overline{\mathcal{R}}_0$ with respect to various parameters reveals that the DENV transmission rate κ, the viral production rate η, and the source rate of uninfected monocytes ϕ all exhibit positive sensitivity indices that should be reduced to effectively limit DENV transmission. This reduction can be achieved through various intervention strategies, such as vaccination programs, efficacious antiviral treatments, and strengthened public health initiatives. Conversely, parameters such as the death

rate constants ρ and ϱ, which are associated with negative sensitivity indices, should be enhanced to suppress viral proliferation within the host.

Table 6. Sensitivity index of $\overline{\mathcal{R}}_0$.

Parameter	$S_\gamma^{\overline{\mathcal{R}}_0}$	Numerical simulation of $S_\gamma^{\overline{\mathcal{R}}_0}$
η	1	1
κ	1	1
ϕ	1	1
μ	$\mu\left(-\frac{1}{\mu+\varphi}+\frac{1}{\mu+\varepsilon\varphi}\right)$	0.1302
ξ	$\frac{\xi\varphi}{\mu+\xi\varphi}$	0.0698
ν_S	$\frac{\zeta_s\alpha_S}{\delta v_S\left(1+\frac{\zeta_N\alpha_N}{\delta v_N}+\frac{\zeta_S\alpha_S}{\delta v_S}\right)}$	0.0012
ν_N	$\frac{\zeta_N\alpha_N}{\delta v_N\left(1+\frac{\zeta_N\alpha_N}{\delta v_N}+\frac{\zeta_S\alpha_S}{\delta v_S}\right)}$	0.0003
ζ_N	$-\frac{\zeta_N\alpha_N}{\delta v_N(1+\frac{\zeta_N\alpha_N}{\delta v_N}+\frac{\zeta_S\alpha_S}{\delta v_S})}$	−0.0003
α_N	$-\frac{\zeta_N\alpha_N}{\delta v_N\left(1+\frac{\zeta_N\alpha_N}{\delta v_N}+\frac{\zeta_S\alpha_S}{\delta v_S}\right)}$	−0.0003
ζ_S	$-\frac{\zeta_S\alpha_S}{\delta v_S\left(1+\frac{\zeta_N\alpha_N}{\delta v_N}+\frac{\zeta_S\alpha_S}{\delta v_S}\right)}$	−0.0012
α_S	$-\frac{\zeta_S\alpha_S}{\delta v_S\left(1+\frac{\zeta_N\alpha_N}{\delta v_N}+\frac{\zeta_S\alpha_S}{\delta v_S}\right)}$	−0.0012
φ	$\frac{\mu\varphi(-1+\xi)}{(\mu+\varphi)(\mu+\xi\varphi)}$	−0.1302
δ	$-\frac{\delta v_N v_S}{\zeta_S\alpha_S v_N+\zeta_N\alpha_N v_S+\delta v_N v_S}$	−0.9984
ρ	−1	−1
ϱ	−1	−1

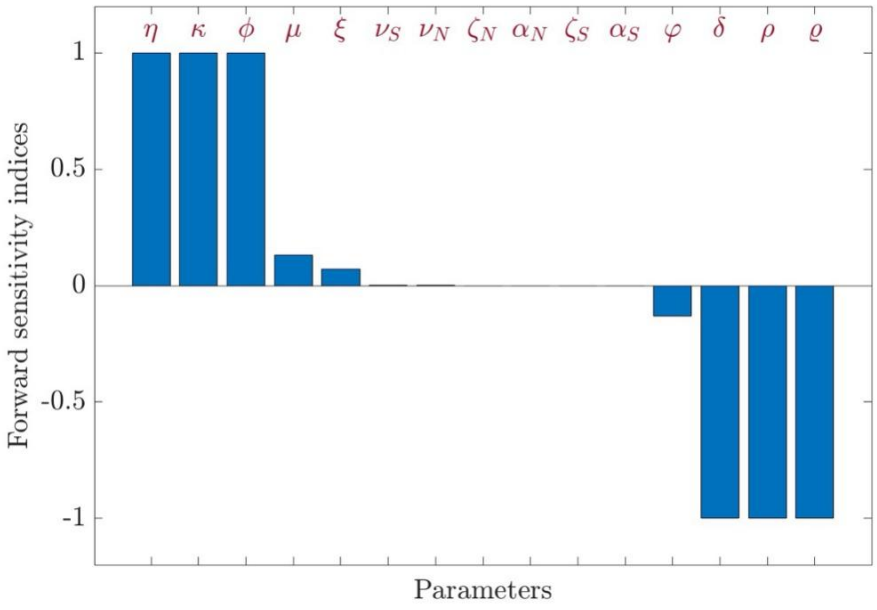


Figure 5. Sensitivity analysis of the basic reproduction number $\overline{\mathcal{R}}_0$.

4.4. Implications for control and intervention

Parameters with high positive sensitivity-such as the DENV transmission rate (κ) and viral production rate (η)-highlight targets for interventions. Reducing these parameters through antiviral therapy, can effectively lower $\overline{\mathcal{R}}_0$ and limit infection spread. Conversely, enhancing parameters with negative sensitivity indices, such as the

death rates of infected cells (ρ and ϱ), can suppress viral proliferation. These findings provide actionable guidance for designing public health strategies and therapeutic approaches, focusing on the most influential factors to optimize infection control and improve patient outcomes.

The antibody-based and CTL-based formulations show distinct mechanisms and outcomes. In the antibody model, the immune response acts by neutralizing free virus through complex formation, which reduces viral particles but may saturate at high viral loads. In the CTL model, the response targets and destroys infected cells, lowering viral production through a slower but more sustained mechanism. Although both models can lead to either viral clearance or an endemic equilibrium, the thresholds governing these transitions differ: antibody dynamics depend on neutralization efficiency, while CTL behavior relies on activation and killing rates. These differences highlight how humoral and cellular immunity shape viral dynamics in complementary but mechanistically distinct ways.

5. Conclusion and model extensions

This study provides a detailed comparative and numerical analysis of two models describing the host immune response to DENV infection. The first model emphasizes the role of antibodies in neutralizing viral particles and preventing further infection of host cells. The second model focuses on the CTLs, which identify and eliminate infected monocytes. Both models are formulated as nonlinear PDEs, capturing the spatial movement of viruses and host cells, and consider both activated and latent forms of infected monocytes.

The analysis confirms that the solutions of the proposed models are non–negative and bounded.

Two equilibrium points are identified: the disease–free equilibrium (EP0) and the endemic equilibrium (EP1). The stability of these points is determined by the basic reproduction number, $\mathcal{R}_0$. When $\mathcal{R}_0 \leq 1$, the infection is cleared, reflecting the efficacy of the immune response. When $\mathcal{R}_0 > 1$, the disease persists within the host. Using Lyapunov stability theory and LaSalle's invariance principle, the global asymptotic stability of both equilibria is rigorously established. The main findings are summarized as follows:

1. The disease–free equilibrium (EP_0) always exists and is globally asymptotically stable when $\mathcal{R}_0 \leq 1$.
2. The endemic equilibrium (EP_1) exists and is globally asymptotically stable for $\mathcal{R}_0 > 1$.

These theoretical results are supported by numerical simulations, and a sensitivity analysis highlights that the infection rate and viral production rate are the most influential parameters affecting $\mathcal{R}_0$, thereby shaping DENV transmission dynamics. Such insights could guide the development of antiviral strategies targeting viral entry and replication.

Proposed model extensions

The model can be further extended in several directions:

- Virus-antibody complexes: the virus-non-specific antibody complex and the virus-strain-specific antibody complex C^S. These complexes play a crucial role in regulating the subsequent regeneration of antibody responses [55,56,58]:

$$\frac{\partial M}{\partial t} = D_M \Delta M(x,t) + \phi - \rho_M M(x,t) - \kappa M(x,t) V(x,t),$$

$$\frac{\partial E^L}{\partial t} = D_{E^L} \Delta E^L(x,t) + (1-\xi)\kappa M(x,t) V(x,t) - (\mu+\varphi) E^L(x,t),$$

$$\frac{\partial E^A}{\partial t} = D_{E^A} \Delta E^A(x,t) + \xi\kappa M(x,t) V(x,t) + \mu E^L(x,t) - \delta E^A(x,t),$$

$$\frac{\partial V}{\partial t} = D_V \Delta V(x,t) + \eta E^A(x,t) - \rho_V V(x,t) - \beta_N V(x,t) W^N(x,t) - \beta_S V(x,t) W^S(x,t),$$

$$\frac{\partial C^N}{\partial t} = D_{C^N} \Delta C^N(x,t) + \beta_N V(x,t) W^N(x,t) - \rho_N C^N(x,t),$$

$$\frac{\partial C^S}{\partial t} = D_{C^S} \Delta C^S(x,t) + \beta_S V(x,t) W^S(x,t) - \rho_S C^S(x,t),$$

$$\frac{\partial W^N}{\partial t} = D_{W^N} \Delta W^N(x,t) + \gamma^N - \beta_N V(x,t) W^N(x,t) + \alpha C^N(x,t) - \psi_N W^N(x,t),$$

$$\frac{\partial W^S}{\partial t} = D_{W^S} \Delta W^S(x,t) + \gamma^S - \beta_S V(x,t) W^S(x,t) + \alpha C^S(x,t) - \psi_S W^S(x,t).$$

The non-specific complex C^N *i*s produced through the binding of free virus with non-specific antibodies at rate $\beta_N V W^N$, and is cleared at a rate $\rho N C^N$. Similarly, the strain-specific complex forms when free virus binds to strain-specific antibodies at rate $\beta_S V W^S$, and is removed at a clearance rate $\rho_S C^S$. The concentration of non-specific antibodies is enhanced in response to virus-non-specific complexes at stimulation rate αC^N, while these antibodies are consumed during the formation of at rate $\beta_N V W^N$. Likewise, the population of strain-specific antibodies is stimulated by virus-strain-specific complexes at rate and is depleted through its binding with free virus to form at rate $\beta_S V W^S$. A full analytical study of existence, positivity, boundedness and equilibria for this extended model is left for future work.

- Immune memory: Incorporating B-cell and T-cell memory could capture key immunological phenomena and longer-term host protection [55,56].
- Alternative incidence rates: The model could be generalized to include other incidence forms, such as saturated, Michaelis-Menten, Beddington-DeAngelis, or general incidence functions.
- Stochastic effects: Random fluctuations in viral dynamics could be incorporated using stochastic modeling approaches, which may reveal behaviors not captured by deterministic PDEs.
- Time delay: Incorporating intracellular or immune-response delays can account for the finite time required for viral replication, antibody production, and CTL activation. Time delays have been successfully employed in both virological [36]

and epidemiological [59] models to capture these biological lags, often revealing richer dynamics such as oscillations, transient instability, or delayed immune clearance. Extending the present PDE framework to include such delays would provide a more realistic description of DENV progression and merits further investigation.

- Heterogeneous diffusion: While the current model assumes uniform diffusion coefficients, allowing for heterogeneous diffusion or spatially varying parameters could provide additional biological insights. This extension requires significant additional work and is therefore suggested as a direction for future research.
- Memory effects: Fractional differential equations can be used to incorporate long-term memory and non-local interactions in the immune response. Such formulations have been applied successfully in biological and epidemiological modeling. Extending the model to a fractional framework could reveal additional features of DENV dynamics.

Author contributions: All authors contributed equally to the conception, design, data collection, analysis, and writing of this study. All authors have read and agreed to the published version of the manuscript.

Funding: This research did not receive any external funding.

Institutional review board statement: Not applicable.

Informed consent statement: Not applicable.

Data availability statement: No data associated with the manuscript.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Haider N, Hasan MN, Onyango J, et al. Global dengue epidemic worsens with record 14 million cases and 9,000 deaths reported in 2024. International Journal of Infectious Diseases. 2025; 158: 107940.
2. Sasmal SK, Dong Y, Takeuchi Y. Mathematical modeling on T-cell mediated adaptive immunity in primary dengue infections. Journal of Theoretical Biology. 2017; 429: 229–240.
3. Ahman QO, Aja RO, Omale D, et al. Mathematical modeling of dengue virus transmission: exploring vector, vertical, and sexual pathways with sensitivity and bifurcation analysis. BMC Infectious Diseases. 2025; 25(1): 999.
4. Guzmán MG, Kouri G. Dengue: An update. The Lancet Infectious Diseases. 2002; 2(1): 33–42.
5. Nuraini N, Tasman H, Soewono E, et al. A with-in host dengue infection model with immune response. Mathematical and Computer Modelling. 2009; 49(5–6): 1148–1155.
6. Perera SD, Perera SSN. Impact of innate and cell mediated immune responses on dengue virus dynamics. International Journal of Pure and Applied Mathematics. 2018; 118(6): 353–360.
7. Perera SD, Perera SSN. Simulation model for dynamics of dengue with innate and humoral immune responses. Computational and Mathematical Methods in Medicine. 2018; 2018(1): 8798057.
8. Perera SD, Perera SSN. Mathematical modeling and analysis of innate and humoral immune responses to dengue infections. International Journal of Biomathematics. 2019; 12(7): 1950077.
9. Clapham HE, Tricou V, Van Vinh Chau N, et al. Within-host viral dynamics of dengue serotype 1 infection. Journal of the Royal Society Interface. 2014; 11(96): 20140094.
10. Ansari H, Hesaaraki M. A with-in host dengue infection model with immune response and Beddington–DeAngelis incidence rate. Applied Mathematics. 2012; 3: 177–184.
11. Thibodeaux JJ, Nunez D, Rivera A. A generalized within-host model of dengue infection with a non-constant

monocyte production rate. Journal of Biological Dynamics. 2020; 14(1): 143–161.
12. Modak B, Muthu P. Stochastic approach to a delayed in-host model of DENV transmission. Physica Scripta. 2024; 99(7): 075006.
13. Mishra A, Gakkhar S. A micro-epidemic model for primary dengue infection. Communications in Nonlinear Science and Numerical Simulation. 2017; 47: 426–437.
14. Cerón Gómez M, Yang HM. Mathematical model of the immune response to dengue virus. Journal of Applied Mathematics and Computing. 2020; 63: 455–478.
15. Sasmal SK, Takeuchi Y, Nakaoka S. T-cell mediated adaptive immunity and antibody-dependent enhancement in secondary dengue infection. Journal of Theoretical Biology. 2019; 470: 50–63.
16. Borisov M, Dimitriu G, Rashkov P. Modelling the host immune response to mature and immature dengue viruses. Bulletin of Mathematical Biology. 2019; 81: 4951–4976.
17. de A Camargo F, Adimy M, Esteva L, et al. Modeling the relationship between antibody-dependent enhancement and disease severity in secondary dengue infection. Bulletin of Mathematical Biology. 2021; 83(8): 85.
18. Nikin-Beers R, Ciupe SM. Modelling original antigenic sin in dengue viral infection. Mathematical Medicine and Biology: A Journal of the IMA. 2018; 35(2): 257–272.
19. Nikin-Beers R, Ciupe SM. The role of antibody in enhancing dengue virus infection. Mathematical Biosciences. 2015; 263: 83–92.
20. Ben-Shachar R, Koelle K. Minimal within-host dengue models highlight the specific roles of the immune response in primary and secondary dengue infections. Journal of the Royal Society Interface. 2015; 12: 20140886.
21. Alves Rubio F, Yang HM. A mathematical model to describe antibody-dependent enhancement and assess the effect of limiting cloning for plasma cells in heterologous secondary dengue infection. Mathematical Medicine and Biology: A Journal of the IMA. 2022; 39(2): 169–196.
22. Rashid S, Jarad F, El-Marouf SA, et al. Global dynamics of deterministic-stochastic dengue infection model including multi specific receptors via crossover effects. AIMS Mathematics. 2023; 8(3): 6466–6503.
23. Gujarati TP, Ambika G. Virus antibody dynamics in primary and secondary dengue infections. Journal of Mathematical Biology. 2014; 69: 1773–1800.
24. Alshaikh MA, Elnahary E, Elaiw AM. Stability of a secondary dengue viral infection model with multi-target cells. Alexandria Engineering Journal. 2022; 61(9): 7075–7087.
25. Elaiw AM, Raezah AA, Alshaikh MA. Global dynamics of viral infection with two distinct populations of antibodies. Mathematics. 2023; 11(14): 3138.
26. Raezah AA, Elaiw AM, Alshaikh MA. Global stability of secondary DENV infection models with non-specific and strain-specific CTLs. Heliyon. 2024; 10(3): e25391.
27. Brainard DM, Tager AM, Misdraji J, et al. Decreased CXCR3+ CD8 T cells in advanced human immunodeficiency virus infection suggest that a homing defect contributes to cytotoxic T-lymphocyte dysfunction. Journal of Virology. 2007; 81(16): 8439–8450.
28. Tattermusch S, Bangham CRM. HTLV-1 infection: what determines the risk of inflammatory disease? Trends in Microbiology. 2012; 20(10): 494–500.
29. Bellomo N, Painter KJ, Tao Y, et al. Occurrence vs. absence of taxis-driven instabilities in a May-Nowak model for virus infection. SIAM Journal on Applied Mathematics. 2019; 79(5): 1990–2010.
30. Elaiw AM, Alofi AS. Global dynamics of secondary DENV infection with diffusion. Journal of Mathematics. 2021; 2021: 5585175.
31. Raezah AA. Dynamical analysis of secondary dengue viral infection with multiple target cells and diffusion by mathematical model. Discrete Dynamics in Nature and Society. 2022; 2022(1): 2106910.
32. Nowak MA, May RM. Virus Dynamics. Oxford University Press; 2000.
33. Dubey B, Dubey P, Dubey US. Modeling the intracellular pathogen-immune interaction with cure rate. Communications in Nonlinear Science and Numerical Simulation. 2016; 38: 72–90.
34. Xu Z, Zhang H, Yang D, et al. The mathematical modeling of the host-virus interaction in dengue virus infection: A quantitative study. Viruses. 2024; 16(2): 216.
35. Wang H, Tian X. Dynamics of a delayed within host model for dengue infection with immune response and Beddington–DeAngelis incidence. International Journal of Biomathematics. 2022; 15(3): 2250002.
36. Huang G, Takeuchi Y, Ma W. Lyapunov functionals for delay differential equations model of viral infections. SIAM Journal of Applied Mathematics. 2010; 70(7): 2693–2708.
37. Zhang Y, Xu Z. Dynamics of a diffusive HBV model with delayed Beddington–DeAngelis response. Nonlinear

Analysis: Real World Applications. 2014; 15: 118–139.
38. Xu Z, Xu Y. Stability of a CD4+ T cell viral infection model with diffusion. International Journal of Biomathematics. 2018; 11(05): 1850071.
39. Chukukere EC, Omame A, Onyenegecha CP, et al. Mathematical analysis of a model for Chlamydia and Gonorrhea codynamics with optimal control. Results in Physics. 2021; 27: 104566.
40. Smith HL. Monotone Dynamical Systems: An Introduction to the Theory of Competitive and Cooperative Systems. American Mathematical Society; 1995.
41. Protter MH, Weinberger HF. Maximum Principles in Differential Equations. Prentice Hall; 1967.
42. Henry D. Geometric Theory of Semilinear Parabolic Equations. Springer; 1993.
43. Nampala H, Luboobi LS, Mugisha JY, et al. Modelling hepatotoxicity and antiretroviral therapeutic effect in HIV/HBV co-infection. Mathematical Biosciences. 2018; 302: 67–79.
44. Van den Driessche P, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical Biosciences. 2002; 180(1–2): 29–48.
45. Hattaf K, Yousfi N. Global stability for reaction-diffusion equations in biology. Computers & Mathematics with Applications. 2013; 66(8): 1488–1497.
46. AlAgha AD, Elaiw AM. Stability of a general reaction-diffusion HIV-1 dynamics model with humoral immunity. The European Physical Journal Plus. 2019; 134(8): 390.
47. Hale JK, Lunel SM. Introduction to Functional Differential Equations. Springer; 1993.
48. Mapalagamage M, Weiskopf D, Sette A, et al. Current understanding of the role of T cells in chikungunya, dengue and zika infections. Viruses. 2022; 14(2): 242.
49. Rothman AL. Immunity to dengue virus: A tale of original antigenic sin and tropical cytokine storms. Nature Reviews Immunology. 2011; 11(8): 532–543.
50. Sardar P, Biswas S, Das KP, et al. Stability, sensitivity, and bifurcation analysis of a fractional-order HIV model of CD4+ T cells with memory and external virus transmission from macrophages. The European Physical Journal Plus. 2025; 140(2): 160.
51. Yaagoub Z. Fractional two-strain SVLIR epidemic model with vaccination and quarantine strategies. International Journal of Dynamics and Control. 2025; 13(2): 55.
52. Butt AIK, Ahmad W, Rafiq M, et al. Optimally analyzed fractional Coronavirus model with Atangana-Baleanu derivative. Results in Physics. 2023; 53: 106929.
53. Butt AIK, Ahmad W, Rabbani HG, et al. Exploring optimal control strategies in a nonlinear fractional bi-susceptible model for COVID-19 dynamics using Atangana-Baleanu derivative. Scientific Reports. 2024; 14(1): 31617.
54. Zeb S, Yatim SAM, Ahmad A, et al. Numerical modelling of SEIR on two-dose vaccination against the rubella virus. Malaysian Journal of Fundamental and Applied Sciences. 2025; 21(1): 1577–1601.
55. Xu Z, Wei D. A comprehensive mathematical model simulating the adaptive immune response. bioRxiv preprint. 2025. doi: 10.1101/2025.10.14.682330
56. Xu Z, Song J, Liu W, et al. An agent-based model with antibody dynamics information in COVID-19 epidemic simulation. Infectious Disease Modelling. 2023; 8(4): 1151–1168.
57. Xu Z, Peng Q, Xu J, et al. Dynamic modeling of antibody repertoire reshaping in response to viral infections. Computers in Biology and Medicine. 2025; 184: 109475.
58. Xu Z, Song J, Zhang H, et al. A mathematical model simulating the adaptive immune response in various vaccines and vaccination strategies. Scientific Reports. 2024; 14(1): 23995.
59. Zeb S, Yatim SAM, Rafiq M, et al. Treatment and delay control strategy for a non-linear Rift Valley fever epidemic model. AIP Advances. 2024; 14(11): 115104.