Networks and Heterogeneous Media

https://www.aimspress.com/journal/nhm

NHM, 21(4): 1262–1333.
DOI: 10.3934/nhm.2026050
Received: 23 April 2026
Revised: 05 June 2026
Accepted: 15 June 2026
Published: 26 June 2026

Research article

Mathematical analysis of DENV–ZIKV co-infection with CTL-mediated immune response and time delays

Ahmed Elaiw[1,*], **Zainab Alkhudhari**[1] **and Ebtehal Almohaimeed**[2]

[1] Department of Mathematics, Faculty of Science, King Abdulaziz University, P. O. Box 80203, Jeddah 21589, Saudi Arabia

[2] Department of Mathematics, College of Science, Qassim University, P.O. Box 6644, Buraydah 51452, Saudi Arabia

* **Correspondence:** Email: aelaiwksu.edu.sa@kau.edu.sa.

Abstract: In this study, we formulated and analyzed a within-host co-infection model of Dengue virus (DENV) and Zika virus (ZIKV) that incorporated CTL-mediated immunity, and four types of distributed time delays. The model described the dynamics of uninfected cells, latently, and productively infected cells for each virus, along with free DENV and ZIKV particles and virus-targeted CTL responses. We first proved that all model solutions remained nonnegative and bounded. We computed the basic reproduction numbers R_D^L for DENV and R_Z^L for ZIKV, together with the invasion reproduction numbers $R_D^{L,inv}$ and $R_Z^{L,inv}$, which determined invasion capability under pre-existing infection. These numbers governed the existence and the global asymptotic stability of model equilibria. Global stability was established using the Lyapunov method, and numerical simulations were performed to validate the analytical results. In addition, sensitivity analysis identified the most influential parameters affecting viral clearance. The effects of antiviral therapy, time delays, and latent infection stages on the DENV–ZIKV co-dynamics were investigated. The results showed that treatment intervention, prolonged delays, and the inclusion of latent infection stages led to a reduction in R_D^L and R_Z^L. Furthermore, neglecting intracellular delays or latent infection stages leads to an overestimation of R_D^L and R_Z^L and the antiviral efficacy required for infection control. This suggests that therapeutic strategies aimed at prolonging intracellular delay phases and accounting for latent-stage dynamics may decrease these reproduction numbers below unity, thereby promoting viral elimination within the host.

Keywords: co-infection; dengue virus; zika virus; time delay; drug therapy; sensitivity analysis; basic and invasion reproduction numbers

1. Introduction

Dengue virus (DENV) and Zika virus (ZIKV) are among the most epidemiologically significant flaviviruses worldwide. Both viruses are primarily transmitted by *Aedes aegypti* and *Aedes albopictus*, mosquito species that are widely distributed in tropical and subtropical climates and facilitate sustained viral circulation in densely populated regions. While dengue transmission is largely vector-dependent, ZIKV also exhibits additional transmission routes, including sexual and vertical transmission during pregnancy, thereby increasing its public health complexity and creating additional challenges for epidemiological surveillance systems [1, 2].

According to the World Health Organization, the global burden of dengue has increased substantially over the past two decades, with reported cases rising from approximately 505,000 in 2000 to more than 14.6 million in 2024, representing the highest annual incidence recorded to date [2]. Cartographic modeling estimates indicate that the number of dengue cases exceeded twice the 7 million reported in 2023 and was nearly twelvefold higher than the 1.2 million cases documented in 2014 [3]. In the same year, 9,508 deaths were attributed to Dengue, corresponding to a global case-fatality rate of 0.07% [3]. In contrast, Zika virus incidence declined markedly following the major epidemic waves of 2015–2016; however, its presence in more than 90 countries in 2023 continued to underscore its persistent epidemic potential and capacity for resurgence [4].

DENV and ZIKV are positive-sense, single-stranded RNA viruses classified within the genus *Flavivirus*. Both viruses elicit innate and adaptive immune responses that shape infection outcomes and contribute to host defense by limiting viral replication and persistence [5, 6]. Adaptive immunity consists of two principal arms: The humoral response, mediated by B lymphocytes that produce antibodies capable of binding to and neutralizing viral particles, and the cellular response, mediated by cytotoxic T lymphocytes (CTLs), that recognize and eliminate infected cells. CTLs are particularly critical in mosquito-borne viral infections, where effective clearance of infected cells is essential for controlling viral load and limiting disease progression. In dengue infection, CTL responses have been shown to influence viral control and disease severity [7], and similar cellular immune mechanisms are implicated in ZIKV infection outcomes [8]. DENV consists of four antigenically distinct serotypes (DENV-1 to DENV-4). Infection with one serotype induces long-lasting homologous immunity against that specific serotype; however, it confers only partial and transient protection against the remaining serotypes. As a result, secondary infections can occur and are frequently associated with heightened disease severity due to immune-mediated mechanisms [9]. In addition, the limited cross-protective immunity between DENV and ZIKV permits sequential infections and co-infections. These events have been documented in several endemic regions and may substantially influence viral dynamics and host immune interactions within the infected individual [10–12].

At the cellular scale, mathematical modeling provides a powerful framework for investigating within-host viral dynamics in primary, secondary, and co-infection scenarios. These models facilitate a mechanistic understanding of the interactions among viruses, target cells, and immune components, and are especially valuable when examining co-infections such as DENV and ZIKV, which compete for similar cellular targets. Moreover, within-host models enable researchers to explore biological mechanisms that are challenging to measure experimentally and to predict infection trajectories, including viral persistence or clearance. Such predictive insights are instrumental in guiding antiviral drug development and vaccine strategies.

The simple target cell limited framework has served as the foundational structure for modeling within-host viral dynamics, capturing the interactions among susceptible target cells, infected cells, and free virions. Building upon a simple foundational model, this approach has been extensively applied to DENV infections [13, 14] and to ZIKV infections [15–17]. Extensions of this framework have progressively incorporated immunological mechanisms. Nikin-Beers and Ciupe [18] formulated this basic framework to elucidate the underlying mechanisms governing viral amplification and clearance during both primary and secondary dengue infections. In addition, Ben Shachar and Koelle [13] demonstrated that T cell–mediated cytokine responses may exacerbate disease severity during secondary DENV infection. For ZIKV, Osuna et al. [15] calibrated the model using primate data, while Best et al. [16] evaluated antiviral treatment effects. Best and Perelson [17] later integrated innate immune mediators such as interferon-α and natural killer cells. Tuncer and Martcheva [19] developed coupled within-host and within-vector models that distinguish pregnant and non-pregnant hosts, and validated them using primate data. Moreover, Best et al. [20] emphasized viral interference with host innate defenses, underscoring the growing recognition of immune-virus feedback mechanisms in shaping infection trajectories.

Subsequent developments entailed structural limitations of the classical framework, particularly the absence of target cell renewal and natural death. Models incorporating target cell recruitment and turnover were advanced by Nuraini et al. [21], who explicitly modeled CTL-mediated viral control. The combined action of innate immunity and CTLs was further analyzed by S. Perera and S. S. N. Perera [22], with subsequent computations in [23] and asymptotic investigations in [24]. Nonlinear interaction structures were introduced using Beddington-DeAngelis functional responses in [25], while Thibodeaux et al. [26] extended CTL-driven models by incorporating monocyte dynamics regulated by macrophage colony-stimulating factor. Stochastic effects were incorporated to capture biological variability [27], and delayed stochastic perturbations were examined by Modak and Muthu [28].

Parallel studies entailed immune complexity during secondary infection, including models integrating both CTL and antibody-mediated responses as in [29–31], and explicit treatment of secondary DENV dynamics [32, 33]. Antibody competition and cross-reactivity mechanisms contributing to antibody-dependent enhancement were investigated in [18, 34]. Extensions to multi-target cell infection structures were proposed by Alshaikh et al. [35] and later expanded spatially by [36]. Additional refinements included antibody-dependent enhancement with constrained plasma cell proliferation [37] and hybrid deterministic-stochastic formulations using piecewise fractional differential equations to capture nonlinear transmission and logistic target cell growth [38]. Gujarati and Ambika [39] further examined the dynamics of antibody classes during secondary DENV infection. Furthermore, Aldubiban et al. [40] advanced secondary DENV within-host modeling by incorporating CTL immunity together with explicit time-delay mechanisms, and then refining the formulation using distributed delays to better capture heterogeneity in infection progression and virion maturation.

Regarding DENV–ZIKV co-infection, considerable attention has been devoted to population-level epidemiological modeling (see e.g. [41–43]). Despite these extensive contributions addressing dengue-Zika co-infection at the population scale, within-host dynamics remain insufficiently investigated. Tang et al. [44] proposed a within-host DENV–ZIKV co-infection model incorporating antibodies to characterize humoral immune responses and cross-immune effects, including antibody-dependent enhancement (ADE) and antibody-dependent neutralization (ADN). While

this framework provides valuable insight into antibody-mediated interactions, several biologically important mechanisms and mathematical aspects remain unexplored.

First, CTL-mediated elimination of infected cells is not explicitly incorporated. Experimental and immunological evidence indicates that CTLs play a crucial role in controlling flaviviral infections through the recognition and clearance of infected cells, thereby contributing to viral elimination and disease regulation [7, 8].

Second, the model neglects latently infected cells, in which infected cells harbor the virus before becoming productively infectious. Since latency constitutes an important stage in intracellular viral progression, neglecting this compartment may limit the representation of viral persistence and delayed infection dynamics.

Third, the model assumes instantaneous transitions among infection stages. However, several biological processes involved in DENV–ZIKV infection are intrinsically time-dependent, including the establishment of latent infection, progression to productive infection, activation of latently infected cells, and maturation of newly produced virions prior to infectivity. To better capture these mechanisms, we incorporate four biologically motivated distributed intracellular delays corresponding to: (i) latent infection establishment, (ii) productive infection establishment, (iii) activation of latent cells, and (iv) virion maturation. Unlike instantaneous or discrete-delay formulations, distributed time delays enable temporal heterogeneity in intracellular progression, thereby providing a more realistic description of viral development across infected cells and virions.

Fourth, a comprehensive mathematical analysis of DENV–ZIKV co-infection, including well-posedness, equilibrium structure, stability, and antiviral treatment effects, remains limited.

The researchers in [45], developed and analyzed DENV–ZIKV co-infection model with CTL-mediated immunity; however, latent infection and intracellular time delays were not considered.

Motivated by the limitations of [44, 45], we develop a within-host DENV–ZIKV co-infection model integrating CTL-mediated immunity, latent infection stages, and four biologically motivated distributed intracellular time delays. The proposed framework enables investigation of how cellular immune responses and delayed intracellular viral progression influence invasion thresholds, viral persistence, competitive outcomes, and long-term co-infection dynamics.

Contributions of this study:

- We develop a within-host DENV–ZIKV co-infection model integrating CTL-mediated immunity, latent infection stages, and four biologically motivated distributed intracellular time delays describing latent-cell establishment, productive-cell establishment, latent-cell activation, and virion maturation.

- A rigorous qualitative investigation of the proposed system is performed to establish its fundamental mathematical properties.

- The basic and invasion reproduction numbers are derived and analytically shown to govern the existence and stability of all equilibrium states.

- The global stability behavior of the co-infection system is thoroughly examined.

- An antiviral treatment strategy is integrated into the model to evaluate its impact on viral progression and immune dynamics.

- A detailed sensitivity analysis is conducted to identify the most influential parameters affecting viral persistence and clearance.
- Numerical simulations are implemented to support the theoretical analysis and to assess the effectiveness of therapeutic interventions as well as time delay.

In this study, we provide a mechanistic framework for understanding the role of CTL-mediated immunity and intracellular delay heterogeneity in shaping DENV–ZIKV co-infection dynamics and establish a foundation for future mathematical, immunological, and data-driven investigations.

2. Model formulation

In this section, we present the formulation of the DENV–ZIKV within-host co-infection model with CTL immunity, latently infected cells, and multi-distributed time delays. The model is developed under the following assumptions:

A1. The within-host system consists of nine interacting compartments: uninfected cells X, latently DENV-infected cells Y_D^L, productively DENV-infected cells Y_D^A, latently ZIKV-infected cells Y_Z^L, productively ZIKV-infected cells Y_Z^A, free DENV virions V_D, free ZIKV virions V_Z, DENV-targeted CTLs U_D, and ZIKV-targeted CTLs U_Z. These compartments are removed at rates d, b_D, a_D, b_Z, a_Z, c_D, c_Z, ψ_D, and ψ_Z, respectively.

A2. Uninfected cells are produced at a constant rate λ and become infected by DENV and ZIKV through bilinear incidence terms $\beta_D X V_D$ and $\beta_Z X V_Z$, respectively. Infection results in the depletion of uninfected cells, and the formation of latent and active infected cell compartments Y_D^L, Y_D^A, Y_Z^L, and Y_Z^A are described by Eqs (2.1)–(2.5).

A3. For each $i \in \{D, Z\}$, a fraction $\theta_i \in [0, 1]$ of newly infected cells immediately enters the productively infected class, while the remaining fraction $(1 - \theta_i)$ becomes latently infected. Latently infected cells transition to the productive class at rates η_D and η_Z, respectively (see Eqs (2.2)–(2.5)).

A4. Productively infected cells Y_D^A and Y_Z^A produce new DENV and ZIKV virions at rates k_D and k_Z, respectively (see Eqs (2.6) and (2.7)). CTLs contribute to viral control by killing productively infected cells at rates $\delta_D Y_D^A U_D$ and $\delta_Z Y_Z^A U_Z$, as described in Eqs (2.3) and (2.5).

A5. DENV- and ZIKV-targeted CTLs U_D and U_Z are produced at basal rates φ_D and φ_Z, respectively, and undergo clonal expansion in response to antigenic stimulation at rates $\rho_D Y_D^A U_D$ and $\rho_Z Y_Z^A U_Z$. The CTL immune response dynamics are governed by Eqs (2.8) and (2.9).

A6. The model incorporates eight biologically distinct distributed time delays representing intracellular processes such as cell infection, activation of latent cells, and maturation of virions. For each delay process $i = 1, 2, \ldots, 8$, the delay variable τ is characterized by a probability density function $f_i(\tau)$ supported on $[0, S_i]$, where S_i denotes the upper bound of the corresponding delay interval. These functions satisfy standard probabilistic assumptions and admit the following interpretations:

- The probability that uninfected cells contacted by DENV or ZIKV at time $t-\tau$ survive for τ time units and become latently infected at time t is given by $f_i(\tau)e^{-n_i\tau}$ for $i = 1, 4$, where $1/n_i$ denotes the average time required for latent infection to establish.
- The probability that viral-contacted cells require τ time units and become productively infected is represented by $f_i(\tau)e^{-n_i\tau}$ for $i = 2, 5$, where $1/n_i$ denotes the average time required for productive infection to establish.
- The probability that latently infected cells become productive after a delay τ is represented by $f_i(\tau)e^{-n_i\tau}$ for $i = 3, 6$, where $1/n_i$ is the average time for the activation of latently infected cells.
- The probability that new produced virions at time $t-\tau$ and become mature at time t is given by $f_i(\tau)e^{-n_i\tau}$ for $i = 7, 8$, where $1/n_i$ represents the average maturation time.

We denote

$$\Psi = \Psi(t), \qquad \Psi_\tau = \Psi(t-\tau), \quad \text{for} \quad \Psi \in \left\{X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z\right\}.$$

Define

$$\Pi_i(\tau) = f_i(\tau)e^{-n_i\tau}, \text{ and } F_i = \int_0^{S_i} \Pi_i(\tau)\, d\tau, \quad i = 1, 2, \ldots, 8,$$

which satisfy $0 < F_i \leq 1$. Based on Assumptions A1–A6, the proposed DENV–ZIKV co-infection model is given by

$$\frac{dX}{dt} = \lambda - dX - \beta_D X V_D - \beta_Z X V_Z, \tag{2.1}$$

$$\frac{dY_D^L}{dt} = (1-\theta_D)\beta_D \int_0^{S_1} \Pi_1(\tau) X_\tau V_{D\tau}\, d\tau - (\eta_D + b_D) Y_D^L, \tag{2.2}$$

$$\frac{dY_D^A}{dt} = \theta_D\beta_D \int_0^{S_2} \Pi_2(\tau) X_\tau V_{D\tau}\, d\tau + \eta_D \int_0^{S_3} \Pi_3(\tau) Y_{D\tau}^L\, d\tau - a_D Y_D^A - \delta_D Y_D^A U_D, \tag{2.3}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z \int_0^{S_4} \Pi_4(\tau) X_\tau V_{Z\tau}\, d\tau - (\eta_Z + b_Z) Y_Z^L, \tag{2.4}$$

$$\frac{dY_Z^A}{dt} = \theta_Z\beta_Z \int_0^{S_5} \Pi_5(\tau) X_\tau V_{Z\tau}\, d\tau + \eta_Z \int_0^{S_6} \Pi_6(\tau) Y_{Z\tau}^L\, d\tau - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z, \tag{2.5}$$

$$\frac{dV_D}{dt} = k_D \int_0^{S_7} \Pi_7(\tau) Y_{D\tau}^A\, d\tau - c_D V_D, \tag{2.6}$$

$$\frac{dV_Z}{dt} = k_Z \int_0^{S_8} \Pi_8(\tau) Y_{Z\tau}^A\, d\tau - c_Z V_Z, \tag{2.7}$$

$$\frac{dU_D}{dt} = \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D, \tag{2.8}$$

$$\frac{dU_Z}{dt} = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z. \tag{2.9}$$

The initial conditions for system in Eqs (2.1)–(2.9) are given by

$$\begin{cases} X(\varkappa) = \phi_1(\varkappa), Y_D^L(\varkappa) = \phi_2(\varkappa), Y_D^A(\varkappa) = \phi_3(\varkappa), Y_Z^L(\varkappa) = \phi_4(\varkappa), Y_Z^A(\varkappa) = \phi_5(\varkappa), \\ V_D(\varkappa) = \phi_6(\varkappa), V_Z(\varkappa) = \phi_7(\varkappa), U_D(\varkappa) = \phi_8(\varkappa), U_Z(\varkappa) = \phi_9(\varkappa), \\ \quad \phi_i(\varkappa) \geq 0, i = 1, 2, \ldots, 9, \ \varkappa \in [-S^*, 0], \end{cases} \tag{2.10}$$

where $S^* = \max\{S_1, S_2, \ldots, S_8\}$ and $\phi_i \in C([-S^*, 0], \mathbb{R}_{\geq 0})$. Here, C denotes the Banach space of continuous functions mapping $[-S^*, 0]$ into $\mathbb{R}_{\geq 0}$ with norm $\|\phi_i\| = \sup_{-S^* \leq \varkappa \leq 0} |\phi_i(\varkappa)|$. By standard results for functional differential equations [46, 47] system in Eqs (2.1)–(2.9) with initial data in Eq (2.10) admits a unique continuous solution. The definitions and values of the model parameters and variables are listed in Table 1. Figure 1 illustrates the within-host dynamics of DENV and ZIKV co-infection, highlighting the interactions between viral populations, latent and actively infected cells, and CTL-mediated immune responses with time delays.

Table 1. Model parameters.

Symbol	Description	Value
X	Uninfected target cells	cells mm^{-3}
Y_D^L	Latently DENV-infected cells	cells mm^{-3}
Y_Z^L	Latently ZIKV-infected cells	cells mm^{-3}
Y_D^A	Productively DENV-infected cells	cells mm^{-3}
Y_Z^A	Productively ZIKV-infected cells	cells mm^{-3}
V_D	Free DENVs	viruses mm^{-3}
V_Z	Free ZIKVs	viruses mm^{-3}
U_D	DENV-targeted CTLs	cells mm^{-3}
U_Z	ZIKV-targeted CTLs	cells mm^{-3}
λ	Production rate of uninfected cells	10 cells mm^{-3} day^{-1}
d	Death rate of uninfected cells	0.14 day^{-1}
β_D	DENV-cells incidence rate	varied
β_Z	ZIKV-cells incidence rate	varied
θ_D	Probability of productive DENV infection	0.3
θ_Z	Probability of productive ZIKV infection	0.25
η_D	Conversion rate of latently DENV-infected to productive cells	0.1 day^{-1}
η_Z	Conversion rate of latently ZIKV-infected to productive cells	0.2 day^{-1}
b_D	Death rate of latently DENV-infected cells	0.14 day^{-1}
b_Z	Death rate of latently ZIKV-infected cells	0.14 day^{-1}
a_D	Death rate of productively DENV-infected cells	0.14 day^{-1}
a_Z	Death rate of productively ZIKV-infected cells	0.1483 day^{-1}
k_D	DENV virion production rate	10 viruses cells^{-1} day^{-1}
k_Z	ZIKV virion production rate	8 viruses cells^{-1} day^{-1}
c_D	Rate of DENV clearance	3.48 day^{-1}
c_Z	Rate of ZIKV clearance	2 day^{-1}
δ_D	CTL killing rate of DENV-infected cells	0.001 cells^{-1} mm^3 day^{-1}
δ_Z	CTL killing rate of ZIKV-infected cells	0.002 cells^{-1} mm^3 day^{-1}
φ_D	Production rate of DENV-targeted CTLs	30 cells day^{-1}
φ_Z	Production rate of ZIKV-targeted CTLs	25 cells day^{-1}
ρ_D	Activation rate of DENV-targeted CTLs	0.03 cell^{-1} mm^3 day^{-1}
ρ_Z	Activation rate of ZIKV-targeted CTLs	0.02 cell^{-1} mm^3 day^{-1}
ψ_D	Death rate of DENV-targeted CTLs	0.5 day^{-1}
ψ_Z	Death rate of ZIKV-targeted CTLs	0.4 day^{-1}
τ	Time delay parameter	varied
$1/n_i$	Average lifetime of the cell or virus during delay period	1 day

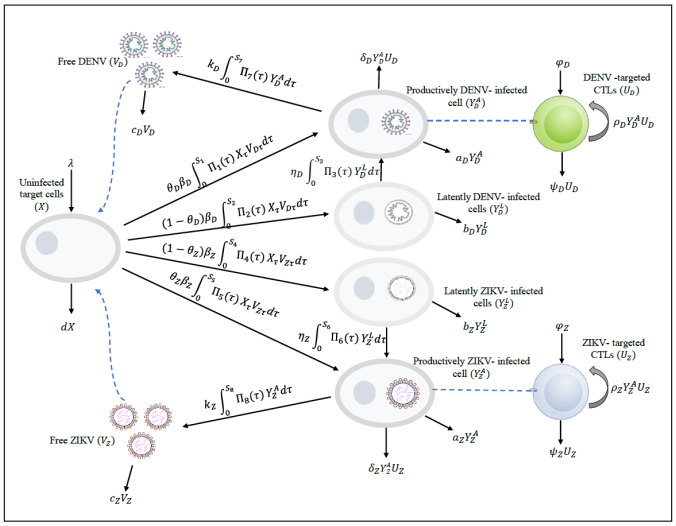

Figure 1. Structural framework of the proposed within-host DENV–ZIKV co-infection model.

Parameter values are selected from available literature whenever possible and, in the absence of direct experimental estimates for DENV–ZIKV within-host co-infection, biologically plausible values are adopted to ensure realistic intracellular viral dynamics. In particular, the infection rates (β_D) and (β_Z), as well as the delay-related parameters (τ) and (n_i), are chosen within biologically reasonable ranges and vary to investigate their effects on system dynamics. The delay parameters are selected to reflect characteristic timescales associated with intracellular viral progression, including latent-cell establishment, productive infection development, latent-cell activation, and virion maturation. Numerical simulations under different parameter settings are performed to illustrate and support the theoretical results and to assess the sensitivity of the dynamical outcomes to parameter variation.

Remark 1. In this work, we employ a bilinear incidence function, which is commonly adopted in mathematical virology and epidemiology due to its mathematical tractability and its biological interpretation based on direct interactions between susceptible target cells (X) (or individuals ($\mathcal{S}$)) and virus particles (V) (or infected individuals ($\mathcal{I}$)). The term βXV (or $\beta \mathcal{S}\mathcal{I}$) assumes that the generation of new infections is proportional to the encounter rate between these two populations.

Nevertheless, a variety of alternative incidence functions have been proposed in the literature to capture more realistic infection mechanisms. Some of these include:

- Saturated incidence [48, 49]:
$$\frac{\beta XV}{1+\upsilon V}, \ \upsilon \geq 0,$$
which incorporates saturation effects at high viral levels and yields a maximal infection rate bounded by $\frac{\beta}{\upsilon}X$.

- Michaelis-Menten incidence [50, 51]:
$$\frac{\beta XV}{K+V}, \ K > 0,$$
which also introduces saturation, with the infection rate approaching βX as $V \to \infty$.

- Standard incidence [52–55]:

$$\frac{\beta XV}{X+Y},$$

which describes a frequency-dependent infection process in which virus-cell interactions are normalized by the total cell population. This formulation may account for limited infection efficiency and may prevent unrealistically large infection rates at high cell densities.

- Beddington-DeAngelis incidence [56, 57]:

$$\frac{\beta XV}{1+\upsilon V+\varpi X},\ \varpi \geq 0,$$

where υV accounts for viral interference and ϖX reflects crowding effects among susceptible cells.

- General incidence [58, 59]:

$$\Psi(X,V),$$

where Ψ denotes a general nonlinear incidence function covering a broad class of infection dynamics.

3. Preliminaries

This section is dedicated to the analysis of the fundamental qualitative properties of system in Eqs (2.1)–(2.9) subject to the initial conditions in Eq (2.10). Specifically, we establish the non-negativity and boundedness of all state variables and subsequently identify all biologically relevant equilibrium points of the model, together with the threshold conditions governing their existence.

3.1. Basic properties

Lemma 1. *Solutions of model in Eqs (2.1)–(2.9) with the initial states in Eq (2.10) are non-negative and ultimately bounded.*

Proof. Let us first show the non-negativity of solutions of model in Eqs (2.1)–(2.9). Equations (2.1), (2.8), and (2.9) give

$$\left(\frac{dX}{dt}|_{X=0}, \frac{dU_D}{dt}|_{U_D=0}, \frac{dU_Z}{dt}|_{U_Z=0}\right) = (\lambda, \varphi_D, \varphi_Z) > 0.$$

Hence, $X(t) > 0$, $U_D(t) > 0$ and $U_Z(t) > 0$, for all $t \geq 0$. From Eqs (2.2)–(2.7), we have

$$Y_D^L(t) = \phi_2(0)e^{-(\eta_D+b_D)t} + (1-\theta_D)\beta_D \int_0^t e^{-(\eta_D+b_D)(t-\zeta)} \int_0^{S_1} \Pi_1(\tau)X(\zeta-\tau)V_D(\zeta-\tau)d\tau d\zeta \geq 0,$$

$$Y_D^A(t) = \phi_3(0)e^{-\int_0^t (a_D+\delta_D U_D(x))dx} + \int_0^t e^{-\int_\zeta^t (a_D+\delta_D U_D(x))dx}$$

$$\times \left[\theta_D\beta_D \int_0^{S_2} \Pi_2(\tau)X(\zeta-\tau)V_D(\zeta-\tau)d\tau + \eta_D \int_0^{S_3} \Pi_3(\tau)Y_D^L(\zeta-\tau)d\tau\right] d\zeta \geq 0,$$

$$Y_Z^L(t) = \phi_4(0)e^{-(\eta_Z+b_Z)t} + (1-\theta_Z)\beta_Z \int_0^t e^{-(\eta_Z+b_Z)(t-\zeta)} \int_0^{S_4} \Pi_4(\tau)X(\zeta-\tau)V_Z(\zeta-\tau)d\tau d\zeta \geq 0,$$

$$Y_Z^A(t) = \phi_5(0)e^{-\int_0^t (a_Z+\delta_Z U_Z(x))dx} + \int_0^t e^{-\int_\zeta^t (a_Z+\delta_Z U_Z(x))dx}$$
$$\times \left[\theta_Z\beta_Z \int_0^{S_5} \Pi_5(\tau)X(\zeta-\tau)V_Z(\zeta-\tau)d\tau + \eta_Z \int_0^{S_6} \Pi_6(\tau)Y_Z^L(\zeta-\tau)d\tau\right] d\zeta \geq 0,$$

$$V_D(t) = \phi_6(0)e^{-c_D t} + k_D \int_0^t e^{-c_D(t-\zeta)} \int_0^{S_7} \Pi_7(\tau)Y_D^A(\zeta-\tau)d\tau d\zeta \geq 0,$$

$$V_Z(t) = \phi_7(0)e^{-c_Z t} + k_Z \int_0^t e^{-c_Z(t-\zeta)} \int_0^{S_8} \Pi_8(\tau)Y_Z^A(\zeta-\tau)d\tau d\zeta \geq 0,$$

for all $t \in [0, S^*]$ [60]. Hence, by recursive argumentation, we obtain that

$$Y_D^L(t), Y_D^A(t), Y_Z^L(t), Y_Z^A(t), V_D(t), V_Z(t) \geq 0 \text{ for all } t \geq 0.$$

Hence, $X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D$ and, U_Z are non-negative.

Now, we prove the ultimate boundedness of $X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D$, and U_Z. From Eq (2.1), we have, $\limsup_{t\to\infty} X(t) \leq \Omega_1$, where $\Omega_1 = \frac{\lambda}{d}$. To prove the ultimate boundedness of $Y_D^L(t)$ and $Y_Z^L(t)$, we define

$$\Psi_1(t) = (1-\theta_D) \int_0^{S_1} \Pi_1(\tau)X_\tau d\tau + Y_D^L \text{ and } \Psi_2(t) = (1-\theta_Z) \int_0^{S_4} \Pi_4(\tau)X_\tau d\tau + Y_Z^L.$$

Then, we get

$$\begin{aligned}
\frac{d\Psi_1}{dt}(t) &= (1-\theta_D) \int_0^{S_1} \Pi_1(\tau)\frac{dX_\tau}{dt}d\tau + \frac{dY_D^L}{dt} \\
&= (1-\theta_D) \int_0^{S_1} \Pi_1(\tau)\left[\lambda - dX_\tau - \beta_D X_\tau V_{D\tau} - \beta_Z X_\tau V_{Z\tau}\right] d\tau \\
&+ (1-\theta_D)\beta_D \int_0^{S_1} \Pi_1(\tau)X_\tau V_{D\tau}d\tau - (\eta_D + b_D)Y_D^L \\
&= (1-\theta_D)\lambda \int_0^{S_1} \Pi_1(\tau)d\tau - (1-\theta_D)d \int_0^{S_1} \Pi_1(\tau)X_\tau d\tau \\
&- (1-\theta_D)\beta_Z \int_0^{S_1} \Pi_1(\tau)X_\tau V_{Z\tau}d\tau - (\eta_D + b_D)Y_D^L \\
&\leq (1-\theta_D)\lambda F_1 - (1-\theta_D)d \int_0^{S_1} \Pi_1(\tau)X_\tau d\tau - (\eta_D + b_D)Y_D^L \\
&\leq (1-\theta_D)\lambda - \zeta_1 \left[(1-\theta_D) \int_0^{S_1} \Pi_1(\tau)X_\tau d\tau + Y_D^L\right] \\
&= (1-\theta_D)\lambda - \zeta_1\Psi_1(t).
\end{aligned}$$

Similarly, we get

$$\frac{d\Psi_2}{dt}(t) \leq (1-\theta_Z)\lambda - \zeta_2\Psi_2(t),$$

where $\zeta_1 = \min\{d, \eta_D + b_D\}$ and $\zeta_2 = \min\{d, \eta_Z + b_Z\}$. It follows that, $\limsup_{t\to\infty} \Psi_1(t) \le \Omega_2$ and $\limsup_{t\to\infty} \Psi_2(t) \le \Omega_3$, where $\Omega_2 = \frac{(1-\theta_D)\lambda}{\zeta_1}$ and $\Omega_3 = \frac{(1-\theta_Z)\lambda}{\zeta_2}$. Since $(1-\theta_D)\int_0^{S_1} \Pi_1(\tau)X_\tau d\tau$, Y_D^L, $(1-\theta_Z)\int_0^{S_4} \Pi_4(\tau)X_\tau d\tau$ and Y_Z^L are non-negative, then $\limsup_{t\to\infty} Y_D^L(t) \le \Omega_2$ and $\limsup_{t\to\infty} Y_Z^L(t) \le \Omega_3$.

Define

$$\Psi_3(t) = \theta_D \int_0^{S_2} \Pi_2(\tau)X_\tau d\tau + Y_D^A + \frac{\delta_D}{\rho_D}U_D \text{ and } \Psi_4(t) = \theta_Z \int_0^{S_5} \Pi_5(\tau)X_\tau d\tau + Y_Z^A + \frac{\delta_Z}{\rho_Z}U_Z.$$

Then, we get

$$\begin{aligned}
\frac{d\Psi_3(t)}{dt} &= \theta_D \int_0^{S_2} \Pi_2(\tau)\frac{dX_\tau}{dt}d\tau + \frac{dY_D^A}{dt} + \frac{\delta_D}{\rho_D}\frac{dU_D}{dt} \\
&= \theta_D \int_0^{S_2} \Pi_2(\tau)\left[\lambda - dX_\tau - \beta_D X_\tau V_{D\tau} - \beta_Z X_\tau V_{Z\tau}\right]d\tau + \theta_D\beta_D \int_0^{S_2} \Pi_2(\tau)X_\tau V_{D\tau}d\tau \\
&+ \eta_D \int_0^{S_3} \Pi_3(\tau)Y_{D\tau}^L d\tau - a_D Y_D^A - \delta_D Y_D^A U_D + \frac{\delta_D}{\rho_D}\left(\varphi_D + \rho_D Y_D^A U_D - \psi_D U_D\right) \\
&= \theta_D\lambda \int_0^{S_2} \Pi_2(\tau)d\tau - d\theta_D \int_0^{S_2} \Pi_2(\tau)X_\tau d\tau - \theta_D\beta_Z \int_0^{S_2} \Pi_2(\tau)X_\tau V_{Z\tau}d\tau \\
&+ \eta_D \int_0^{S_3} \Pi_3(\tau)Y_{D\tau}^L d\tau - a_D Y_D^A + \frac{\delta_D\varphi_D}{\rho_D} - \frac{\delta_D\psi_D}{\rho_D}U_D \\
&\le \theta_D\lambda F_2 - d\theta_D \int_0^{S_2} \Pi_2(\tau)X_\tau d\tau + \eta_D F_3\Omega_2 - a_D Y_D^A + \frac{\delta_D\varphi_D}{\rho_D} - \frac{\delta_D\psi_D}{\rho_D}U_D \\
&\le \theta_D\lambda + \eta_D\Omega_2 + \frac{\delta_D\varphi_D}{\rho_D} - \zeta_3\left[\theta_D \int_0^{S_2} \Pi_2(\tau)X_\tau d\tau + Y_D^A + \frac{\delta_D}{\rho_D}U_D\right] \\
&= \theta_D\lambda + \eta_D\Omega_2 + \frac{\delta_D\varphi_D}{\rho_D} - \zeta_3\Psi_3(t).
\end{aligned}$$

Similarly, we get

$$\frac{d\Psi_4(t)}{dt} \le \theta_Z\lambda + \eta_Z\Omega_3 + \frac{\delta_Z\varphi_Z}{\rho_Z} - \zeta_4\Psi_4(t),$$

where $\zeta_3 = \min\{d, a_D, \psi_D\}$ and $\zeta_4 = \min\{d, a_Z, \psi_Z\}$. It follows that $\limsup_{t\to\infty} \Psi_3(t) \le \Omega_4$ and $\limsup_{t\to\infty} \Psi_4(t) \le \Omega_5$, where $\Omega_4 = \frac{\rho_D\theta_D\lambda + \rho_D\eta_D\Omega_2 + \delta_D\varphi_D}{\rho_D\zeta_3}$ and $\Omega_5 = \frac{\rho_Z\theta_Z\lambda + \rho_Z\eta_Z\Omega_3 + \delta_Z\varphi_Z}{\rho_Z\zeta_4}$, so $\limsup_{t\to\infty} Y_D^A(t) \le \Omega_4$, $\limsup_{t\to\infty} Y_Z^A(t) \le \Omega_5$, $\limsup_{t\to\infty} U_D(t) \le \Omega_6$, and $\limsup_{t\to\infty} U_Z(t) \le \Omega_7$, where $\Omega_6 = \frac{\rho_D}{\delta_D}\Omega_4$ and $\Omega_7 = \frac{\rho_Z}{\delta_Z}\Omega_5$. Now, let us define

$$\Psi_5(t) = V_D + V_Z.$$

Then, we obtain

$$\begin{aligned}
\frac{d\Psi_5(t)}{dt} &= \frac{dV_D}{dt} + \frac{dV_Z}{dt} \\
&= k_D \int_0^{S_7} \Pi_7(\tau)Y_{D\tau}^A d\tau - c_D V_D + k_Z \int_0^{S_8} \Pi_8(\tau)Y_{Z\tau}^A d\tau - c_Z V_Z
\end{aligned}$$

$$\leq k_D F_7 \Omega_4 + k_Z F_8 \Omega_5 - \zeta_5 (V_D + V_Z)$$
$$\leq k_D \Omega_4 + k_Z \Omega_5 - \zeta_5 \Psi_5(t),$$

where $\zeta_5 = \min\{c_D, c_Z\}$. It follows that, $\limsup_{t\to\infty} \Psi_5(t) \leq \Omega_8$, where $\Omega_8 = \frac{k_D\Omega_4 + k_Z\Omega_5}{\zeta_5}$, then $\limsup_{t\to\infty} V_D(t) \leq \Omega_8$, $\limsup_{t\to\infty} V_Z(t) \leq \Omega_8$. Consequently, according to the Lemma 1, the region

$$\Gamma = \left\{\left(X, Y_D^L, Y_Z^L, Y_D^A, Y_Z^A, V_D, V_Z, U_D, U_Z\right) \in \mathbb{R}^9_{\geq 0} : \|X\| \leq \Omega_1, \|Y_D^L\| \leq \Omega_2, \|Y_Z^L\| \leq \Omega_3, \|Y_D^A\| \leq \Omega_4, \right.$$
$$\left. \|Y_Z^A\| \leq \Omega_5, \|V_D\| \leq \Omega_8, \|V_Z\| \leq \Omega_8, \|U_D\| \leq \Omega_6, \|U_Z\| \leq \Omega_7\right\}$$

is positively invariant with respect to model in Eqs (2.1)–(2.9).

4. Existence and global stability of equilibria

We determine the equilibrium points of the proposed model and investigate the conditions required for their existence. These conditions are characterized in terms of the basic reproduction numbers.

The basic reproduction number R_0^L for the DENV–ZIKV co-infection system is determined using the next-generation matrix approach proposed [61] (see Appendix A). The analysis leads to the following expression

$$R_0^L = \max\{R_D^L, R_Z^L\},$$

where

$$R_D^L = \frac{k_D \beta_D \lambda \psi_D F_7 \sigma_D}{d c_D (\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D)}, \qquad R_Z^L = \frac{k_Z \beta_Z \lambda \psi_Z F_8 \sigma_Z}{d c_Z (\eta_Z + b_Z)(a_Z \psi_Z + \delta_Z \varphi_Z)},$$

where $\sigma_D = (\eta_D + b_D)\theta_D F_2 + \eta_D(1-\theta_D)F_1F_3$ and $\sigma_Z = (\eta_Z + b_Z)\theta_Z F_5 + \eta_Z(1-\theta_Z)F_4F_6$. It is noteworthy that R_D^L and R_Z^L correspond to the basic reproduction numbers of the DENV and ZIKV mono-infection submodels, respectively.

Furthermore, the invasion reproduction numbers $R_D^{L,inv}$ and $R_Z^{L,inv}$, which describe the ability of one virus to invade when the other is already at endemic equilibrium, are derived for the system in Eqs (2.1)–(2.9) and are reported in detail in the Appendix (see Appendix B). Specifically, they are given by

$$R_D^{L,inv} = \frac{k_D \beta_D \lambda \psi_D F_7 \sigma_D}{d c_D (a_D \psi_D + \delta_D \varphi_D)(\eta_D + b_D)\left(1 + \frac{k_Z \beta_Z F_8}{d c_Z} \overline{Y}_Z^A\right)} = \frac{R_D^L}{1 + \frac{k_Z \beta_Z F_8}{d c_Z} \overline{Y}_Z^A},$$
$$R_Z^{L,inv} = \frac{k_Z \beta_Z \lambda \psi_Z F_8 \sigma_Z}{d c_Z (a_Z \psi_Z + \delta_Z \varphi_Z)(\eta_Z + b_Z)\left(1 + \frac{k_D \beta_D F_7}{d c_D} Y_D^{A*}\right)} = \frac{R_Z^L}{1 + \frac{k_D \beta_D F_7}{d c_D} Y_D^{A*}}.$$

Thus,

$$R_D^{L,inv} = \frac{R_D^L}{1 + \frac{k_Z \beta_Z F_8}{d c_Z} \overline{Y}_Z^A} < R_D^L, \qquad R_Z^{L,inv} = \frac{R_Z^L}{1 + \frac{k_D \beta_D F_7}{d c_D} Y_D^{A*}} < R_Z^L.$$

Biologically, the invasion reproduction numbers quantify the ability of one virus to establish infection when the other virus is already maintained at its endemic equilibrium. The additional

denominator terms involving $(\overline{Y}_Z^A)$ and (Y_D^{A*}) reflect the reduction in available susceptible target cells caused by the resident virus, as well as the modified within-host environment associated with ongoing infection and immune activity. Consequently, the effective transmission potential of the invading virus is reduced compared with the disease-free setting, which explains why $R_D^{L,inv} < R_D^L$ and $(R_Z^{L,inv} < R_Z^L)$. Therefore, successful invasion requires sufficiently strong transmission potential to overcome the competitive effects generated by the pre-existing infection.

4.1. Existence of equilibria

Lemma 2. The system in Eqs (2.1)–(2.9), admits four possible equilibria:

(I) Disease-free equilibrium: $EQ^0 = (X^0, 0, 0, 0, 0, 0, 0, U_D^0, U_Z^0)$ which always exists.

(II) DENV mono-infection equilibrium: If $R_D^L > 1$, then there exists $EQ^* = (X^*, Y_D^{L*}, Y_D^{A*}, 0, 0, V_D^*, 0, U_D^*, U_Z^*)$, in addition to EQ^0.

(III) ZIKV mono-infection equilibrium: If $R_Z^L > 1$, then there exists $\overline{EQ} = (\overline{X}, 0, 0, \overline{Y}_Z^L, \overline{Y}_Z^A, 0, \overline{V}_Z, \overline{U}_D, \overline{U}_Z)$, in addition to EQ^0.

(IV) DENV–ZIKV co-infection equilibrium: If $R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$ then there exists $\widetilde{EQ} = (\widetilde{X}, \widetilde{Y}_D^L, \widetilde{Y}_D^A, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{V}_D, \widetilde{V}_Z, \widetilde{U}_D, \widetilde{U}_Z)$, in addition to EQ^0, EQ^* and $\overline{EQ}$.

Proof. Setting the right-hand sides of Eqs (2.1)–(2.9) equal to zero gives:

$$0 = \lambda - dX - \beta_D X V_D - \beta_Z X V_Z, \tag{4.1}$$
$$0 = (1-\theta_D)\beta_D F_1 X V_D - (\eta_D + b_D) Y_D^L, \tag{4.2}$$
$$0 = \theta_D \beta_D F_2 X V_D + \eta_D F_3 Y_D^L - a_D Y_D^A - \delta_D Y_D^A U_D, \tag{4.3}$$
$$0 = (1-\theta_Z)\beta_Z F_4 X V_Z - (\eta_Z + b_Z) Y_Z^L, \tag{4.4}$$
$$0 = \theta_Z \beta_Z F_5 X V_Z + \eta_Z F_6 Y_Z^L - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z, \tag{4.5}$$
$$0 = k_D F_7 Y_D^A - c_D V_D, \tag{4.6}$$
$$0 = k_Z F_8 Y_Z^A - c_Z V_Z, \tag{4.7}$$
$$0 = \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D, \tag{4.8}$$
$$0 = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z. \tag{4.9}$$

From Eqs (4.1), (4.2), (4.4), (4.8), and (4.9) we have

$$\begin{aligned}
X &= \frac{\lambda c_D c_Z}{d c_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A}, \\
Y_D^L &= \frac{(1-\theta_D)\beta_D k_D F_1 F_7 c_Z \lambda Y_D^A}{(\eta_D + b_D)(d c_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)}, \\
Y_Z^L &= \frac{(1-\theta_Z)\beta_Z k_Z F_4 F_8 c_D \lambda Y_Z^A}{(\eta_Z + b_Z)(d c_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)}, \\
V_D &= \frac{k_D F_7}{c_D} Y_D^A, \; V_Z = \frac{k_Z F_8}{c_Z} Y_Z^A, \\
U_D &= \frac{\varphi_D}{\psi_D - \rho_D Y_D^A} \text{ and } U_Z = \frac{\varphi_Z}{\psi_Z - \rho_Z Y_Z^A}.
\end{aligned} \tag{4.10}$$

We note that $U_D > 0$ and $U_Z > 0$, when $Y_D^A \in \left[0, \frac{\psi_D}{\rho_D}\right)$ and $Y_Z^A \in \left[0, \frac{\psi_Z}{\rho_Z}\right)$, respectively. Substituting in Eqs (4.3) and (4.5), we obtain

$$\left(\frac{\beta_D \lambda k_D c_Z F_7 \sigma_D}{(\eta_D + b_D)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)} - a_D + \frac{\delta_D \varphi_D}{\rho_D Y_D^A - \psi_D}\right) Y_D^A = 0, \tag{4.11}$$

$$\left(\frac{\beta_Z \lambda k_Z c_D F_8 \sigma_Z}{(\eta_Z + b_Z)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)} - a_Z + \frac{\delta_Z \varphi_Z}{\rho_Z Y_Z^A - \psi_Z}\right) Y_Z^A = 0. \tag{4.12}$$

Equations (4.11) and (4.12) have four possibilities:

(I) $Y_D^A = 0$ and $Y_Z^A = 0$, which gives disease-free equilibrium. $EQ^0 = (X^0, 0, 0, 0, 0, 0, 0, U_D^0, U_Z^0)$, where $X^0 = \frac{\lambda}{d}$, $U_D^0 = \frac{\varphi_D}{\psi_D}$, and $U_Z^0 = \frac{\varphi_Z}{\psi_Z}$.

(II) $Y_D^A \neq 0$ and $Y_Z^A = 0$, so from Eq (4.11), we get

$$\frac{\beta_D \lambda k_D F_7 \sigma_D}{(\eta_D + b_D)(dc_D + \beta_D k_D F_7 Y_D^A)} - a_D + \frac{\delta_D \varphi_D}{\rho_D Y_D^A - \psi_D} = 0,$$

which gives

$$\frac{A_D^L (Y_D^A)^2 + B_D^L Y_D^A + C_D^L}{\rho_D Y_D^A - \psi_D} = 0, \tag{4.13}$$

where

$$\begin{aligned}
A_D^L &= a_D \beta_D k_D \rho_D F_7 (\eta_D + b_D),\\
B_D^L &= a_D dc_D \rho_D (\eta_D + b_D) - k_D \beta_D \lambda \rho_D F_7 \sigma_D - \beta_D k_D F_7 (\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D),\\
C_D^L &= k_D \beta_D \lambda \psi_D F_7 \sigma_D - dc_D (\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D).
\end{aligned}$$

We define a continuous function H^{L*} as:

$$H^{L*}(Y_D^A) = \frac{A_D^L (Y_D^A)^2 + B_D^L Y_D^A + C_D^L}{\rho_D Y_D^A - \psi_D},\ Y_D^A \in \left[0, \frac{\psi_D}{\rho_D}\right).$$

Then we have

$$H^{L*}(0) = \frac{dc_D (\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D)}{\psi_D} \left(1 - R_D^L\right) < 0, \text{ if } R_D^L > 1.$$

Moreover

$$\lim_{Y_D^A \to \left(\frac{\psi_D}{\rho_D}\right)^-} H^{L*}(Y_D^A) = \infty,$$

so there exists $Y_D^{A*} \in \left(0, \frac{\psi_D}{\rho_D}\right)$ such that $H^{L*}(Y_D^{A*}) = 0$.

For $R_D^L > 1$, we have

$$C_D^L = dc_D (\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D)\left(R_D^L - 1\right) > 0.$$

Moreover,

$$k_D \beta_D \lambda F_7 \sigma_D > dc_D a_D (\eta_D + b_D).$$

This implies that $B_D^L < 0$. Hence, there exist two positive solutions

$$Y_D^{A\pm} = \frac{-B_D^L \pm \sqrt{\left(B_D^L\right)^2 - 4A_D^L C_D^L}}{2A_D^L}.$$

If $R_D^L > 1$, implies that $B_D^L < 0$ and $C_D^L > 0$.
We have

$$\lim_{Y_D^A \to \left(\frac{\psi_D}{\rho_D}\right)^+} H^{L*}(Y_D^A) = -\infty, \qquad \lim_{Y_D^A \to \infty} H^{L*}(Y_D^A) = \infty.$$

Then

$$Y_D^{A-} \in \left(0, \frac{\psi_D}{\rho_D}\right) \text{ and } Y_D^{A+} \in \left(\frac{\psi_D}{\rho_D}, \infty\right).$$

Then we take

$$Y_D^{A*} = \frac{-B_D^L - \sqrt{\left(B_D^L\right)^2 - 4A_D^L C_D^L}}{2A_D^L}.$$

Hence,

$$X^* = \frac{\lambda c_D}{dc_D + \beta_D k_D F_7 Y_D^{A*}} > 0,\ Y_D^{L*} = \frac{(1-\theta_D)\beta_D k_D F_1 F_7 \lambda Y_D^{A*}}{(\eta_D + b_D)(dc_D + \beta_D k_D F_7 Y_D^{A*})} > 0,$$
$$Y_Z^{L*} = 0,\ Y_Z^{A*} = 0, V_D^* = \frac{k_D F_7}{c_D} Y_D^{A*} > 0,\ V_Z^* = 0,$$
$$U_D^* = \frac{\varphi_D}{\psi_D - \rho_D Y_D^{A*}} > 0 \text{ and } U_Z^* = \frac{\varphi_Z}{\psi_Z} > 0.$$

It follows that, a DENV mono-infection equilibrium $EQ^* = (X^*, Y_D^{L*}, Y_D^{A*}, 0, 0, V_D^*, 0, U_D^*, U_Z^*)$ when $R_D^L > 1$.

(III) $Y_D^A = 0$ and $Y_Z^A \neq 0$, then from Eq (4.12), we have

$$\frac{\beta_Z \lambda k_Z F_8 \sigma_Z}{(\eta_Z + b_Z)(dc_Z + \beta_Z k_Z F_8 Y_Z^A)} - a_Z + \frac{\delta_Z \varphi_Z}{\rho_Z Y_Z^A - \psi_Z} = 0,$$

which gives

$$\frac{A_Z^L \left(Y_Z^A\right)^2 + B_Z^L Y_Z^A + C_Z^L}{\rho_Z Y_Z^A - \psi_Z} = 0,\ Y_Z^A \in \left[0, \frac{\psi_Z}{\rho_Z}\right), \tag{4.14}$$

where

$$A_Z^L = a_Z \beta_Z k_Z \rho_Z F_8 (\eta_Z + b_Z),$$
$$B_Z^L = a_Z dc_Z \rho_Z (\eta_Z + b_Z) - k_Z \beta_Z \lambda \rho_Z F_8 \sigma_Z - \beta_Z k_Z F_8 (\eta_Z + b_Z)(a_Z \psi_Z + \delta_Z \varphi_Z),$$
$$C_Z^L = k_Z \beta_Z \lambda \psi_Z F_8 \sigma_Z - dc_Z (\eta_Z + b_Z)(a_Z \psi_Z + \delta_Z \varphi_Z).$$

We define a continuous function $\overline{H}^L$ as:

$$\overline{H}^L(Y_Z^A) = \frac{A_Z^L \left(Y_Z^A\right)^2 + B_Z^L Y_Z^A + C_Z^L}{\rho_Z Y_Z^A - \psi_Z}, \text{ where } Y_Z^A \in \left[0, \frac{\psi_Z}{\rho_Z}\right).$$

We get

$$\overline{H}^L(0) = -\frac{C_Z^L}{\psi_Z} = \frac{dc_Z(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z) - k_Z\beta_Z\lambda\psi_Z F_8\sigma_Z}{\psi_Z}$$
$$= \frac{dc_Z(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}{\psi_Z}\left(1 - R_Z^L\right).$$

We have $\overline{H}^L(0) < 0$ if $R_Z^L > 1$. Moreover

$$\lim_{Y_Z^A \to \left(\frac{\psi_Z}{\rho_Z}\right)^-} \overline{H}^L(Y_Z^A) = \infty,$$

then there exists $\overline{Y}_Z^A \in \left(0, \frac{\psi_Z}{\rho_Z}\right)$ such that $\overline{H}^L(\overline{Y}_Z^A) = 0$.

Similar to Case (II), one can show that if $R_Z^L > 1$, then $C_Z^L > 0$ and $B_Z^L < 0$.

Then there exist two positive solutions

$$Y_Z^{A\pm} = \frac{-B_Z^L \pm \sqrt{\left(B_Z^L\right)^2 - 4A_Z^L C_Z^L}}{2A_Z^L}.$$

We have

$$\lim_{Y_Z^A \to \left(\frac{\psi_Z}{\rho_Z}\right)^+} \overline{H}^L(Y_Z^A) = -\infty, \qquad \lim_{Y_Z^A \to \infty} \overline{H}^L(Y_Z^A) = \infty.$$

Then

$$Y_Z^{A-} \in \left(0, \frac{\psi_Z}{\rho_Z}\right) \text{ and } Y_Z^{A+} \in \left(\frac{\psi_Z}{\rho_Z}, \infty\right).$$

Then we take

$$\overline{Y}_Z^A = \frac{-B_Z^L - \sqrt{\left(B_Z^L\right)^2 - 4A_Z^L C_Z^L}}{2A_Z^L}.$$

Hence,

$$\overline{X} = \frac{\lambda c_Z}{dc_Z + \beta_Z k_Z F_8 \overline{Y}_Z^A} > 0,\ \overline{Y}_D^L = 0,\ \overline{Y}_Z^L = \frac{(1-\theta_Z)\beta_Z k_Z F_4 F_8 \lambda \overline{Y}_Z^A}{(\eta_Z + b_Z)(dc_Z + \beta_Z k_Z F_8 \overline{Y}_Z^A)} > 0,$$
$$\overline{V}_D = 0,\ \overline{V}_Z = \frac{k_Z F_8}{c_Z}\overline{Y}_Z^A > 0,\ \overline{U}_D = \frac{\varphi_D}{\psi_D} > 0 \text{ and } \overline{U}_Z = \frac{\varphi_Z}{\psi_Z - \rho_Z \overline{Y}_Z^A} > 0.$$

Consequently a ZIKV mono-infection equilibrium $\overline{EQ} = (\overline{X}, 0, 0, \overline{Y}_Z^L, \overline{Y}_Z^A, 0, \overline{V}_Z, \overline{U}_D, \overline{U}_Z)$ exists when $R_Z^L > 1$.

(IV) $Y_D^A \neq 0$ and $Y_Z^A \neq 0$, so from Eqs (4.11) and (4.12), we have

$$\frac{\beta_D \lambda k_D c_Z F_7 \sigma_D}{(\eta_D + b_D)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)} - a_D + \frac{\delta_D \varphi_D}{\rho_D Y_D^A - \psi_D} = 0, \tag{4.15}$$

$$\frac{\beta_Z \lambda k_Z c_D F_8 \sigma_Z}{(\eta_Z + b_Z)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)} - a_Z + \frac{\delta_Z \varphi_Z}{\rho_Z Y_Z^A - \psi_Z} = 0. \tag{4.16}$$

We solve Eqs (4.15) and (4.16) using the isocline method [62]. Let us consider

$$F_1^L(Y_D^A, Y_Z^A) = \frac{\beta_D \lambda k_D c_Z F_7 \sigma_D}{(\eta_D + b_D)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)} - a_D + \frac{\delta_D \varphi_D}{\rho_D Y_D^A - \psi_D} = 0, \tag{4.17}$$

$$Y_D^A \in \left[0, \frac{\psi_D}{\rho_D}\right).$$

$$F_2^L(Y_D^A, Y_Z^A) = \frac{\beta_Z \lambda k_Z c_D F_8 \sigma_Z}{(\eta_Z + b_Z)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)} - a_Z + \frac{\delta_Z \varphi_Z}{\rho_Z Y_Z^A - \psi_Z} = 0, \tag{4.18}$$

$$Y_Z^A \in \left[0, \frac{\psi_Z}{\rho_Z}\right).$$

From Eq (4.17), we note the following:
(a) When $Y_D^A = 0$, then

$$\frac{\beta_D \lambda k_D c_Z F_7 \sigma_D}{(\eta_D + b_D)(dc_D c_Z + \beta_Z k_Z F_8 c_D Y_Z^A)} - a_D - \frac{\delta_D \varphi_D}{\psi_D} = 0,$$

$$\implies Y_Z^A = \frac{dc_Z}{\beta_Z k_Z F_8}\left(\frac{k_D \beta_D \lambda \psi_D F_7 \sigma_D}{dc_D(\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D)} - 1\right),$$

$$\implies Y_Z^A = \frac{dc_Z}{\beta_Z k_Z F_8}(R_D^L - 1) =: \widehat{Y}_Z^A,$$

which is positive if $R_D^L > 1$.
(b) When $Y_Z^A = 0$, then

$$\frac{\beta_D \lambda k_D F_7 \sigma_D}{(\eta_D + b_D)(dc_D + \beta_D k_D F_7 Y_D^A)} - a_D + \frac{\delta_D \varphi_D}{\rho_D Y_D^A - \psi_D} = 0,$$

From Eq (4.13), we get

$$Y_D^A = Y_D^{A*} = \frac{-B_D^L - \sqrt{\left(B_D^L\right)^2 - 4A_D^L C_D^L}}{2A_D^L}.$$

(c)

$$\frac{dY_Z^A}{dY_D^A} = -\frac{\partial F_1^L / \partial Y_D^A}{\partial F_1^L / \partial Y_Z^A}$$

$$= -\frac{k_D^2 \beta_D^2 \lambda c_Z^2 F_7^2 \sigma_D (\rho_D Y_D^A - \psi_D)^2 + \delta_D \varphi_D \rho_D (\eta_D + b_D)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)^2}{k_D k_Z \beta_D \beta_Z \lambda c_Z c_D F_7 F_8 \sigma_D (\rho_D Y_D^A - \psi_D)^2}$$

$$< 0, \; Y_D^A \in \left(0, \frac{\psi_D}{\rho_D}\right),$$

then Y_Z^A is a decreasing function of Y_D^A. It follows that $F_1^L(Y_D^A, Y_Z^A)$ intersects the Y_D^A-axis in $Y_D^A = Y_D^{A*}$ and Y_Z^A-axis in $Y_Z^A = \widehat{Y}_Z^A = \frac{dc_Z}{\beta_Z k_Z F_8}(R_D^L - 1)$.

Now, from Eq (4.18), we note the following:

(d) When $Y_Z^A = 0$, then

$$\frac{\beta_Z \lambda k_Z c_D F_8 \sigma_Z}{(\eta_Z + b_Z)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A)} - a_Z - \frac{\delta_Z \varphi_Z}{\psi_Z} = 0,$$

$$\implies Y_D^A = \frac{dc_D}{\beta_D k_D F_7}\left(\frac{k_Z \beta_Z \lambda \psi_Z F_8 \sigma_Z}{dc_Z(\eta_Z + b_Z)(a_Z \psi_Z + \delta_Z \varphi_Z)} - 1\right),$$
$$\implies Y_D^A = \frac{dc_D}{\beta_D k_D F_7}(R_Z^L - 1) =: \widehat{Y}_D^A,$$

which is positive if $R_Z^L > 1$.

(e) When $Y_D^A = 0$, then

$$\frac{\beta_Z \lambda k_Z F_8 \sigma_Z}{(\eta_Z + b_Z)(dc_Z + \beta_Z k_Z F_8 Y_Z^A)} - a_Z + \frac{\delta_Z \varphi_Z}{\rho_Z Y_Z^A - \psi_Z} = 0.$$

From Eq (4.14), we get

$$Y_Z^A = \overline{Y}_Z^A = \frac{-B_Z^L - \sqrt{\left(B_Z^L\right)^2 - 4A_Z^L C_Z^L}}{2A_Z^L}.$$

(f)

$$\begin{aligned}\frac{dY_Z^A}{dY_D^A} &= -\frac{\partial F_2^L/\partial Y_D^A}{\partial F_2^L/\partial Y_Z^A}\\ &= -\frac{k_D k_Z \beta_D \beta_Z \lambda c_Z c_D F_7 F_8 \sigma_Z (\rho_Z Y_Z^A - \psi_Z)^2}{k_Z^2 \beta_Z^2 \lambda c_D^2 F_8^2 \sigma_Z (\rho_Z Y_Z^A - \psi_Z)^2 + \delta_Z \varphi_Z \rho_Z (\eta_Z + b_Z)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D Y_Z^A)^2}\\ &< 0, \quad Y_D^A \in \left(0, \frac{\psi_D}{\rho_D}\right).\end{aligned}$$

Then Y_Z^A decreases as Y_D^A increases. As a result, the function $F_2^L(Y_D^A, Y_Z^A)$ intersects the Y_Z^A-axis in $Y_Z^A = \overline{Y}_Z^A$ and Y_D^A-axis in $Y_D^A = \widehat{Y}_D^A = \frac{dc_D}{\beta_D k_D F_7}(R_Z^L - 1)$.

The above analysis shows that the two isoclines in Eqs (4.17) and (4.18) intersect each other in $(\widetilde{Y}_D^A, \widetilde{Y}_Z^A)$, where $\widetilde{Y}_D^A \in \left(0, \frac{\psi_D}{\rho_D}\right)$ and $\widetilde{Y}_Z^A \in \left(0, \frac{\psi_Z}{\rho_Z}\right)$, provided the following conditions hold:

$$\widehat{Y}_Z^A > \overline{Y}_Z^A \implies R_D^L > 1 + \frac{\beta_Z k_Z F_8}{dc_Z}\overline{Y}_Z^A \implies R_D^{L,inv} > 1,$$
$$\widehat{Y}_D^A > Y_D^{A*} \implies R_Z^L > 1 + \frac{\beta_D k_D F_7}{dc_D} Y_D^{A*} \implies R_Z^{L,inv} > 1.$$

Hence,

$$\widetilde{X} = \frac{\lambda c_D c_Z}{dc_D c_Z + \beta_D k_D F_7 c_Z \widetilde{Y}_D^A + \beta_Z k_Z F_8 c_D \widetilde{Y}_Z^A},$$

$$\widetilde{Y}_D^L = \frac{(1-\theta_D)\beta_D k_D F_1 F_7 c_Z \lambda \widetilde{Y}_D^A}{(\eta_D + b_D)(dc_D c_Z + \beta_D k_D F_7 c_Z \widetilde{Y}_D^A + \beta_Z k_Z F_8 c_D \widetilde{Y}_Z^A)},$$
$$\widetilde{Y}_Z^L = \frac{(1-\theta_Z)\beta_Z k_Z F_4 F_8 c_D \lambda \widetilde{Y}_Z^A}{(\eta_Z + b_Z)(dc_D c_Z + \beta_D k_D F_7 c_Z Y_D^A + \beta_Z k_Z F_8 c_D \widetilde{Y}_Z^A)},$$
$$\widetilde{V}_D = \frac{k_D F_7}{c_D}\widetilde{Y}_D^A,\ \widetilde{V}_Z = \frac{k_Z F_8}{c_Z}\widetilde{Y}_Z^A,$$
$$\widetilde{U}_D = \frac{\varphi_D}{\psi_D - \rho_D \widetilde{Y}_D^A} \text{ and } \widetilde{U}_Z = \frac{\varphi_Z}{\psi_Z - \rho_Z \widetilde{Y}_Z^A}.$$

Thus, the DENV–ZIKV co-infection equilibrium $\widetilde{EQ} = (\widetilde{X}, \widetilde{Y}_D^L, \widetilde{Y}_D^A, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{V}_D, \widetilde{V}_Z, \widetilde{U}_D, \widetilde{U}_Z)$ exists if $R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$.

5. Global stability analysis

In this section, we investigate the global stability of all equilibrium points of the co-infection model in Eqs (2.1)–(2.9). For each equilibrium, an appropriate Lyapunov function is constructed, and the Lyapunov–LaSalle's invariance principle (L-LAS), as formulated in [63], is employed to establish global asymptotic stability. We employ the Volterra-type function

$$\mathcal{L}(x) = x - 1 - \ln x, \quad x > 0,$$

which satisfies

$$\mathcal{L}(x) \geq 0 \text{ and } \mathcal{L}(1) = 0.$$

To incorporate the effects of distributed intracellular delays, the Lyapunov functionals are augmented with suitable integral components involving delayed variables. These integral terms are introduced to represent the hereditary nature of the delayed processes embedded in the system. Upon differentiation, they are constructed to offset the corresponding distributed-delay terms arising from the model equations, thereby yielding a negative semi-definite Lyapunov derivative and enabling the application of the L-LAS.

Let Υ_j' be the largest invariant subset of

$$\Upsilon_j = \left\{ \left(X, Y_D^L, Y_Z^L, Y_D^A, Y_Z^A, V_D, V_Z, U_D, U_Z \right) : \frac{d\Theta_j^L}{dt} = 0 \right\},\ j = 0, 1, 2, 3,$$

where Θ_j^L is a Lyapunov function.

Theorem 1. The disease-free equilibrium $EQ^0 = (X^0, 0, 0, 0, 0, 0, 0, U_D^0, U_Z^0)$ is globally asymptotically stable (G.A.S) when $R_0^L \leq 1$; if $R_0^L > 1$, the equilibrium becomes unstable.

Proof. Define the Lyapunov functional

$$\Theta_0^L(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z) = \Theta_{01}^L + \Theta_{02}^L,$$

where Θ_{01}^L is the algebraic part and Θ_{02}^L is integral delay part, given as:

$$\Theta_{01}^L = X^0 \mathcal{L}\left(\frac{X}{X^0}\right) + \frac{\eta_D F_3}{\sigma_D} Y_D^L + \frac{\eta_D + b_D}{\sigma_D} Y_D^A + \frac{\eta_Z F_6}{\sigma_Z} Y_Z^L$$

$$+\frac{\eta_Z+b_Z}{\sigma_Z}Y_Z^A+\frac{\beta_D X^0}{c_D}V_D+\frac{\beta_Z X^0}{c_Z}V_Z+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}U_D^0\mathcal{L}\left(\frac{U_D}{U_D^0}\right)$$
$$+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}U_Z^0\mathcal{L}\left(\frac{U_Z}{U_Z^0}\right),$$

and

$$\begin{aligned}\Theta_{02}^L=&\frac{\eta_D F_3\beta_D(1-\theta_D)}{\sigma_D}\int_0^{S_1}\Pi_1(\tau)\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau\\&+\frac{\beta_D\theta_D(\eta_D+b_D)}{\sigma_D}\int_0^{S_2}\Pi_2(\tau)\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau\\&+\frac{\eta_D(\eta_D+b_D)}{\sigma_D}\int_0^{S_3}\Pi_3(\tau)\int_{t-\tau}^{t}Y_D^L(\phi)d\phi d\tau\\&+\frac{\eta_Z F_6\beta_Z(1-\theta_Z)}{\sigma_Z}\int_0^{S_4}\Pi_4(\tau)\int_{t-\tau}^{t}X(\phi)V_Z(\phi)d\phi d\tau\\&+\frac{\beta_Z\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\int_0^{S_5}\Pi_5(\tau)\int_{t-\tau}^{t}X(\phi)V_Z(\phi)d\phi d\tau\\&+\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\int_0^{S_6}\Pi_6(\tau)\int_{t-\tau}^{t}Y_Z^L(\phi)d\phi d\tau\\&+\frac{\beta_D k_D X^0}{c_D}\int_0^{S_7}\Pi_7(\tau)\int_{t-\tau}^{t}Y_D^A(\phi)d\phi d\tau\\&+\frac{\beta_Z k_Z X^0}{c_Z}\int_0^{S_8}\Pi_8(\tau)\int_{t-\tau}^{t}Y_Z^A(\phi)d\phi d\tau.\end{aligned}$$

It is straightforward to verify that $\Theta_0^L(X,Y_D^L,Y_D^A,Y_Z^L,Y_Z^A,V_D,V_Z,U_D,U_Z) > 0$ for all $\left(X,Y_D^L,Y_D^A,Y_Z^L,Y_Z^A,V_D,V_Z,U_D,U_Z\right)>0$ and $\Theta_0^L(X^0,0,0,0,0,0,0,U_D^0,U_Z^0)=0$. Differentiating Θ_0^L along the trajectories of system in Eqs (2.1)–(2.9) yields:

$$\frac{d\Theta_0^L}{dt}=\frac{d\Theta_{01}^L}{dt}+\frac{d\Theta_{02}^L}{dt},$$

where

$$\begin{aligned}\frac{d\Theta_{01}^L}{dt}=&\left(1-\frac{X^0}{X}\right)\frac{dX}{dt}+\frac{\eta_D F_3}{\sigma_D}\frac{dY_D^L}{dt}+\frac{\eta_D+b_D}{\sigma_D}\frac{dY_D^A}{dt}+\frac{\eta_Z F_6}{\sigma_Z}\frac{dY_Z^L}{dt}\\&+\frac{\eta_Z+b_Z}{\sigma_Z}\frac{dY_Z^A}{dt}+\frac{\beta_D X^0}{c_D}\frac{dV_D}{dt}+\frac{\beta_Z X^0}{c_Z}\frac{dV_Z}{dt}\\&+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{U_D^0}{U_D}\right)\frac{dU_D}{dt}+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{U_Z^0}{U_Z}\right)\frac{dU_Z}{dt},\end{aligned}$$

and

$$\frac{d\Theta_{02}^L}{dt}=\frac{\eta_D F_3\beta_D(1-\theta_D)}{\sigma_D}\frac{d}{dt}\int_0^{S_1}\Pi_1(\tau)\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau$$

$$
\begin{aligned}
&+\frac{\beta_D\theta_D(\eta_D+b_D)}{\sigma_D}\frac{d}{dt}\int_0^{S_2}\Pi_2(\tau)\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau\\
&+\frac{\eta_D(\eta_D+b_D)}{\sigma_D}\frac{d}{dt}\int_0^{S_3}\Pi_3(\tau)\int_{t-\tau}^{t}Y_D^L(\phi)d\phi d\tau\\
&+\frac{\eta_Z F_6\beta_Z(1-\theta_Z)}{\sigma_Z}\frac{d}{dt}\int_0^{S_4}\Pi_4(\tau)\int_{t-\tau}^{t}X(\phi)V_Z(\phi)d\phi d\tau\\
&+\frac{\beta_Z\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\frac{d}{dt}\int_0^{S_5}\Pi_5(\tau)\int_{t-\tau}^{t}X(\phi)V_Z(\phi)d\phi d\tau\\
&+\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\frac{d}{dt}\int_0^{S_6}\Pi_6(\tau)\int_{t-\tau}^{t}Y_Z^L(\phi)d\phi d\tau\\
&+\frac{\beta_D k_D X^0}{c_D}\frac{d}{dt}\int_0^{S_7}\Pi_7(\tau)\int_{t-\tau}^{t}Y_D^A(\phi)d\phi d\tau\\
&+\frac{\beta_Z k_Z X^0}{c_Z}\frac{d}{dt}\int_0^{S_8}\Pi_8(\tau)\int_{t-\tau}^{t}Y_Z^A(\phi)d\phi d\tau.
\end{aligned}
$$

Using Leibniz's rule, for example,

$$
\begin{aligned}
\frac{d}{dt}\int_0^{S_1}\Pi_1(\tau)\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau &= \int_0^{S_1}\Pi_1(\tau)\frac{d}{dt}\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau\\
&= \int_0^{S_1}\Pi_1(\tau)\left[X(t)V_D(t)-X(t-\tau)V_D(t-\tau)\right]d\tau\\
&= F_1XV_D-\int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau.
\end{aligned}
$$

Similarly, we obtain analogous expressions for the remaining delay integrals as:

$$
\begin{aligned}
\frac{d\Theta_{02}^L}{dt} &= \frac{\eta_D F_3\beta_D(1-\theta_D)}{\sigma_D}\left[F_1XV_D-\int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau\right]\\
&+\frac{\beta_D\theta_D(\eta_D+b_D)}{\sigma_D}\left[F_2XV_D-\int_0^{S_2}\Pi_2(\tau)X_\tau V_{D\tau}d\tau\right]\\
&+\frac{\eta_D(\eta_D+b_D)}{\sigma_D}\left[F_3Y_D^L-\int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau\right]\\
&+\frac{\eta_Z F_6\beta_Z(1-\theta_Z)}{\sigma_Z}\left[F_4XV_Z-\int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau\right]\\
&+\frac{\beta_Z\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\left[F_5XV_Z-\int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau\right]\\
&+\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\left[F_6Y_Z^L-\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau\right]\\
&+\frac{\beta_D k_D X^0}{c_D}\left[F_7Y_D^A-\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau\right]\\
&+\frac{\beta_Z k_Z X^0}{c_Z}\left[F_8Y_Z^A-\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau\right].
\end{aligned}
$$

From Eqs (2.1)–(2.9), we get

$$\begin{aligned}
\frac{d\Theta_0^L}{dt} &= \left(1-\frac{X^0}{X}\right)(\lambda - dX - \beta_D X V_D - \beta_Z X V_Z)\\
&+ \frac{\eta_D F_3}{\sigma_D}\left((1-\theta_D)\beta_D\int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau - (\eta_D+b_D)Y_D^L\right)\\
&+ \frac{\eta_D+b_D}{\sigma_D}\left(\theta_D\beta_D\int_0^{S_2}\Pi_2(\tau)X_\tau V_{D\tau}d\tau + \eta_D\int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau - a_D Y_D^A - \delta_D Y_D^A U_D\right)\\
&+ \frac{\eta_Z F_6}{\sigma_Z}\left((1-\theta_Z)\beta_Z\int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau - (\eta_Z+b_Z)Y_Z^L\right)\\
&+ \frac{\eta_Z+b_Z}{\sigma_Z}\left(\theta_Z\beta_Z\int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau + \eta_Z\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z\right)\\
&+ \frac{\beta_D X^0}{c_D}\left(k_D\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau - c_D V_D\right) + \frac{\beta_Z X^0}{c_Z}\left(k_Z\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau - c_Z V_Z\right)\\
&+ \frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{U_D^0}{U_D}\right)(\varphi_D + \rho_D Y_D^A U_D - \psi_D U_D)\\
&+ \frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{U_Z^0}{U_Z}\right)(\varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z)\\
&+ \frac{\eta_D F_3\beta_D(1-\theta_D)}{\sigma_D}\left[F_1 X V_D - \int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau\right]\\
&+ \frac{\beta_D\theta_D(\eta_D+b_D)}{\sigma_D}\left[F_2 X V_D - \int_0^{S_2}\Pi_2(\tau)X_\tau V_{D\tau}d\tau\right]\\
&+ \frac{\eta_D(\eta_D+b_D)}{\sigma_D}\left[F_3 Y_D^L - \int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau\right]\\
&+ \frac{\eta_Z F_6\beta_Z(1-\theta_Z)}{\sigma_Z}\left[F_4 X V_Z - \int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau\right]\\
&+ \frac{\beta_Z\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\left[F_5 X V_Z - \int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau\right]\\
&+ \frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\left[F_6 Y_Z^L - \int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau\right]\\
&+ \frac{\beta_D k_D X^0}{c_D}\left[F_7 Y_D^A - \int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau\right]\\
&+ \frac{\beta_Z k_Z X^0}{c_Z}\left[F_8 Y_Z^A - \int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau\right].
\end{aligned}$$

Collecting terms, we find that the distributed-delay terms cancel pairwise. Then we get

$$\begin{aligned}
\frac{d\Theta_0^L}{dt} &= \left(1-\frac{X^0}{X}\right)(\lambda - dX) + \left(\frac{\beta_D k_D X^0 F_7}{c_D} - \frac{a_D(\eta_D+b_D)}{\sigma_D} - \frac{\delta_D(\eta_D+b_D)}{\sigma_D}U_D^0\right)Y_D^A\\
&+ \left(\frac{\beta_Z k_Z X^0 F_8}{c_Z} - \frac{a_Z(\eta_Z+b_Z)}{\sigma_Z} - \frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}U_Z^0\right)Y_Z^A
\end{aligned}$$

$$+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{U_D^0}{U_D}\right)(\varphi_D-\psi_D U_D)+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{U_Z^0}{U_Z}\right)(\varphi_Z-\psi_Z U_Z).$$

Using $\lambda = dX^0$, $\varphi_D = \psi_D U_D^0$ and $\varphi_Z = \psi_Z U_Z^0$, we obtain

$$\begin{aligned}
\frac{d\Theta_0^L}{dt} &= -\frac{d(X-X^0)^2}{X}+\left(\frac{\beta_D\lambda k_D F_7}{dc_D}-\frac{a_D(\eta_D+b_D)}{\sigma_D}-\frac{\delta_D\varphi_D(\eta_D+b_D)}{\psi_D\sigma_D}\right)Y_D^A\\
&+\left(\frac{\beta_Z\lambda k_Z F_8}{dc_Z}-\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}-\frac{\delta_Z\varphi_Z(\eta_Z+b_Z)}{\psi_Z\sigma_Z}\right)Y_Z^A\\
&-\frac{\delta_D\psi_D(\eta_D+b_D)}{\rho_D\sigma_D}\frac{(U_D-U_D^0)^2}{U_D}-\frac{\delta_Z\psi_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z-U_Z^0)^2}{U_Z}\\
&= -\frac{d(X-X^0)^2}{X}-\frac{\delta_D\psi_D(\eta_D+b_D)}{\rho_D\sigma_D}\frac{(U_D-U_D^0)^2}{U_D}-\frac{\delta_Z\psi_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z-U_Z^0)^2}{U_Z}\\
&+\frac{(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D\sigma_D}\left(\frac{\beta_D k_D\psi_D\lambda F_7\sigma_D}{dc_D(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}-1\right)Y_D^A\\
&+\frac{(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{\psi_Z\sigma_Z}\left(\frac{\beta_Z k_Z\psi_Z\lambda F_8\sigma_Z}{dc_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}-1\right)Y_Z^A\\
&= -\frac{d(X-X^0)^2}{X}-\frac{\delta_D\psi_D(\eta_D+b_D)}{\rho_D\sigma_D}\frac{(U_D-U_D^0)^2}{U_D}-\frac{\delta_Z\psi_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z-U_Z^0)^2}{U_Z}\\
&+\frac{(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D\sigma_D}\left(R_D^L-1\right)Y_D^A+\frac{(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{\psi_Z\sigma_Z}\left(R_Z^L-1\right)Y_Z^A.
\end{aligned}$$

If $R_D^L \le 1$ and $R_Z^L \le 1$, then $\frac{d\Theta_0^L}{dt} \le 0$, for all $\left(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z\right) > 0$. Furthermore, $\frac{d\Theta_0^L}{dt} = 0$ holds only when $X = X^0$, $U_D = U_D^0$, and $U_Z = U_Z^0$, together with $(R_D^L - 1)Y_D^A = 0$ and $(R_Z^L - 1)Y_Z^A = 0$. The trajectories of system in Eqs (2.1)–(2.9) converge to Υ_0' [47]. This set has elements satisfying $X = X^0, U_D = U_D^0, U_Z = U_Z^0$, so

$$(R_D^L - 1)Y_D^A = 0 \text{ and } (R_Z^L - 1)Y_Z^A = 0. \tag{5.1}$$

There are four cases:

(i) $R_D^L = 1$ and $R_Z^L = 1$. Then from Eq (2.1), we get

$$\begin{aligned}
0 = \frac{dX}{dt} &= \lambda - dX^0 - \beta_D X^0 V_D - \beta_Z X^0 V_Z \Longrightarrow (\beta_D V_D + \beta_Z V_Z)X^0 = 0, \\
&\Longrightarrow V_D(t) = 0,\ V_Z(t) = 0 \text{ for any } t,
\end{aligned} \tag{5.2}$$

and then $\frac{dV_D}{dt} = \frac{dV_Z}{dt} = 0$. From Eqs (2.6) and (2.7), we find that

$$0 = \frac{dV_D}{dt} = k_D\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau \Rightarrow Y_D^A(t) = 0 \text{ for any } t, \tag{5.3}$$

$$0 = \frac{dV_Z}{dt} = k_Z\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau \Rightarrow Y_Z^A(t) = 0 \text{ for any } t, \tag{5.4}$$

and so we have $\frac{dY_D^A}{dt} = \frac{dY_Z^A}{dt} = 0$. From Eqs (2.3) and (2.5), we find that

$$0 = \frac{dY_D^A}{dt} = \eta_D \int_0^{S_3} \Pi_3(\tau) Y_{D\tau}^L d\tau \Rightarrow Y_D^L(t) = 0 \text{ for any } t, \tag{5.5}$$

$$0 = \frac{dY_Z^A}{dt} = \eta_Z \int_0^{S_6} \Pi_6(\tau) Y_{Z\tau}^L d\tau \Rightarrow Y_Z^L(t) = 0 \text{ for any } t. \tag{5.6}$$

Thus, $\Upsilon_0' = \{EQ^0\}$.

(ii) $R_D^L < 1$ and $R_Z^L < 1$. Then from Eq (5.1), we have $Y_D^A = Y_Z^A = 0$, from Eq (5.2), we have $V_D = V_Z = 0$, and from Eqs (5.5) and (5.6), we have $Y_D^L = Y_Z^L = 0$. Thus, $\Upsilon_0' = \{EQ^0\}$.

(iii) $R_D^L = 1$ and $R_Z^L < 1$. Then from Eq (5.1), we have $Y_Z^A = 0$ and from Eq (5.2), we have $V_D = V_Z = 0$. Equations (5.3), (5.5) and (5.6) imply that $Y_D^A = Y_Z^A = Y_D^L = Y_Z^L = 0$. Thus, $\Upsilon_0' = \{EQ^0\}$.

(iv) $R_D^L < 1$ and $R_Z^L = 1$. Then from Eq (5.1), we have $Y_D^A = 0$, and from Eq (5.2), we have $V_D = V_Z = 0$. Equations (5.4)–(5.6) imply that $Y_D^A = Y_Z^A = Y_D^L = Y_Z^L = 0$. Thus, $\Upsilon_0' = \{EQ^0\}$.

Applying L-LAS, we obtain that EQ^0 is G.A.S. To establish the instability of EQ^0 if $R_0^L > 1$, we compute the Jacobian matrix at the disease-free equilibrium EQ^0, and then we calculate the characteristic equation as:

$$\det(J(EQ^0) - \xi I) = \begin{vmatrix} -d-\xi & 0 & 0 & 0 & 0 & -\beta_D X^0 & -\beta_Z X^0 & 0 & 0 \\ 0 & -(\eta_D + b_D) - \xi & 0 & 0 & 0 & (1-\theta_D)\bar{F}_1\beta_D X^0 & 0 & 0 & 0 \\ 0 & \bar{F}_3\eta_D & -a_D - \delta_D U_D^0 - \xi & 0 & 0 & \theta_D\bar{F}_2\beta_D X^0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\eta_Z + b_Z) - \xi & 0 & 0 & (1-\theta_Z)\bar{F}_4\beta_Z X^0 & 0 & 0 \\ 0 & 0 & 0 & \bar{F}_6\eta_Z & -a_Z - \delta_Z U_Z^0 - \xi & 0 & \theta_Z\bar{F}_5\beta_Z X^0 & 0 & 0 \\ 0 & 0 & \bar{F}_7 k_D & 0 & 0 & -c_D - \xi & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \bar{F}_8 k_Z & 0 & -c_Z - \xi & 0 & 0 \\ 0 & 0 & \rho_D U_D^0 & 0 & 0 & 0 & 0 & -\psi_D - \xi & 0 \\ 0 & 0 & 0 & 0 & \rho_Z U_Z^0 & 0 & 0 & 0 & -\psi_Z - \xi \end{vmatrix} = 0, \tag{5.7}$$

where ξ is the eigenvalue and I is the identity matrix and $\bar{F}_i = \int_0^{S_i} f_i(\tau) e^{-(\xi+n_i)\tau} d\tau, i = 1, 2, ..., 8$. Expanding the determinant, we obtain:

$$(d+\xi)(\psi_D + \xi)(\psi_Z + \xi)M(\xi) = 0, \tag{5.8}$$

where $M(\xi) = M_1(\xi)M_2(\xi)$ is defined for interval $[0, \infty)$ as:

$$M_1(\xi) = \xi^3 + \hat{m}_2^L\xi^2 + \hat{m}_1^L\xi + \hat{m}_0^L, \qquad M_2(\xi) = \xi^3 + \hat{n}_2^L\xi^2 + \hat{n}_1^L\xi + \hat{n}_0^L,$$

and

$$\begin{aligned}
\hat{m}_2^L &= a_D + b_D + c_D + \eta_D + \delta_D U_D^0, \\
\hat{m}_1^L &= a_D(b_D + c_D + \eta_D) + c_D(b_D + \eta_D) + (b_D + c_D + \eta_D)\delta_D U_D^0 - \theta_D\beta_D\bar{F}_2\bar{F}_7 k_D X^0, \\
\hat{m}_0^L &= c_D(\eta_D + b_D)(a_D + \delta_D U_D^0) - \beta_D k_D\bar{F}_7 X^0((\eta_D + b_D)\theta_D\bar{F}_2 + \eta_D(1-\theta_D)\bar{F}_1\bar{F}_3) \\
&= c_D(\eta_D + b_D)\left(a_D + \frac{\delta_D\varphi_D}{\psi_D}\right) - \beta_D k_D\bar{F}_7\bar{\sigma}_D X^0, \\
\hat{n}_2^L &= a_Z + b_Z + c_Z + \eta_Z + \delta_Z U_Z^0, \\
\hat{n}_1^L &= a_Z(b_Z + c_Z + \eta_Z) + c_Z(b_Z + \eta_Z) + (b_Z + c_Z + \eta_Z)\delta_Z U_Z^0 - \theta_Z\beta_Z\bar{F}_5\bar{F}_8 k_Z X^0,
\end{aligned}$$

$$\hat{n}_0^L = c_Z(\eta_Z + b_Z)(a_Z + \delta_Z U_Z^0) - \beta_Z k_Z \bar{F}_8 X^0((\eta_Z + b_Z)\theta_Z \bar{F}_5 + \eta_Z(1-\theta_Z)\bar{F}_4\bar{F}_6)$$
$$= c_Z(\eta_Z + b_Z)\left(a_Z + \frac{\delta_Z \varphi_Z}{\psi_Z}\right) - \beta_Z k_Z \bar{F}_8 \bar{\sigma}_Z X^0,$$

where $\bar{\sigma}_D = (\eta_D + b_D)\theta_D\bar{F}_2 + \eta_D(1-\theta_D)\bar{F}_1\bar{F}_3$, $\bar{\sigma}_Z = (\eta_Z + b_Z)\theta_Z\bar{F}_5 + \eta_Z(1-\theta_Z)\bar{F}_4\bar{F}_6$. Thus $M_1(0) = -\frac{c_D(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D}\left(R_D^L - 1\right) < 0$ if $R_D^L > 1$, and $M_2(0) = -\frac{c_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{\psi_Z}\left(R_Z^L - 1\right) < 0$ if $R_Z^L > 1$ and $\lim_{\xi\to\infty} M_i(\xi) = \infty$, $i = 1, 2$. Then $M_i(\xi)$ has a positive real root. Thus, when $R_D^L > 1$ and/or $R_Z^L > 1$ (i.e., $R_0^L > 1$), Eq (5.8) has a positive root, and so EQ^0 is unstable.

Theorem 2. The DENV mono-infection equilibrium $EQ^* = (X^*, Y_D^{L*}, Y_D^{A*}, 0, 0, V_D^*, 0, U_D^*, U_Z^*)$ is G.A.S if $R_D^L > 1$ and $R_Z^{L,inv} \le 1$. Moreover, if $R_Z^{L,inv} > 1$, then EQ^* is unstable.

Proof. Define $\Theta_1^L(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z)$ as:

$$\begin{aligned}
\Theta_1^L = {} & X^*\mathcal{L}\left(\frac{X}{X^*}\right) + \frac{\eta_D F_3}{\sigma_D} Y_D^{L*}\mathcal{L}\left(\frac{Y_D^L}{Y_D^{L*}}\right) + \frac{\eta_D + b_D}{\sigma_D} Y_D^{A*}\mathcal{L}\left(\frac{Y_D^A}{Y_D^{A*}}\right) \\
& + \frac{\eta_Z F_6}{\sigma_Z} Y_Z^L + \frac{\eta_Z + b_Z}{\sigma_Z} Y_Z^A + \frac{\beta_D X^*}{c_D} V_D^*\mathcal{L}\left(\frac{V_D}{V_D^*}\right) + \frac{\beta_Z X^*}{c_Z} V_Z \\
& + \frac{\delta_D(\eta_D + b_D)}{\rho_D\sigma_D} U_D^*\mathcal{L}\left(\frac{U_D}{U_D^*}\right) + \frac{\delta_Z(\eta_Z + b_Z)}{\rho_Z\sigma_Z} U_Z^*\mathcal{L}\left(\frac{U_Z}{U_Z^*}\right) \\
& + \frac{\eta_D F_3\beta_D(1-\theta_D)}{\sigma_D} X^* V_D^* \int_0^{S_1} \Pi_1(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{X(\phi)V_D(\phi)}{X^*V_D^*}\right) d\phi d\tau \\
& + \frac{\beta_D\theta_D(\eta_D + b_D)}{\sigma_D} X^* V_D^* \int_0^{S_2} \Pi_2(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{X(\phi)V_D(\phi)}{X^*V_D^*}\right) d\phi d\tau \\
& + \frac{\eta_D(\eta_D + b_D)}{\sigma_D} Y_D^{L*} \int_0^{S_3} \Pi_3(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{Y_D^L(\phi)}{Y_D^{L*}}\right) d\phi d\tau \\
& + \frac{\eta_Z F_6\beta_Z(1-\theta_Z)}{\sigma_Z} \int_0^{S_4} \Pi_4(\tau) \int_{t-\tau}^t X(\phi)V_Z(\phi) d\phi d\tau \\
& + \frac{\beta_Z\theta_Z(\eta_Z + b_Z)}{\sigma_Z} \int_0^{S_5} \Pi_5(\tau) \int_{t-\tau}^t X(\phi)V_Z(\phi) d\phi d\tau \\
& + \frac{\eta_Z(\eta_Z + b_Z)}{\sigma_Z} \int_0^{S_6} \Pi_6(\tau) \int_{t-\tau}^t Y_Z^L(\phi) d\phi d\tau \\
& + \frac{\beta_D k_D X^*}{c_D} Y_D^{A*} \int_0^{S_7} \Pi_7(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{Y_D^A(\phi)}{Y_D^{A*}}\right) d\phi d\tau \\
& + \frac{\beta_Z k_Z X^*}{c_Z} \int_0^{S_8} \Pi_8(\tau) \int_{t-\tau}^t Y_Z^A(\phi) d\phi d\tau.
\end{aligned}$$

We observe that $\Theta_1^L(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z) > 0$ for all $(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z) > 0$ and $\Theta_1^L(X^*, Y_D^{L*}, Y_D^{A*}, 0, 0, V_D^*, 0, U_D^*, U_Z^*) = 0$. Calculating $\frac{d\Theta_1^L}{dt}$ along the solutions of system in Eqs (2.1)–(2.9) as:

$$\frac{d\Theta_1^L}{dt} = \left(1 - \frac{X^*}{X}\right)(\lambda - dX - \beta_D X V_D - \beta_Z X V_Z) + \frac{\eta_D F_3}{\sigma_D}\left(1 - \frac{Y_D^{L*}}{Y_D^L}\right)$$

$$
\begin{aligned}
&\times\left((1-\theta_D)\beta_D\int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau-(\eta_D+b_D)Y_D^L\right)+\frac{\eta_D+b_D}{\sigma_D}\left(1-\frac{Y_D^{A*}}{Y_D^A}\right)\\
&\times\left(\theta_D\beta_D\int_0^{S_2}\Pi_2(\tau)X_\tau V_{D\tau}d\tau+\eta_D\int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau-a_DY_D^A-\delta_DY_D^AU_D\right)\\
&+\frac{\eta_ZF_6}{\sigma_Z}\left((1-\theta_Z)\beta_Z\int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau-(\eta_Z+b_Z)Y_Z^L\right)\\
&+\frac{\eta_Z+b_Z}{\sigma_Z}\left(\theta_Z\beta_Z\int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau+\eta_Z\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau-a_ZY_Z^A-\delta_ZY_Z^AU_Z\right)\\
&+\frac{\beta_DX^*}{c_D}\left(1-\frac{V_D^*}{V_D}\right)\left(k_D\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau-c_DV_D\right)+\frac{\beta_ZX^*}{c_Z}\left(k_Z\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau-c_ZV_Z\right)\\
&+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{U_D^*}{U_D}\right)(\varphi_D+\rho_DY_D^AU_D-\psi_DU_D)\\
&+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{U_Z^*}{U_Z}\right)(\varphi_Z+\rho_ZY_Z^AU_Z-\psi_ZU_Z)\\
&+\frac{\eta_DF_3\beta_D(1-\theta_D)}{\sigma_D}X^*V_D^*\int_0^{S_1}\Pi_1(\tau)\left[\frac{XV_D}{X^*V_D^*}-\frac{X_\tau V_{D\tau}}{X^*V_D^*}+\ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right)\right]d\tau\\
&+\frac{\beta_D\theta_D(\eta_D+b_D)}{\sigma_D}X^*V_D^*\int_0^{S_2}\Pi_2(\tau)\left[\frac{XV_D}{X^*V_D^*}-\frac{X_\tau V_{D\tau}}{X^*V_D^*}+\ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right)\right]d\tau\\
&+\frac{\eta_D(\eta_D+b_D)}{\sigma_D}Y_D^{L*}\int_0^{S_3}\Pi_3(\tau)\left[\frac{Y_D^L}{Y_D^{L*}}-\frac{Y_{D\tau}^L}{Y_D^{L*}}+\ln\left(\frac{Y_{D\tau}^L}{Y_D^L}\right)\right]d\tau\\
&+\frac{\eta_ZF_6\beta_Z(1-\theta_Z)}{\sigma_Z}\int_0^{S_4}\Pi_4(\tau)(XV_Z-X_\tau V_{Z\tau})d\tau\\
&+\frac{\beta_Z\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\int_0^{S_5}\Pi_5(\tau)(XV_Z-X_\tau V_{Z\tau})d\tau\\
&+\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\int_0^{S_6}\Pi_6(\tau)(Y_Z^L-Y_{Z\tau}^L)d\tau\\
&+\frac{\beta_Dk_DX^*}{c_D}Y_D^{A*}\int_0^{S_7}\Pi_7(\tau)\left[\frac{Y_D^A}{Y_D^{A*}}-\frac{Y_{D\tau}^A}{Y_D^{A*}}+\ln\left(\frac{Y_{D\tau}^A}{Y_D^A}\right)\right]d\tau\\
&+\frac{\beta_Zk_ZX^*}{c_Z}\int_0^{S_8}\Pi_8(\tau)(Y_Z^A-Y_{Z\tau}^A)d\tau.
\end{aligned}
$$

It follows that

$$
\begin{aligned}
\frac{d\Theta_1^L}{dt}&=\left(1-\frac{X^*}{X}\right)(\lambda-dX)+\left(\frac{\beta_Dk_DF_7X^*}{c_D}-\frac{a_D(\eta_D+b_D)}{\sigma_D}-\frac{\delta_D(\eta_D+b_D)}{\sigma_D}U_D^*\right)Y_D^A\\
&+\left(\frac{\beta_Zk_ZF_8X^*}{c_Z}-\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}-\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}U_Z^*\right)Y_Z^A\\
&-\frac{\eta_D(1-\theta_D)\beta_DF_3}{\sigma_D}\int_0^{S_1}\Pi_1(\tau)\frac{X_\tau V_{D\tau}Y_D^{L*}}{Y_D^L}d\tau+\frac{\eta_DF_3(\eta_D+b_D)}{\sigma_D}Y_D^{L*}
\end{aligned}
$$

$$
\begin{aligned}
&- \frac{(\eta_D + b_D)\theta_D\beta_D}{\sigma_D} \int_0^{S_2} \Pi_2(\tau) \frac{X_\tau V_{D\tau} Y_D^{A*}}{Y_D^A} d\tau + \frac{a_D(\eta_D + b_D)}{\sigma_D} Y_D^{A*} \\
&- \frac{\eta_D(\eta_D + b_D)}{\sigma_D} \int_0^{S_3} \Pi_3(\tau) \frac{Y_{D\tau}^L Y_D^{A*}}{Y_D^A} d\tau - \frac{\beta_D k_D X^*}{c_D} \int_0^{S_7} \Pi_7(\tau) \frac{Y_{D\tau}^A V_D^*}{V_D} d\tau + \beta_D X^* V_D^* \\
&+ \frac{\delta_D(\eta_D + b_D)}{\sigma_D} Y_D^{A*} U_D + \frac{\delta_D(\eta_D + b_D)}{\rho_D \sigma_D} \left(1 - \frac{U_D^*}{U_D}\right)(\varphi_D - \psi_D U_D) \\
&+ \frac{\delta_Z(\eta_Z + b_Z)}{\rho_Z \sigma_Z} \left(1 - \frac{U_Z^*}{U_Z}\right)(\varphi_Z - \psi_Z U_Z) + \frac{\eta_D(1-\theta_D)F_3}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_1} \Pi_1(\tau) \ln\left(\frac{X_\tau V_{D\tau}}{X V_D}\right) d\tau \\
&+ \frac{\theta_D(\eta_D + b_D)}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_2} \Pi_2(\tau) \ln\left(\frac{X_\tau V_{D\tau}}{X V_D}\right) d\tau + \frac{\eta_D(\eta_D + b_D)}{\sigma_D} Y_D^{L*} \int_0^{S_3} \Pi_3(\tau) \ln\left(\frac{Y_{D\tau}^L}{Y_D^L}\right) d\tau \\
&+ \frac{\beta_D k_D X^*}{c_D} Y_D^{A*} \int_0^{S_7} \Pi_7(\tau) \ln\left(\frac{Y_{D\tau}^A}{Y_D^A}\right) d\tau.
\end{aligned}
$$

Equilibrium EQ^* satisfies

$$
\begin{aligned}
\lambda &= dX^* + \beta_D X^* V_D^*, \\
(1-\theta_D)\beta_D F_1 X^* V_D^* &= (\eta_D + b_D) Y_D^{L*}, \\
a_D Y_D^{A*} &= \theta_D \beta_D F_2 X^* V_D^* + \eta_D F_3 Y_D^{L*} - \delta_D Y_D^{A*} U_D^*, \\
k_D F_7 Y_D^{A*} &= c_D V_D^*, \\
\varphi_D &= \psi_D U_D^* - \rho_D Y_D^{A*} U_D^*, \\
\varphi_Z &= \psi_Z U_Z^*,
\end{aligned}
$$

we obtain

$$
\begin{aligned}
&\left(\frac{\beta_D k_D F_7 X^*}{c_D} - \frac{a_D(\eta_D + b_D)}{\sigma_D} - \frac{\delta_D(\eta_D + b_D)}{\sigma_D} U_D^*\right) Y_D^A \\
&= \left(\frac{\beta_D k_D F_7 X^*}{c_D} Y_D^{A*} - \frac{a_D(\eta_D + b_D)}{\sigma_D} Y_D^{A*} - \frac{\delta_D(\eta_D + b_D)}{\sigma_D} U_D^* Y_D^{A*}\right) \frac{Y_D^A}{Y_D^{A*}} = 0,
\end{aligned}
$$

and

$$
\left(\frac{\beta_Z k_Z F_8 X^*}{c_Z} - \frac{a_Z(\eta_Z + b_Z)}{\sigma_Z} - \frac{\delta_Z(\eta_Z + b_Z)}{\sigma_Z} U_Z^*\right) Y_Z^A = \frac{(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}{\psi_Z \sigma_Z} \left(R_Z^{L,inv} - 1\right) Y_Z^A,
$$

and using the following equalities

$$
\begin{aligned}
\ln\left(\frac{X_\tau V_{D\tau}}{X V_D}\right) &= \ln\left(\frac{X_\tau V_{D\tau} Y_D^{L*}}{X^* V_D^* Y_D^L}\right) + \ln\left(\frac{X^*}{X}\right) + \ln\left(\frac{Y_D^L V_D^*}{Y_D^{L*} V_D}\right), \\
\ln\left(\frac{X_\tau V_{D\tau}}{X V_D}\right) &= \ln\left(\frac{X_\tau V_{D\tau} Y_D^{A*}}{X^* V_D^* Y_D^A}\right) + \ln\left(\frac{X^*}{X}\right) + \ln\left(\frac{Y_D^A V_D^*}{Y_D^{A*} V_D}\right), \\
\ln\left(\frac{Y_{D\tau}^L}{Y_D^L}\right) &= \ln\left(\frac{Y_{D\tau}^L Y_D^{A*}}{Y_D^{L*} Y_D^A}\right) + \ln\left(\frac{Y_D^{L*} Y_D^A}{Y_D^L Y_D^{A*}}\right),
\end{aligned}
$$

$$\ln\left(\frac{Y_{D\tau}^{A}}{Y_{D}^{A}}\right)=\ln\left(\frac{Y_{D\tau}^{A}V_{D}^{*}}{Y_{D}^{A*}V_{D}}\right)+\ln\left(\frac{Y_{D}^{A*}V_{D}}{Y_{D}^{A}V_{D}^{*}}\right).$$

So,

$$\begin{aligned}
\frac{d\Theta_1^L}{dt}&=\left(1-\frac{X^*}{X}\right)(dX^*+\beta_D X^*V_D^*-dX)+\frac{(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{\psi_Z\sigma_Z}\left(R_Z^{L,inv}-1\right)Y_Z^A\\
&-\frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_1}\Pi_1(\tau)\frac{X_\tau V_{D\tau}Y_D^{L*}}{X^*V_D^*Y_D^L}d\tau+2\frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D}\beta_D X^*V_D^*\\
&+\frac{\theta_D(\eta_D+b_D)F_2}{\sigma_D}\beta_D X^*V_D^*-\frac{\delta_D(\eta_D+b_D)}{\sigma_D}Y_D^{A*}U_D^*-\frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D X^*V_D^*\\
&\times\int_0^{S_2}\Pi_2(\tau)\frac{X_\tau V_{D\tau}Y_D^{A*}}{X^*V_D^*Y_D^A}d\tau-\frac{\eta_D F_1(1-\theta_D)}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_3}\Pi_3(\tau)\frac{Y_{D\tau}^LY_D^{A*}}{Y_D^{L*}Y_D^A}d\tau\\
&-\frac{\beta_D}{F_7}X^*V_D^*\int_0^{S_7}\Pi_7(\tau)\frac{Y_{D\tau}^AV_D^*}{Y_D^{A*}V_D}d\tau+\beta_D X^*V_D^*+\frac{\delta_D(\eta_D+b_D)}{\sigma_D}Y_D^{A*}U_D\\
&+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{U_D^*}{U_D}\right)(\psi_DU_D^*-\rho_DY_D^{A*}U_D^*-\psi_DU_D)+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{U_Z^*}{U_Z}\right)(\psi_ZU_Z^*-\psi_ZU_Z)\\
&+\frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_1}\Pi_1(\tau)\left[\ln\left(\frac{X_\tau V_{D\tau}Y_D^{L*}}{X^*V_D^*Y_D^L}\right)+\ln\left(\frac{X^*}{X}\right)+\ln\left(\frac{Y_D^LV_D^*}{Y_D^{L*}V_D}\right)\right]d\tau\\
&+\frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_2}\Pi_2(\tau)\left[\ln\left(\frac{X_\tau V_{D\tau}Y_D^{A*}}{X^*V_D^*Y_D^A}\right)+\ln\left(\frac{X^*}{X}\right)+\ln\left(\frac{Y_D^AV_D^*}{Y_D^{A*}V_D}\right)\right]d\tau\\
&+\frac{\eta_D F_1(1-\theta_D)}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_3}\Pi_3(\tau)\left[\ln\left(\frac{Y_{D\tau}^LY_D^{A*}}{Y_D^{L*}Y_D^A}\right)+\ln\left(\frac{Y_D^{L*}Y_D^A}{Y_D^LY_D^{A*}}\right)\right]d\tau\\
&+\frac{\beta_D}{F_7}X^*V_D^*\int_0^{S_7}\Pi_7(\tau)\left[\ln\left(\frac{Y_{D\tau}^AV_D^*}{Y_D^{A*}V_D}\right)+\ln\left(\frac{Y_D^{A*}V_D}{Y_D^AV_D^*}\right)\right]d\tau.
\end{aligned}$$

It follows that

$$\begin{aligned}
\frac{d\Theta_1^L}{dt}&=\left(1-\frac{X^*}{X}\right)(dX^*-dX)+\beta_D X^*V_D^*\left(1-\frac{X^*}{X}\right)\\
&+\frac{(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{\psi_Z\sigma_Z}\left(R_Z^{L,inv}-1\right)Y_Z^A+\frac{\delta_D(\eta_D+b_D)}{\sigma_D}Y_D^{A*}(U_D-U_D^*)\\
&+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{U_D^*}{U_D}\right)(\psi_DU_D^*-\psi_DU_D)\\
&-\frac{\delta_D(\eta_D+b_D)}{\sigma_D}Y_D^{A*}U_D^*\left(1-\frac{U_D^*}{U_D}\right)+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{U_Z^*}{U_Z}\right)(\psi_ZU_Z^*-\psi_ZU_Z)\\
&-\frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_1}\Pi_1(\tau)\left[\frac{X_\tau V_{D\tau}Y_D^{L*}}{X^*V_D^*Y_D^L}-1-\ln\left(\frac{X_\tau V_{D\tau}Y_D^{L*}}{X^*V_D^*Y_D^L}\right)\right]d\tau\\
&-\frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_2}\Pi_2(\tau)\left[\frac{X_\tau V_{D\tau}Y_D^{A*}}{X^*V_D^*Y_D^A}-1-\ln\left(\frac{X_\tau V_{D\tau}Y_D^{A*}}{X^*V_D^*Y_D^A}\right)\right]d\tau\\
&-\frac{\eta_D F_1(1-\theta_D)}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_3}\Pi_3(\tau)\left[\frac{Y_{D\tau}^LY_D^{A*}}{Y_D^{L*}Y_D^A}-1-\ln\left(\frac{Y_{D\tau}^LY_D^{A*}}{Y_D^{L*}Y_D^A}\right)\right]d\tau
\end{aligned}$$

$$
\begin{aligned}
&- \frac{\beta_D}{F_7} X^* V_D^* \int_0^{S_7} \Pi_7(\tau) \left[\frac{Y_{D\tau}^A V_D^*}{Y_D^{A*} V_D} - 1 - \ln\left(\frac{Y_{D\tau}^A V_D^*}{Y_D^{A*} V_D} \right) \right] d\tau \\
&+ \frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D} \beta_D X^* V_D^* \ln\left(\frac{X^*}{X} \right) + \frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D} \beta_D X^* V_D^* \ln\left(\frac{Y_D^L V_D^*}{Y_D^{L*} V_D} \right) \\
&+ \frac{\theta_D(\eta_D + b_D)F_2}{\sigma_D} \beta_D X^* V_D^* \ln\left(\frac{X^*}{X} \right) + \frac{\theta_D(\eta_D + b_D)F_2}{\sigma_D} \beta_D X^* V_D^* \ln\left(\frac{Y_D^A V_D^*}{Y_D^{A*} V_D} \right) \\
&+ \frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D} \beta_D X^* V_D^* \ln\left(\frac{Y_D^{L*} Y_D^A}{Y_D^L Y_D^{A*}} \right) + \beta_D X^* V_D^* \ln\left(\frac{Y_D^{A*} V_D}{Y_D^A V_D^*} \right).
\end{aligned}
$$

Then we get

$$
\begin{aligned}
\frac{d\Theta_1^L}{dt} &= -\frac{d(X - X^*)^2}{X} + \beta_D X^* V_D^* \left(1 - \frac{X^*}{X} \right) + \frac{(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}{\psi_Z \sigma_Z} \left(R_Z^{L,inv} - 1 \right) Y_Z^A \\
&- \frac{\delta_D \psi_D (\eta_D + b_D)}{\rho_D \sigma_D} \frac{(U_D - U_D^*)^2}{U_D} - \frac{\delta_Z \psi_Z (\eta_Z + b_Z)}{\rho_Z \sigma_Z} \frac{(U_Z - U_Z^*)^2}{U_Z} \\
&- \frac{\delta_D(\eta_D + b_D)}{\sigma_D} Y_D^{A*} U_D^* \left(2 - \frac{U_D^*}{U_D} - \frac{U_D}{U_D^*} \right) \\
&- \frac{\eta_D(1-\theta_D)F_3}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_1} \Pi_1(\tau) \mathcal{L}\left(\frac{X_\tau V_{D\tau} Y_D^{L*}}{X^* V_D^* Y_D^L} \right) d\tau \\
&- \frac{\theta_D(\eta_D + b_D)}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_2} \Pi_2(\tau) \mathcal{L}\left(\frac{X_\tau V_{D\tau} Y_D^{A*}}{X^* V_D^* Y_D^A} \right) d\tau \\
&- \frac{\eta_D F_1(1-\theta_D)}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_3} \Pi_3(\tau) \mathcal{L}\left(\frac{Y_{D\tau}^L Y_D^{A*}}{Y_D^{L*} Y_D^A} \right) d\tau \\
&- \frac{\beta_D}{F_7} X^* V_D^* \int_0^{S_7} \Pi_7(\tau) \mathcal{L}\left(\frac{Y_{D\tau}^A V_D^*}{Y_D^{A*} V_D} \right) d\tau + \beta_D X^* V_D^* \ln\left(\frac{X^*}{X} \right) \\
&= -\frac{d(X - X^*)^2}{X} + \frac{(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}{\psi_Z \sigma_Z} \left(R_Z^{L,inv} - 1 \right) Y_Z^A \\
&- \frac{\delta_D \psi_D (\eta_D + b_D)}{\rho_D \sigma_D} \frac{(U_D - U_D^*)^2}{U_D} - \frac{\delta_Z \psi_Z (\eta_Z + b_Z)}{\rho_Z \sigma_Z} \frac{(U_Z - U_Z^*)^2}{U_Z} \\
&+ \frac{\delta_D(\eta_D + b_D)}{\sigma_D} Y_D^{A*} \frac{(U_D - U_D^*)^2}{U_D} - \beta_D X^* V_D^* \mathcal{L}\left(\frac{X^*}{X} \right) \\
&- \frac{\eta_D(1-\theta_D)F_3}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_1} \Pi_1(\tau) \mathcal{L}\left(\frac{X_\tau V_{D\tau} Y_D^{L*}}{X^* V_D^* Y_D^L} \right) d\tau \\
&- \frac{\theta_D(\eta_D + b_D)}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_2} \Pi_2(\tau) \mathcal{L}\left(\frac{X_\tau V_{D\tau} Y_D^{A*}}{X^* V_D^* Y_D^A} \right) d\tau \\
&- \frac{\eta_D F_1(1-\theta_D)}{\sigma_D} \beta_D X^* V_D^* \int_0^{S_3} \Pi_3(\tau) \mathcal{L}\left(\frac{Y_{D\tau}^L Y_D^{A*}}{Y_D^{L*} Y_D^A} \right) d\tau \\
&- \frac{\beta_D}{F_7} X^* V_D^* \int_0^{S_7} \Pi_7(\tau) \mathcal{L}\left(\frac{Y_{D\tau}^A V_D^*}{Y_D^{A*} V_D} \right) d\tau.
\end{aligned}
$$

From equilibrium conditions of EQ^*, we have $Y_D^{A*} - \frac{\psi_D}{\rho_D} = -\frac{\varphi_D}{\rho_D U_D^*}$. It follows that

$$\begin{aligned}\frac{d\Theta_1^L}{dt} &= -\frac{d(X-X^*)^2}{X} + \frac{(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}{\psi_Z\sigma_Z}\left(R_Z^{L,inv} - 1\right)Y_Z^A \\ &- \frac{\delta_D\varphi_D(\eta_D + b_D)}{\rho_D\sigma_D}\frac{(U_D - U_D^*)^2}{U_D^*U_D} - \frac{\delta_Z\psi_Z(\eta_Z + b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z - U_Z^*)^2}{U_Z} \\ &- \beta_D X^* V_D^* \mathcal{L}\left(\frac{X^*}{X}\right) - \frac{\eta_D(1-\theta_D)F_3\beta_D}{\sigma_D}X^*V_D^*\int_0^{S_1}\Pi_1(\tau)\mathcal{L}\left(\frac{X_\tau V_{D\tau}Y_D^{L*}}{X^*V_D^*Y_D^L}\right)d\tau \\ &- \frac{\theta_D(\eta_D + b_D)}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_2}\Pi_2(\tau)\mathcal{L}\left(\frac{X_\tau V_{D\tau}Y_D^{A*}}{X^*V_D^*Y_D^A}\right)d\tau \\ &- \frac{\eta_D F_1(1-\theta_D)}{\sigma_D}\beta_D X^*V_D^*\int_0^{S_3}\Pi_3(\tau)\mathcal{L}\left(\frac{Y_{D\tau}^L Y_D^{A*}}{Y_D^{L*}Y_D^A}\right)d\tau \\ &- \frac{\beta_D}{F_7}X^*V_D^*\int_0^{S_7}\Pi_7(\tau)\mathcal{L}\left(\frac{Y_{D\tau}^A V_D^*}{Y_D^{A*}V_D}\right)d\tau.\end{aligned}$$

Consequently, if $R_Z^{L,inv} \le 1$, then $\frac{d\Theta_1^L}{dt} \le 0$, for all $\left(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z\right) > 0$. Moreover, $\frac{d\Theta_1^L}{dt} = 0$ when $X = X^*$, $Y_D^L = Y_D^{L*}$, $Y_D^A = Y_D^{A*}$, $V_D = V_D^*$, $U_D = U_D^*$, $U_Z = U_Z^*$, and $(R_Z^{L,inv} - 1)Y_Z^A = 0$. The solutions of system in Eqs (2.1)–(2.9) converge to Υ_1', which has elements satisfying $X = X^*$, $Y_D^L = Y_D^{L*}$, $Y_D^A = Y_D^{A*}$, $V_D = V_D^*$, $U_D = U_D^*$, $U_Z = U_Z^*$, and

$$(R_Z^{L,inv} - 1)Y_Z^A = 0. \tag{5.9}$$

We have two cases: (i) $R_Z^{L,inv} < 1$, then Eq (5.9) implies that $Y_Z^A = 0$, and Eq (2.1) gives

$$0 = \frac{dX}{dt} = \lambda - dX^* - \beta_D X^* V_D^* - \beta_Z X^* V_Z \Longrightarrow V_Z(t) = 0 \text{ for any t.} \tag{5.10}$$

From Eq (2.5), we have

$$0 = \frac{dY_Z^A}{dt} = \eta_Z\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau \Rightarrow Y_Z^L(t) = 0 \text{ for any t.} \tag{5.11}$$

Hence, $\Upsilon_1' = \{EQ^*\}$. (ii) $R_Z^{L,inv} = 1$, then from Eq (5.10), we have $V_Z = 0$, and from Eq (2.7), we get

$$0 = \frac{dV_Z}{dt} = k_Z\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau \Rightarrow Y_Z^A(t) = 0 \text{ for any t.}$$

Additionally, from Eq (5.11), we have $Y_Z^L = 0$. Hence, $\Upsilon_1' = \{EQ^*\}$. Applying the L-LAS theorem implies that EQ^* is G.A.S.

To determine whether EQ^* is unstable when $R_Z^{L,inv} > 1$, we compute the characteristic equation at EQ^* as:

$$\begin{aligned}\det(J(EQ^*) - \xi I) = (\psi_Z + \xi)N(\xi)[&\delta_D U_D^*(c_D + \xi)(d + \beta_D V_D^* + \xi) \\ &\times (b_D + \eta_D + \xi)(\psi_D + \xi) + (\psi_D - \rho_D Y_D^{A*} + \xi)((c_D + \xi)(a_D + \xi)\end{aligned}$$

$$\times (d+\beta_D V_D^* + \xi)(b_D + \eta_D + \xi) - k_D\beta_D X^*(d+\xi) + \bar{\sigma}_D + \bar{F}_2\theta_D\xi)]$$
$$= 0, \tag{5.12}$$

where $N(\xi)$ is defined for interval $[0,\infty)$ as:

$$N(\xi) = \xi^3 + \hat{\varepsilon}_2^L\xi^2 + \hat{\varepsilon}_1^L\xi + \hat{\varepsilon}_0^L,$$

and

$$\begin{aligned}
\hat{\varepsilon}_2^L &= a_Z + b_Z + c_Z + \eta_Z + \delta_Z U_Z^*,\\
\hat{\varepsilon}_1^L &= a_Z(b_Z + c_Z + \eta_Z) + c_Z(b_Z + \eta_Z) + (b_Z + c_Z + \eta_Z)\delta_Z U_Z^* - \theta_Z\beta_Z k_Z\bar{F}_5\bar{F}_8 X^*,\\
\hat{\varepsilon}_0^L &= c_Z(\eta_Z + b_Z)(a_Z + \delta_Z U_Z^*) - \beta_Z k_Z\bar{F}_8 X^*((\eta_Z + b_Z)\theta_Z\bar{F}_5 + \eta_Z(1-\theta_Z)\bar{F}_4\bar{F}_6)\\
&= c_Z(\eta_Z + b_Z)\left(a_Z + \delta_Z U_Z^*\right) - \beta_Z k_Z\bar{F}_8 X^*\bar{\sigma}_Z.
\end{aligned}$$

If $R_Z^{L,inv} > 1$, then $N(0) < 0$ since $N(0) = -\frac{c_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{\psi_Z}\left(R_Z^{L,inv} - 1\right)$ and $\lim_{\xi\to\infty} N(\xi) = \infty$, so, Eq (5.12) has a positive root and hence EQ^* is unstable.

Theorem 3. The ZIKV mono-infection equilibrium $\overline{EQ} = (\overline{X}, 0, 0, \overline{Y}_Z^L, \overline{Y}_Z^A, 0, \overline{V}_Z, \overline{U}_D, \overline{U}_Z)$ is G.A.S if $R_Z^L > 1$ and $R_D^{L,inv} \le 1$. Moreover, if $R_D^{L,inv} > 1$, then $\overline{EQ}$ is unstable.

Proof. Define $\Theta_2^L(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z)$ as:

$$\begin{aligned}
\Theta_2^L &= \overline{X}\mathcal{L}\left(\frac{X}{\overline{X}}\right) + \frac{\eta_D F_3}{\sigma_D}Y_D^L + \frac{\eta_D + b_D}{\sigma_D}Y_D^A + \frac{\eta_Z F_6}{\sigma_Z}\overline{Y}_Z^L\mathcal{L}\left(\frac{Y_Z^L}{\overline{Y}_Z^L}\right) + \frac{\eta_Z + b_Z}{\sigma_Z}\overline{Y}_Z^A\mathcal{L}\left(\frac{Y_Z^A}{\overline{Y}_Z^A}\right) + \frac{\beta_D\overline{X}}{c_D}V_D\\
&+ \frac{\beta_Z\overline{X}}{c_Z}\overline{V}_Z\mathcal{L}\left(\frac{V_Z}{\overline{V}_Z}\right) + \frac{\delta_D(\eta_D + b_D)}{\rho_D\sigma_D}\overline{U}_D\mathcal{L}\left(\frac{U_D}{\overline{U}_D}\right) + \frac{\delta_Z(\eta_Z + b_Z)}{\rho_Z\sigma_Z}\overline{U}_Z\mathcal{L}\left(\frac{U_Z}{\overline{U}_Z}\right)\\
&+ \frac{\eta_D F_3\beta_D(1-\theta_D)}{\sigma_D}\int_0^{S_1}\Pi_1(\tau)\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau\\
&+ \frac{\beta_D\theta_D(\eta_D + b_D)}{\sigma_D}\int_0^{S_2}\Pi_2(\tau)\int_{t-\tau}^{t}X(\phi)V_D(\phi)d\phi d\tau + \frac{\eta_D(\eta_D + b_D)}{\sigma_D}\int_0^{S_3}\Pi_3(\tau)\int_{t-\tau}^{t}Y_D^L(\phi)d\phi d\tau\\
&+ \frac{\eta_Z F_6\beta_Z(1-\theta_Z)}{\sigma_Z}\overline{X}\,\overline{V}_Z\int_0^{S_4}\Pi_4(\tau)\int_{t-\tau}^{t}\mathcal{L}\left(\frac{X(\phi)V_Z(\phi)}{\overline{X}\,\overline{V}_Z}\right)d\phi d\tau + \frac{\beta_Z\theta_Z(\eta_Z + b_Z)}{\sigma_Z}\overline{X}\,\overline{V}_Z\int_0^{S_5}\Pi_5(\tau)\\
&\times\int_{t-\tau}^{t}\mathcal{L}\left(\frac{X(\phi)V_Z(\phi)}{\overline{X}\,\overline{V}_Z}\right)d\phi d\tau + \frac{\eta_Z(\eta_Z + b_Z)}{\sigma_Z}\overline{Y}_Z^L\int_0^{S_6}\Pi_6(\tau)\int_{t-\tau}^{t}\mathcal{L}\left(\frac{Y_Z^L(\phi)}{\overline{Y}_Z^L}\right)d\phi d\tau\\
&+ \frac{\beta_D k_D\overline{X}}{c_D}\int_0^{S_7}\Pi_7(\tau)\int_{t-\tau}^{t}Y_D^A(\phi)d\phi d\tau + \frac{\beta_Z k_Z\overline{X}}{c_Z}\overline{Y}_Z^A\int_0^{S_8}\Pi_8(\tau)\int_{t-\tau}^{t}\mathcal{L}\left(\frac{Y_Z^A(\phi)}{\overline{Y}_Z^A}\right)d\phi d\tau.
\end{aligned}$$

We observe that $\Theta_2^L(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z) > 0$ for all $(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z) > 0$ and $\Theta_2^L(\overline{X}, 0, 0, \overline{Y}_Z^L, \overline{Y}_Z^A, 0, \overline{V}_Z, \overline{U}_D, \overline{U}_Z) = 0$. Calculating $\frac{d\Theta_2^L}{dt}$ along the solutions of system in Eqs (2.1)–(2.9) as:

$$\frac{d\Theta_2^L}{dt} = \left(1 - \frac{\overline{X}}{X}\right)(\lambda - dX - \beta_D XV_D - \beta_Z XV_Z) + \frac{\eta_D F_3}{\sigma_D}\left((1-\theta_D)\beta_D\int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau - (\eta_D + b_D)Y_D^L\right)$$

$$
\begin{aligned}
&+\frac{\eta_D+b_D}{\sigma_D}\left(\theta_D\beta_D\int_0^{S_2}\Pi_2(\tau)X_\tau V_{D\tau}d\tau+\eta_D\int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau-a_DY_D^A-\delta_DY_D^AU_D\right)\\
&+\frac{\eta_ZF_6}{\sigma_Z}\left(1-\frac{\overline{Y}_Z^L}{Y_Z^L}\right)\left((1-\theta_Z)\beta_Z\int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau-(\eta_Z+b_Z)Y_Z^L\right)\\
&+\frac{\eta_Z+b_Z}{\sigma_Z}\left(1-\frac{\overline{Y}_Z^A}{Y_Z^A}\right)\left(\theta_Z\beta_Z\int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau+\eta_Z\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau-a_ZY_Z^A-\delta_ZY_Z^AU_Z\right)\\
&+\frac{\beta_D\overline{X}}{c_D}\left(k_D\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau-c_DV_D\right)+\frac{\beta_Z\overline{X}}{c_Z}\left(1-\frac{\overline{V}_Z}{V_Z}\right)\left(k_Z\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau-c_ZV_Z\right)\\
&+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\overline{U}_D}{U_D}\right)(\varphi_D+\rho_DY_D^AU_D-\psi_DU_D)\\
&+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\overline{U}_Z}{U_Z}\right)(\varphi_Z+\rho_ZY_Z^AU_Z-\psi_ZU_Z)\\
&+\frac{\eta_DF_3\beta_D(1-\theta_D)}{\sigma_D}\int_0^{S_1}\Pi_1(\tau)(XV_D-X_\tau V_{D\tau})d\tau\\
&+\frac{\beta_D\theta_D(\eta_D+b_D)}{\sigma_D}\int_0^{S_2}\Pi_2(\tau)(XV_D-X_\tau V_{D\tau})d\tau+\frac{\eta_D(\eta_D+b_D)}{\sigma_D}\int_0^{S_3}\Pi_3(\tau)(Y_D^L-Y_{D\tau}^L)d\tau\\
&+\frac{\eta_ZF_6\beta_Z(1-\theta_Z)}{\sigma_Z}\overline{XV}_Z\int_0^{S_4}\Pi_4(\tau)\left[\frac{XV_Z}{\overline{XV}_Z}-\frac{X_\tau V_{Z\tau}}{\overline{XV}_Z}+\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)\right]d\tau\\
&+\frac{\beta_Z\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\left[\frac{XV_Z}{\overline{XV}_Z}-\frac{X_\tau V_{Z\tau}}{\overline{XV}_Z}+\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)\right]d\tau\\
&+\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^L\int_0^{S_6}\Pi_6(\tau)\left[\frac{Y_Z^L}{\overline{Y}_Z^L}-\frac{Y_{Z\tau}^L}{\overline{Y}_Z^L}+\ln\left(\frac{Y_{Z\tau}^L}{Y_Z^L}\right)\right]d\tau\\
&+\frac{\beta_Dk_D\overline{X}}{c_D}\int_0^{S_7}\Pi_7(\tau)(Y_D^A-Y_{D\tau}^A)d\tau\\
&+\frac{\beta_Zk_Z\overline{X}}{c_Z}\overline{Y}_Z^A\int_0^{S_8}\Pi_8(\tau)\left[\frac{Y_Z^A}{\overline{Y}_Z^A}-\frac{Y_{Z\tau}^A}{\overline{Y}_Z^A}+\ln\left(\frac{Y_{Z\tau}^A}{Y_Z^A}\right)\right]d\tau.
\end{aligned}
$$

It follows that

$$
\begin{aligned}
\frac{d\Theta_2^L}{dt}=&\left(1-\frac{\overline{X}}{X}\right)(\lambda-dX)+\left(\frac{\beta_Dk_DF_7\overline{X}}{c_D}-\frac{a_D(\eta_D+b_D)}{\sigma_D}-\frac{\delta_D(\eta_D+b_D)}{\sigma_D}\overline{U}_D\right)Y_D^A\\
&+\left(\frac{\beta_Zk_ZF_8\overline{X}}{c_Z}-\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}-\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{U}_Z\right)Y_Z^A-\frac{\eta_Z(1-\theta_Z)\beta_ZF_6}{\sigma_Z}\frac{\overline{Y}_Z^L}{Y_Z^L}\int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau\\
&+\frac{\eta_ZF_6(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^L-\frac{(\eta_Z+b_Z)\theta_Z\beta_Z}{\sigma_Z}\frac{\overline{Y}_Z^A}{Y_Z^A}\int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau+\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A\\
&-\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\frac{\overline{Y}_Z^A}{Y_Z^A}\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau-\frac{\beta_Zk_Z\overline{X}}{c_Z}\frac{\overline{V}_Z}{V_Z}\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau+\beta_Z\overline{XV}_Z
\end{aligned}
$$

$$+\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A U_Z+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\overline{U}_D}{U_D}\right)(\varphi_D-\psi_D U_D)$$
$$+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\overline{U}_Z}{U_Z}\right)(\varphi_Z-\psi_Z U_Z)+\frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_4}\Pi_4(\tau)\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)d\tau$$
$$+\frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)d\tau+\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^L\int_0^{S_6}\Pi_6(\tau)\ln\left(\frac{Y^L_{Z\tau}}{Y^L_Z}\right)d\tau$$
$$+\frac{\beta_Z k_Z\overline{X}}{c_Z}\overline{Y}_Z^A\int_0^{S_8}\Pi_8(\tau)\ln\left(\frac{Y^A_{Z\tau}}{Y^A_Z}\right)d\tau.$$

Equilibrium $\overline{EQ}$ satisfies

$$\begin{aligned}\lambda&=d\overline{X}+\beta_Z\overline{X}\,\overline{V}_Z,\\(1-\theta_Z)\beta_Z F_4\overline{X}\,\overline{V}_Z&=(\eta_Z+b_Z)\overline{Y}_Z^L,\\a_Z\overline{Y}_Z^A&=\theta_Z\beta_Z F_5\overline{X}\,\overline{V}_Z+\eta_Z F_6\overline{Y}_Z^L-\delta_Z\overline{Y}_Z^A\overline{U}_Z,\\k_Z F_8\overline{Y}_Z^A&=c_Z\overline{V}_Z,\\\varphi_D&=\psi_D\overline{U}_D,\\\varphi_Z&=\psi_Z\overline{U}_Z-\rho_Z\overline{Y}_Z^A\overline{U}_Z,\end{aligned}$$

we obtain

$$\left(\frac{\beta_D k_D F_7\overline{X}}{c_D}-\frac{a_D(\eta_D+b_D)}{\sigma_D}-\frac{\delta_D(\eta_D+b_D)}{\sigma_D}\overline{U}_D\right)Y_D^A=\frac{(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D\sigma_D}\left(R_D^{L,inv}-1\right)Y_D^A,$$

and

$$\left(\frac{\beta_Z k_Z F_8\overline{X}}{c_Z}-\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}-\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{U}_Z\right)Y_Z^A$$
$$=\left(\frac{\beta_Z k_Z F_8\overline{X}}{c_Z}\overline{Y}_Z^A-\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A-\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{U}_Z\overline{Y}_Z^A\right)\frac{Y_Z^A}{\overline{Y}_Z^A}=0.$$

Using the following equalities

$$\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)=\ln\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}\right)+\ln\left(\frac{\overline{X}}{X}\right)+\ln\left(\frac{Y_Z^L\overline{V}_Z}{\overline{Y}_Z^L V_Z}\right),$$
$$\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)=\ln\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}\right)+\ln\left(\frac{\overline{X}}{X}\right)+\ln\left(\frac{Y_Z^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right),$$
$$\ln\left(\frac{Y^L_{Z\tau}}{Y^L_Z}\right)=\ln\left(\frac{Y^L_{Z\tau}\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}\right)+\ln\left(\frac{\overline{Y}_Z^L Y_Z^A}{Y_Z^L\overline{Y}_Z^A}\right),$$
$$\ln\left(\frac{Y^A_{Z\tau}}{Y^A_Z}\right)=\ln\left(\frac{Y^A_{Z\tau}\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)+\ln\left(\frac{\overline{Y}_Z^A V_Z}{Y_Z^A\overline{V}_Z}\right).$$

Thus,

$$\begin{aligned}
\frac{d\Theta_2^L}{dt} &= \left(1-\frac{\overline{X}}{X}\right)(d\overline{X}+\beta_Z\overline{XV}_Z-dX)+\frac{(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D\sigma_D}\left(R_D^{L,inv}-1\right)Y_D^A\\
&-\frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_4}\Pi_4(\tau)\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}d\tau\\
&+2\frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\overline{XV}_Z+\frac{\theta_Z(\eta_Z+b_Z)F_5}{\sigma_Z}\beta_Z\overline{XV}_Z-\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A\overline{U}_Z\\
&-\frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}d\tau-\frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_6}\Pi_6(\tau)\frac{Y_{Z\tau}^L\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}d\tau\\
&+\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A U_Z-\frac{\beta_Z}{F_8}\overline{XV}_Z\int_0^{S_8}\Pi_8(\tau)\frac{Y_{Z\tau}^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}d\tau+\beta_Z\overline{XV}_Z\\
&-\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\overline{U}_D}{U_D}\right)(\psi_D\overline{U}_D-\psi_D U_D)\\
&+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\overline{U}_Z}{U_Z}\right)(\psi_Z\overline{U}_Z-\rho_Z\overline{Y}_Z^A\overline{U}_Z-\psi_Z U_Z)\\
&+\frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_4}\Pi_4(\tau)\left[\ln\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}\right)+\ln\left(\frac{\overline{X}}{X}\right)+\ln\left(\frac{Y_Z^L\overline{V}_Z}{\overline{Y}_Z^L V_Z}\right)\right]d\tau\\
&+\frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\left[\ln\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}\right)+\ln\left(\frac{\overline{X}}{X}\right)+\ln\left(\frac{Y_Z^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)\right]d\tau\\
&+\frac{\eta_Z F_4(1-\theta_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_6}\Pi_6(\tau)\left[\ln\left(\frac{Y_{Z\tau}^L\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}\right)+\ln\left(\frac{\overline{Y}_Z^L Y_Z^A}{Y_Z^L\overline{Y}_Z^A}\right)\right]d\tau\\
&+\frac{\beta_Z}{F_8}\overline{XV}_Z\int_0^{S_8}\Pi_8(\tau)\left[\ln\left(\frac{Y_{Z\tau}^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)+\ln\left(\frac{\overline{Y}_Z^A V_Z}{Y_Z^A\overline{V}_Z}\right)\right]d\tau.
\end{aligned}$$

It follows that

$$\begin{aligned}
\frac{d\Theta_2^L}{dt} &= \left(1-\frac{\overline{X}}{X}\right)(d\overline{X}-dX)+\beta_Z\overline{XV}_Z\left(1-\frac{\overline{X}}{X}\right)+\frac{(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D\sigma_D}\left(R_D^{L,inv}-1\right)Y_D^A\\
&+\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A(U_Z-\overline{U}_Z)+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\overline{U}_D}{U_D}\right)(\psi_D\overline{U}_D-\psi_D U_D)\\
&+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\overline{U}_Z}{U_Z}\right)(\psi_Z\overline{U}_Z-\psi_Z U_Z)-\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A\overline{U}_Z\left(1-\frac{\overline{U}_Z}{U_Z}\right)\\
&-\frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_4}\Pi_4(\tau)\left[\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}-1-\ln\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}\right)\right]d\tau\\
&-\frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\left[\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}-1-\ln\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}\right)\right]d\tau
\end{aligned}$$

$$
\begin{aligned}
&- \frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_6}\Pi_6(\tau)\left[\frac{Y_{Z\tau}^L\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}-1-\ln\left(\frac{Y_{Z\tau}^L\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}\right)\right]d\tau\\
&- \frac{\beta_Z}{F_8}\overline{XV}_Z\int_0^{S_8}\Pi_8(\tau)\left[\frac{Y_{Z\tau}^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}-1-\ln\left(\frac{Y_{Z\tau}^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)\right]d\tau\\
&+ \frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\ln\left(\frac{\overline{X}}{X}\right)+\frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\ln\left(\frac{Y_Z^L\overline{V}_Z}{\overline{Y}_Z^L V_Z}\right)\\
&+ \frac{\theta_Z(\eta_Z+b_Z)F_5}{\sigma_Z}\beta_Z\overline{XV}_Z\ln\left(\frac{\overline{X}}{X}\right)+\frac{\theta_Z(\eta_Z+b_Z)F_5}{\sigma_Z}\beta_Z\overline{XV}_Z\ln\left(\frac{Y_Z^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)\\
&+ \frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\ln\left(\frac{\overline{Y}_Z^L Y_Z^A}{Y_Z^L\overline{Y}_Z^A}\right)+\beta_Z\overline{XV}_Z\ln\left(\frac{\overline{Y}_Z^A V_Z}{Y_Z^A\overline{V}_Z}\right).
\end{aligned}
$$

Then we get

$$
\begin{aligned}
\frac{d\Theta_2^L}{dt} &= -\frac{d(X-\overline{X})^2}{X}+\beta_Z\overline{XV}_Z\left(1-\frac{\overline{X}}{X}\right)+\frac{(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D\sigma_D}\left(R_D^{L,inv}-1\right)Y_D^A\\
&- \frac{\delta_D\psi_D(\eta_D+b_D)}{\rho_D\sigma_D}\frac{(U_D-\overline{U}_D)^2}{U_D}-\frac{\delta_Z\psi_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z-\overline{U}_Z)^2}{U_Z}\\
&- \frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A\overline{U}_Z\left(2-\frac{\overline{U}_Z}{U_Z}-\frac{U_Z}{\overline{U}_Z}\right)-\frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_4}\Pi_4(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}\right)d\tau\\
&- \frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}\right)d\tau-\frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_6}\Pi_6(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^L\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}\right)d\tau\\
&- \frac{\beta_Z}{F_8}\overline{XV}_Z\int_0^{S_8}\Pi_8(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)d\tau+\beta_Z\overline{XV}_Z\ln\left(\frac{\overline{X}}{X}\right)\\
&= -\frac{d(X-\overline{X})^2}{X}+\frac{(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{\psi_D\sigma_D}\left(R_D^{L,inv}-1\right)Y_D^A\\
&- \frac{\delta_D\psi_D(\eta_D+b_D)}{\rho_D\sigma_D}\frac{(U_D-\overline{U}_D)^2}{U_D}-\frac{\delta_Z\psi_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z-\overline{U}_Z)^2}{U_Z}\\
&+ \frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\overline{Y}_Z^A\frac{(U_Z-\overline{U}_Z)^2}{U_Z}-\beta_Z\overline{XV}_Z\mathcal{L}\left(\frac{\overline{X}}{X}\right)-\frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\\
&\times\int_0^{S_4}\Pi_4(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}\right)d\tau-\frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}\right)d\tau\\
&- \frac{\eta_Z F_4(1-\theta_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_6}\Pi_6(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^L\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}\right)d\tau-\frac{\beta_Z}{F_8}\overline{XV}_Z\int_0^{S_8}\Pi_8(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)d\tau.
\end{aligned}
$$

From Equilibrium conditions of $\overline{EQ}$, we have $\overline{Y}_Z^A - \frac{\psi_Z}{\rho_Z} = -\frac{\varphi_Z}{\rho_Z \overline{U}_Z}$. It follows that

$$\begin{aligned}
\frac{d\Theta_2^L}{dt} &= -\frac{d(X-\overline{X})^2}{X} + \frac{(\eta_D + b_D)(a_D\psi_D + \delta_D\varphi_D)}{\psi_D\sigma_D}\left(R_D^{L,inv} - 1\right)Y_D^A \\
&- \frac{\delta_D\psi_D(\eta_D + b_D)}{\rho_D\sigma_D}\frac{(U_D - \overline{U}_D)^2}{U_D} - \frac{\delta_Z\varphi_Z(\eta_Z + b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z - \overline{U}_Z)^2}{\overline{U}_Z U_Z} \\
&- \beta_Z\overline{XV}_Z\mathcal{L}\left(\frac{\overline{X}}{X}\right) - \frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_4}\Pi_4(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^L}{\overline{XV}_Z Y_Z^L}\right)d\tau \\
&- \frac{\theta_Z(\eta_Z + b_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_5}\Pi_5(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\overline{Y}_Z^A}{\overline{XV}_Z Y_Z^A}\right)d\tau \\
&- \frac{\eta_Z F_4(1-\theta_Z)}{\sigma_Z}\beta_Z\overline{XV}_Z\int_0^{S_6}\Pi_6(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^L\overline{Y}_Z^A}{\overline{Y}_Z^L Y_Z^A}\right)d\tau \\
&- \frac{\beta_Z}{F_8}\overline{XV}_Z\int_0^{S_8}\Pi_8(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^A\overline{V}_Z}{\overline{Y}_Z^A V_Z}\right)d\tau.
\end{aligned}$$

Consequently, if $R_D^{L,inv} \leq 1$, we get $\frac{d\Theta_2^L}{dt} \leq 0$, for all $\left(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z\right) > 0$. Moreover, $\frac{d\Theta_2^L}{dt} = 0$ when $X = \overline{X}$, $Y_Z^L = \overline{Y}_Z^L$, $Y_Z^A = \overline{Y}_Z^A$, $V_Z = \overline{V}_Z$, $U_D = \overline{U}_D$, $U_Z = \overline{U}_Z$ and $\left(R_D^{L,inv} - 1\right)Y_D^A = 0$. The solutions of system in Eqs (2.1)–(2.9) converge to Υ_2', which contains elements with $X = \overline{X}$, $Y_Z^L = \overline{Y}_Z^L$, $Y_Z^A = \overline{Y}_Z^A$, $V_Z = \overline{V}_Z$, $U_D = \overline{U}_D$, $U_Z = \overline{U}_Z$ and,

$$\left(R_D^{L,inv} - 1\right)Y_D^A = 0. \tag{5.13}$$

We have two cases: (i) $R_D^{L,inv} < 1$, then Eq (5.13) implies that $Y_D^A = 0$, and from Eq (2.1), we get

$$0 = \frac{dX}{dt} = \lambda - d\overline{X} - \beta_D\overline{X}V_D - \beta_Z\overline{XV}_Z \Longrightarrow V_D(t) = 0 \text{ for any } t. \tag{5.14}$$

From Eq (2.3), we have

$$0 = \frac{dY_D^A}{dt} = \eta_D\int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau \Rightarrow Y_D^L(t) = 0 \text{ for any } t. \tag{5.15}$$

Hence, $\Upsilon_2' = \{\overline{EQ}\}$.
(ii) $R_D^{L,inv} = 1$, then from Eq (5.14), we have $V_D = 0$, and from Eq (2.6), we have

$$0 = \frac{dV_D}{dt} = k_D\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau \Rightarrow Y_D^A(t) = 0 \text{ for any } t.$$

From Eq (5.15), we have $Y_D^L = 0$. Hence, $\Upsilon_2' = \{\overline{EQ}\}$. Applying the L-LAS theorem implies that $\overline{EQ}$ is G.A.S.

To determine whether $\overline{EQ}$ is unstable when $R_D^{L,inv} > 1$, we compute the characteristic equation at $\overline{EQ}$ as:

$$\begin{aligned}\det(J(\overline{EQ}) - \xi I) = (\psi_D + \xi)W(\xi)[(\delta_Z \overline{U}_Z(c_Z + \xi)(d + \beta_Z \overline{V}_Z + \xi) \\ \times (b_Z + \eta_Z + \xi)(\psi_Z + \xi) + (\psi_Z - \rho_Z \overline{Y}_Z^A + \xi)((c_Z + \xi)(a_Z + \xi) \\ \times (d + \beta_Z \overline{V}_Z + \xi)(b_Z + \eta_Z + \xi) - k_Z \beta_Z \overline{X}(d + \xi) + \bar{\sigma}_Z + \bar{F}_5 \theta_Z \xi)] = 0,\end{aligned} \tag{5.16}$$

where $W(\xi)$ is defined for interval $[0, \infty)$ as:

$$W(\xi) = \xi^3 + \hat{\omega}_2^L \xi^2 + \hat{\omega}_1^L \xi + \hat{\omega}_0^L,$$

and

$$\begin{aligned}\hat{\omega}_2^L &= a_D + b_D + c_D + \eta_D + \delta_D \overline{U}_D, \\ \hat{\omega}_1^L &= a_D(b_D + c_D + \eta_D) + c_D(b_D + \eta_D) + (b_D + c_D + \eta_D)\delta_D \overline{U}_D - \theta_D \beta_D k_D \bar{F}_2 \bar{F}_7 \overline{X}, \\ \hat{\omega}_0^L &= c_D(\eta_D + b_D)(a_D + \delta_D \overline{U}_D) - \beta_D k_D \bar{F}_7 \overline{X}((\eta_D + b_D)\theta_D \bar{F}_2 + \eta_D(1 - \theta_D)\bar{F}_1 \bar{F}_3) \\ &= c_D(\eta_D + b_D)(a_D + \frac{\delta_D \varphi_D}{\psi_D}) - \beta_D k_D \bar{F}_7 \bar{\sigma}_D \overline{X},\end{aligned}$$

if $R_D^{L,inv} > 1$, then $W(0) < 0$, since $W(0) = -\frac{c_D(\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D)}{\psi_D}\left(R_D^{L,inv} - 1\right)$ and $\lim_{\xi \to \infty} W(\xi) = \infty$, so, Eq (5.16) has a positive root and hence $\overline{EQ}$ is unstable.

Theorem 4. A ZIKV-DENV co-infection equilibrium $\widetilde{EQ} = (\widetilde{X}, \widetilde{Y}_D^L, \widetilde{Y}_D^A, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{V}_D, \widetilde{V}_Z, \widetilde{U}_D, \widetilde{U}_Z)$ is G.A.S, if $R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$.

Proof. Define $\Theta_3^L(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z)$ as:

$$\begin{aligned}\Theta_3^L &= \widetilde{X}\mathcal{L}\left(\frac{X}{\widetilde{X}}\right) + \frac{\eta_D F_3}{\sigma_D}\widetilde{Y}_D^L \mathcal{L}\left(\frac{Y_D^L}{\widetilde{Y}_D^L}\right) + \frac{\eta_D + b_D}{\sigma_D}\widetilde{Y}_D^A \mathcal{L}\left(\frac{Y_D^A}{\widetilde{Y}_D^A}\right) + \frac{\eta_Z F_6}{\sigma_Z}\widetilde{Y}_Z^L \mathcal{L}\left(\frac{Y_Z^L}{\widetilde{Y}_Z^L}\right) + \frac{\eta_Z + b_Z}{\sigma_Z}\widetilde{Y}_Z^A \mathcal{L}\left(\frac{Y_Z^A}{\widetilde{Y}_Z^A}\right) \\ &+ \frac{\beta_D}{c_D}\widetilde{X}\widetilde{V}_D \mathcal{L}\left(\frac{V_D}{\widetilde{V}_D}\right) + \frac{\beta_Z}{c_Z}\widetilde{X}\widetilde{V}_Z \mathcal{L}\left(\frac{V_Z}{\widetilde{V}_Z}\right) + \frac{\delta_D(\eta_D + b_D)}{\rho_D \sigma_D}\widetilde{U}_D \mathcal{L}\left(\frac{U_D}{\widetilde{U}_D}\right) + \frac{\delta_Z(\eta_Z + b_Z)}{\rho_Z \sigma_Z}\widetilde{U}_Z \mathcal{L}\left(\frac{U_Z}{\widetilde{U}_Z}\right) \\ &+ \frac{\eta_D F_3 \beta_D(1 - \theta_D)}{\sigma_D}\widetilde{X}\widetilde{V}_D \times \int_0^{S_1} \Pi_1(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{X(\phi)V_D(\phi)}{\widetilde{X}\widetilde{V}_D}\right) d\phi d\tau \\ &+ \frac{\beta_D \theta_D(\eta_D + b_D)}{\sigma_D}\widetilde{X}\widetilde{V}_D \int_0^{S_2} \Pi_2(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{X(\phi)V_D(\phi)}{\widetilde{X}\widetilde{V}_D}\right) d\phi d\tau \\ &+ \frac{\eta_D(\eta_D + b_D)}{\sigma_D}\widetilde{Y}_D^L \int_0^{S_3} \Pi_3(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{Y_D^L(\phi)}{\widetilde{Y}_D^L}\right) d\phi d\tau + \frac{\eta_Z F_6 \beta_Z(1 - \theta_Z)}{\sigma_Z}\widetilde{X}\widetilde{V}_Z \\ &\times \int_0^{S_4} \Pi_4(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{X(\phi)V_Z(\phi)}{\widetilde{X}\widetilde{V}_Z}\right) d\phi d\tau + \frac{\beta_Z \theta_Z(\eta_Z + b_Z)}{\sigma_Z}\widetilde{X}\widetilde{V}_Z \int_0^{S_5} \Pi_5(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{X(\phi)V_Z(\phi)}{\widetilde{X}\widetilde{V}_Z}\right) d\phi d\tau \\ &+ \frac{\eta_Z(\eta_Z + b_Z)}{\sigma_Z}\widetilde{Y}_Z^L \int_0^{S_6} \Pi_6(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{Y_Z^L(\phi)}{\widetilde{Y}_Z^L}\right) d\phi d\tau + \frac{\beta_D k_D \widetilde{X}}{c_D}\widetilde{Y}_D^A \int_0^{S_7} \Pi_7(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{Y_D^A(\phi)}{\widetilde{Y}_D^A}\right) d\phi d\tau \\ &+ \frac{\beta_Z k_Z \widetilde{X}}{c_Z}\widetilde{Y}_Z^A \int_0^{S_8} \Pi_8(\tau) \int_{t-\tau}^t \mathcal{L}\left(\frac{Y_Z^A(\phi)}{\widetilde{Y}_Z^A}\right) d\phi d\tau.\end{aligned}$$

We observe that $\Theta_3^L(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z) > 0$ for all $(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z) > 0$ and $\Theta_3^L(\widetilde{X}, \widetilde{Y}_D^L, \widetilde{Y}_D^A, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{V}_D, \widetilde{V}_Z, \widetilde{U}_D, \widetilde{U}_Z) = 0$. Calculating $\frac{d\Theta_3^L}{dt}$ along the solutions of system in Eqs (2.1)–(2.9) as:

$$
\begin{aligned}
\frac{d\Theta_3^L}{dt} &= \left(1-\frac{\widetilde{X}}{X}\right)(\lambda - dX - \beta_D X V_D - \beta_Z X V_Z) \\
&+ \frac{\eta_D F_3}{\sigma_D}\left(1-\frac{\widetilde{Y}_D^L}{Y_D^L}\right)\left((1-\theta_D)\beta_D\int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau - (\eta_D+b_D)Y_D^L\right) \\
&+ \frac{\eta_D+b_D}{\sigma_D}\left(1-\frac{\widetilde{Y}_D^A}{Y_D^A}\right)\left(\theta_D\beta_D\int_0^{S_2}\Pi_2(\tau)X_\tau V_{D\tau}d\tau + \eta_D\int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau - a_D Y_D^A - \delta_D Y_D^A U_D\right) \\
&+ \frac{\eta_Z F_6}{\sigma_Z}\left(1-\frac{\widetilde{Y}_Z^L}{Y_Z^L}\right)\left((1-\theta_Z)\beta_Z\int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau - (\eta_Z+b_Z)Y_Z^L\right) \\
&+ \frac{\eta_Z+b_Z}{\sigma_Z}\left(1-\frac{\widetilde{Y}_Z^A}{Y_Z^A}\right)\left(\theta_Z\beta_Z\int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau + \eta_Z\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z\right) \\
&+ \frac{\beta_D\widetilde{X}}{c_D}\left(1-\frac{\widetilde{V}_D}{V_D}\right)\left(k_D\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau - c_D V_D\right) + \frac{\beta_Z\widetilde{X}}{c_Z}\left(1-\frac{\widetilde{V}_Z}{V_Z}\right)\left(k_Z\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau - c_Z V_Z\right) \\
&+ \frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\widetilde{U}_D}{U_D}\right)(\varphi_D + \rho_D Y_D^A U_D - \psi_D U_D) + \frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\widetilde{U}_Z}{U_Z}\right)(\varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z) \\
&+ \frac{\eta_D F_3\beta_D(1-\theta_D)}{\sigma_D}\widetilde{X}\widetilde{V}_D\int_0^{S_1}\Pi_1(\tau)\left[\frac{XV_D}{\widetilde{X}\widetilde{V}_D} - \frac{X_\tau V_{D\tau}}{\widetilde{X}\widetilde{V}_D} + \ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right)\right]d\tau \\
&+ \frac{\beta_D\theta_D(\eta_D+b_D)}{\sigma_D}\widetilde{X}\widetilde{V}_D\int_0^{S_2}\Pi_2(\tau)\left[\frac{XV_D}{\widetilde{X}\widetilde{V}_D} - \frac{X_\tau V_{D\tau}}{\widetilde{X}\widetilde{V}_D} + \ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right)\right]d\tau \\
&+ \frac{\eta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}_D^L\int_0^{S_3}\Pi_3(\tau)\left[\frac{Y_D^L}{\widetilde{Y}_D^L} - \frac{Y_{D\tau}^L}{\widetilde{Y}_D^L} + \ln\left(\frac{Y_{D\tau}^L}{Y_D^L}\right)\right]d\tau \\
&+ \frac{\eta_Z F_6\beta_Z(1-\theta_Z)}{\sigma_Z}\widetilde{X}\widetilde{V}_Z\int_0^{S_4}\Pi_4(\tau)\left[\frac{XV_Z}{\widetilde{X}\widetilde{V}_Z} - \frac{X_\tau V_{Z\tau}}{\widetilde{X}\widetilde{V}_Z} + \ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)\right]d\tau \\
&+ \frac{\beta_Z\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{X}\widetilde{V}_Z\int_0^{S_5}\Pi_5(\tau)\left[\frac{XV_Z}{\widetilde{X}\widetilde{V}_Z} - \frac{X_\tau V_{Z\tau}}{\widetilde{X}\widetilde{V}_Z} + \ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)\right]d\tau \\
&+ \frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}_Z^L\int_0^{S_6}\Pi_6(\tau)\left[\frac{Y_Z^L}{\widetilde{Y}_Z^L} - \frac{Y_{Z\tau}^L}{\widetilde{Y}_Z^L} + \ln\left(\frac{Y_{Z\tau}^L}{Y_Z^L}\right)\right]d\tau \\
&+ \frac{\beta_D k_D\widetilde{X}}{c_D}\widetilde{Y}_D^A\int_0^{S_7}\Pi_7(\tau)\left[\frac{Y_D^A}{\widetilde{Y}_D^A} - \frac{Y_{D\tau}^A}{\widetilde{Y}_D^A} + \ln\left(\frac{Y_{D\tau}^A}{Y_D^A}\right)\right]d\tau \\
&+ \frac{\beta_Z k_Z\widetilde{X}}{c_Z}\widetilde{Y}_Z^A\int_0^{S_8}\Pi_8(\tau)\left[\frac{Y_Z^A}{\widetilde{Y}_Z^A} - \frac{Y_{Z\tau}^A}{\widetilde{Y}_Z^A} + \ln\left(\frac{Y_{Z\tau}^A}{Y_Z^A}\right)\right]d\tau.
\end{aligned}
$$

It follows that

$$
\frac{d\Theta_3^L}{dt} = \left(1-\frac{\widetilde{X}}{X}\right)(\lambda - dX) + \left(\frac{\beta_D k_D F_7\widetilde{X}}{c_D} - \frac{a_D(\eta_D+b_D)}{\sigma_D} - \frac{\delta_D(\eta_D+b_D)}{\sigma_D}\widetilde{U}_D\right)Y_D^A
$$

$$
\begin{aligned}
&+\left(\frac{\beta_Z k_Z F_8 \widetilde{X}}{c_Z}-\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}-\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{U}_Z\right)Y_Z^A\\
&-\frac{\eta_D(1-\theta_D)\beta_D F_3}{\sigma_D}\frac{\widetilde{Y}_D^L}{Y_D^L}\int_0^{S_1}\Pi_1(\tau)X_\tau V_{D\tau}d\tau-\frac{\eta_Z(1-\theta_Z)\beta_Z F_6}{\sigma_Z}\frac{\widetilde{Y}_Z^L}{Y_Z^L}\int_0^{S_4}\Pi_4(\tau)X_\tau V_{Z\tau}d\tau\\
&+\frac{\eta_D F_3(\eta_D+b_D)}{\sigma_D}\widetilde{Y}_D^L+\frac{\eta_Z F_6(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}_Z^L-\frac{(\eta_D+b_D)\theta_D\beta_D}{\sigma_D}\frac{\widetilde{Y}_D^A}{Y_D^A}\int_0^{S_2}\Pi_2(\tau)X_\tau V_{D\tau}d\tau\\
&-\frac{(\eta_Z+b_Z)\theta_Z\beta_Z}{\sigma_Z}\frac{\widetilde{Y}_Z^A}{Y_Z^A}\int_0^{S_5}\Pi_5(\tau)X_\tau V_{Z\tau}d\tau+\frac{a_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}_D^A+\frac{a_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}_Z^A\\
&-\frac{\eta_D(\eta_D+b_D)}{\sigma_D}\frac{\widetilde{Y}_D^A}{Y_D^A}\int_0^{S_3}\Pi_3(\tau)Y_{D\tau}^L d\tau-\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\frac{\widetilde{Y}_Z^A}{Y_Z^A}\int_0^{S_6}\Pi_6(\tau)Y_{Z\tau}^L d\tau\\
&-\frac{\beta_D k_D\widetilde{X}}{c_D}\frac{\widetilde{V}_D}{V_D}\int_0^{S_7}\Pi_7(\tau)Y_{D\tau}^A d\tau-\frac{\beta_Z k_Z\widetilde{X}}{c_Z}\frac{\widetilde{V}_Z}{V_Z}\int_0^{S_8}\Pi_8(\tau)Y_{Z\tau}^A d\tau+\beta_D\widetilde{X}\widetilde{V}_D\\
&+\beta_Z\widetilde{X}\widetilde{V}_Z+\frac{\delta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}_D^A U_D+\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}_Z^A U_Z\\
&+\frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\widetilde{U}_D}{U_D}\right)(\varphi_D-\psi_D U_D)+\frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\widetilde{U}_Z}{U_Z}\right)(\varphi_Z-\psi_Z U_Z)\\
&+\frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_1}\Pi_1(\tau)\ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right)d\tau\\
&+\frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_4}\Pi_4(\tau)\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)d\tau\\
&+\frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_2}\Pi_2(\tau)\ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right)d\tau\\
&+\frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_5}\Pi_5(\tau)\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right)d\tau\\
&+\frac{\eta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}_D^L\int_0^{S_3}\Pi_3(\tau)\ln\left(\frac{Y_{D\tau}^L}{Y_D^L}\right)d\tau+\frac{\eta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}_Z^L\int_0^{S_6}\Pi_6(\tau)\ln\left(\frac{Y_{Z\tau}^L}{Y_Z^L}\right)d\tau\\
&+\frac{\beta_D k_D\widetilde{X}}{c_D}\widetilde{Y}_D^A\int_0^{S_7}\Pi_7(\tau)\ln\left(\frac{Y_{D\tau}^A}{Y_D^A}\right)d\tau+\frac{\beta_Z k_Z\widetilde{X}}{c_Z}\widetilde{Y}_Z^A\int_0^{S_8}\Pi_8(\tau)\ln\left(\frac{Y_{Z\tau}^A}{Y_Z^A}\right)d\tau.
\end{aligned}
$$

Equilibrium $\widetilde{EQ}$ satisfies

$$
\begin{aligned}
\lambda &= d\widetilde{X}+\beta_D\widetilde{X}\widetilde{V}_D+\beta_Z\widetilde{X}\widetilde{V}_Z,\\
(1-\theta_D)\beta_D F_1\widetilde{X}\widetilde{V}_D &= (\eta_D+b_D)\widetilde{Y}_D^L,\\
a_D\widetilde{Y}_D^A &= \theta_D\beta_D F_2\widetilde{X}\widetilde{V}_D+\eta_D F_3\widetilde{Y}_D^L-\delta_D\widetilde{Y}_D^A\widetilde{U}_D,\\
(1-\theta_Z)\beta_Z F_4\widetilde{X}\widetilde{V}_Z &= (b_Z+\eta_Z)\widetilde{Y}_Z^L,\\
a_Z\widetilde{Y}_Z^A &= \theta_Z\beta_Z F_5\widetilde{X}\widetilde{V}_Z+\eta_Z F_6\widetilde{Y}_Z^L-\delta_Z\widetilde{Y}_Z^A\widetilde{U}_Z,\\
k_D F_7\widetilde{Y}_D^A &= c_D\widetilde{V}_D,\\
k_Z F_8\widetilde{Y}_Z^A &= c_Z\widetilde{V}_Z,
\end{aligned}
$$

$$\varphi_D = \psi_D \widetilde{U}_D - \rho_D \widetilde{Y}_D^A \widetilde{U}_D,$$
$$\varphi_Z = \psi_Z \widetilde{U}_Z - \rho_Z \widetilde{Y}_Z^A \widetilde{U}_Z,$$

and using the following equalities

$$\ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right) = \ln\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^L}{\widetilde{X}\widetilde{V}_D Y_D^L}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y_D^L \widetilde{V}_D}{\widetilde{Y}_D^L V_D}\right),$$
$$\ln\left(\frac{X_\tau V_{D\tau}}{XV_D}\right) = \ln\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^A}{\widetilde{X}\widetilde{V}_D Y_D^A}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y_D^A \widetilde{V}_D}{\widetilde{Y}_D^A V_D}\right),$$
$$\ln\left(\frac{Y_{D\tau}^L}{Y_D^L}\right) = \ln\left(\frac{Y_{D\tau}^L \widetilde{Y}_D^A}{\widetilde{Y}_D^L Y_D^A}\right) + \ln\left(\frac{\widetilde{Y}_D^L Y_D^A}{Y_D^L \widetilde{Y}_D^A}\right),$$
$$\ln\left(\frac{Y_{D\tau}^A}{Y_D^A}\right) = \ln\left(\frac{Y_{D\tau}^A \widetilde{V}_D}{\widetilde{Y}_D^A V_D}\right) + \ln\left(\frac{\widetilde{Y}_D^A V_D}{Y_D^A \widetilde{V}_D}\right),$$
$$\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right) = \ln\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y_Z^L \widetilde{V}_Z}{\widetilde{Y}_Z^L V_Z}\right),$$
$$\ln\left(\frac{X_\tau V_{Z\tau}}{XV_Z}\right) = \ln\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y_Z^A \widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right),$$
$$\ln\left(\frac{Y_{Z\tau}^L}{Y_Z^L}\right) = \ln\left(\frac{Y_{Z\tau}^L \widetilde{Y}_Z^A}{\widetilde{Y}_Z^L Y_Z^A}\right) + \ln\left(\frac{\widetilde{Y}_Z^L Y_Z^A}{Y_Z^L \widetilde{Y}_Z^A}\right),$$
$$\ln\left(\frac{Y_{Z\tau}^A}{Y_Z^A}\right) = \ln\left(\frac{Y_{Z\tau}^A \widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right) + \ln\left(\frac{\widetilde{Y}_Z^A V_Z}{Y_Z^A \widetilde{V}_Z}\right).$$

We obtain

$$\left(\frac{\beta_D k_D F_7}{c_D}\widetilde{X}\widetilde{Y}_D^A - \frac{a_D(\eta_D + b_D)}{\sigma_D}\widetilde{Y}_D^A - \frac{\delta_D(\eta_D + b_D)}{\sigma_D}\widetilde{U}_D\widetilde{Y}_D^A\right)\frac{Y_D^A}{\widetilde{Y}_D^A} = 0,$$
$$\left(\frac{\beta_Z k_Z F_8}{c_Z}\widetilde{X}\widetilde{Y}_Z^A - \frac{a_Z(\eta_Z + b_Z)}{\sigma_Z}\widetilde{Y}_Z^A - \frac{\delta_Z(\eta_Z + b_Z)}{\sigma_Z}\widetilde{U}_Z\widetilde{Y}_Z^A\right)\frac{Y_Z^A}{\widetilde{Y}_Z^A} = 0.$$

So,

$$\begin{aligned}\frac{d\Theta_3^L}{dt} &= \left(1 - \frac{\widetilde{X}}{X}\right)(d\widetilde{X} + \beta_D\widetilde{X}\widetilde{V}_D + \beta_Z\widetilde{X}\widetilde{V}_Z - dX) - \frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_1}\Pi_1(\tau)\frac{X_\tau V_{D\tau}\widetilde{Y}_D^L}{\widetilde{X}\widetilde{V}_D Y_D}d\tau\\
&- \frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_4}\Pi_4(\tau)\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L}d\tau + 2\frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\\
&+ \frac{\theta_D(\eta_D + b_D)F_2}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D + 2\frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z + \frac{\theta_Z(\eta_Z + b_Z)F_5}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\\
&- \frac{\theta_D(\eta_D + b_D)}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_2}\Pi_2(\tau)\frac{X_\tau V_{D\tau}\widetilde{Y}_D^A}{\widetilde{X}\widetilde{V}_D Y_D^A}d\tau - \frac{\theta_Z(\eta_Z + b_Z)}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_5}\Pi_5(\tau)\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A}d\tau\end{aligned}$$

$$
\begin{aligned}
&- \frac{\eta_D(1-\theta_D)F_1}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_3}\Pi_3(\tau)\frac{Y^L_{D\tau}\widetilde{Y}^A_D}{\widetilde{Y}^L_D Y^A_D}d\tau - \frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_6}\Pi_6(\tau)\frac{Y^L_{Z\tau}\widetilde{Y}^A_Z}{\widetilde{Y}^L_Z Y^A_Z}d\tau\\
&- \frac{\beta_D}{F_7}\widetilde{X}\widetilde{V}_D\int_0^{S_7}\Pi_7(\tau)\frac{Y^A_{D\tau}\widetilde{V}_D}{\widetilde{Y}^A_D V_D}d\tau - \frac{\beta_Z}{F_8}\widetilde{X}\widetilde{V}_Z\int_0^{S_8}\Pi_8(\tau)\frac{Y^A_{Z\tau}\widetilde{V}_Z}{\widetilde{Y}^A_Z V_Z}d\tau + \beta_D\widetilde{X}\widetilde{V}_D + \beta_Z\widetilde{X}\widetilde{V}_Z\\
&+ \frac{\delta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}^A_D U_D + \frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}^A_Z U_Z - \frac{\delta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}^A_D\widetilde{U}_D\\
&- \frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}^A_Z\widetilde{U}_Z + \frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\widetilde{U}_D}{U_D}\right)(\psi_D\widetilde{U}_D - \rho_D\widetilde{Y}^A_D\widetilde{U}_D - \psi_D U_D)\\
&+ \frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\widetilde{U}_Z}{U_Z}\right)(\psi_Z\widetilde{U}_Z - \rho_Z\widetilde{Y}^A_D\widetilde{U}_Z - \psi_Z U_Z) + \frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\\
&\times\int_0^{S_1}\Pi_1(\tau)\left[\ln\left(\frac{X_\tau V_{D\tau}\widetilde{Y}^L_D}{\widetilde{X}\widetilde{V}_D Y^L_D}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y^L_D\widetilde{V}_D}{\widetilde{Y}^L_D V_D}\right)\right]d\tau\\
&+ \frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_4}\Pi_4(\tau)\left[\ln\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}^L_Z}{\widetilde{X}\widetilde{V}_Z Y^L_Z}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y^L_Z\widetilde{V}_Z}{\widetilde{Y}^L_Z V_Z}\right)\right]d\tau\\
&+ \frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_2}\Pi_2(\tau)\left[\ln\left(\frac{X_\tau V_{D\tau}\widetilde{Y}^A_D}{\widetilde{X}\widetilde{V}_D Y^A_D}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y^A_D\widetilde{V}_D}{\widetilde{Y}^A_D V_D}\right)\right]d\tau\\
&+ \frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_5}\Pi_5(\tau)\left[\ln\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}^A_Z}{\widetilde{X}\widetilde{V}_Z Y^A_Z}\right) + \ln\left(\frac{\widetilde{X}}{X}\right) + \ln\left(\frac{Y^A_Z\widetilde{V}_Z}{\widetilde{Y}^A_Z V_Z}\right)\right]d\tau\\
&+ \frac{\eta_D(1-\theta_D)F_1}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_3}\Pi_3(\tau)\left[\ln\left(\frac{Y^L_{D\tau}\widetilde{Y}^A_D}{\widetilde{Y}^L_D Y^A_D}\right) + \ln\left(\frac{\widetilde{Y}^L_D Y^A_D}{Y^L_D\widetilde{Y}^A_D}\right)\right]d\tau\\
&+ \frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_6}\Pi_6(\tau)\left[\ln\left(\frac{Y^L_{Z\tau}\widetilde{Y}^A_Z}{\widetilde{Y}^L_Z Y^A_Z}\right) + \ln\left(\frac{\widetilde{Y}^L_Z Y^A_Z}{Y^L_Z\widetilde{Y}^A_Z}\right)\right]d\tau\\
&+ \frac{\beta_D}{F_7}\widetilde{X}\widetilde{V}_D\int_0^{S_7}\Pi_7(\tau)\left[\ln\left(\frac{Y^A_{D\tau}\widetilde{V}_D}{\widetilde{Y}^A_D V_D}\right) + \ln\left(\frac{\widetilde{Y}^A_D V_D}{Y^A_D\widetilde{V}_D}\right)\right]d\tau\\
&+ \frac{\beta_Z}{F_8}\widetilde{X}\widetilde{V}_Z\int_0^{S_8}\Pi_8(\tau)\left[\ln\left(\frac{Y^A_{Z\tau}\widetilde{V}_Z}{\widetilde{Y}^A_Z V_Z}\right) + \ln\left(\frac{\widetilde{Y}^A_Z V_Z}{Y^A_Z\widetilde{V}_Z}\right)\right]d\tau.
\end{aligned}
$$

It follows that

$$
\begin{aligned}
\frac{d\Theta^L_3}{dt} &= \left(1-\frac{\widetilde{X}}{X}\right)(d\widetilde{X}-dX) + \beta_D\widetilde{X}\widetilde{V}_D\left(1-\frac{\widetilde{X}}{X}\right) + \beta_Z\widetilde{X}\widetilde{V}_Z\left(1-\frac{\widetilde{X}}{X}\right) + \frac{\delta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}^A_D(U_D-\widetilde{U}_D)\\
&+ \frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}^A_Z(U_Z-\widetilde{U}_Z) + \frac{\delta_D(\eta_D+b_D)}{\rho_D\sigma_D}\left(1-\frac{\widetilde{U}_D}{U_D}\right)(\psi_D\widetilde{U}_D-\psi_D U_D)\\
&+ \frac{\delta_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\left(1-\frac{\widetilde{U}_Z}{U_Z}\right)(\psi_Z\widetilde{U}_Z-\psi_Z U_Z)\\
&- \frac{\delta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}^A_D\widetilde{U}_D\left(1-\frac{\widetilde{U}_D}{U_D}\right) - \frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}^A_Z\widetilde{U}_Z\left(1-\frac{\widetilde{U}_Z}{U_Z}\right)
\end{aligned}
$$

$$
\begin{aligned}
&- \frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_1}\Pi_1(\tau)\left[\frac{X_\tau V_{D\tau}\widetilde{Y}_D^L}{\widetilde{X}\widetilde{V}_D Y_D}-\ln\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^L}{\widetilde{X}\widetilde{V}_D Y_D^L}\right)\right]d\tau\\
&- \frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_D\int_0^{S_4}\Pi_4(\tau)\left[\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L}-\ln\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L}\right)\right]d\tau\\
&- \frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_2}\Pi_2(\tau)\left[\frac{X_\tau V_{D\tau}\widetilde{Y}_D^A}{\widetilde{X}\widetilde{V}_D Y_D^A}-\ln\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^A}{\widetilde{X}\widetilde{V}_D Y_D^A}\right)\right]d\tau\\
&- \frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_5}\Pi_5(\tau)\left[\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A}-\ln\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A}\right)\right]d\tau\\
&- \frac{\eta_D(1-\theta_D)F_1}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\int_0^{S_3}\Pi_3(\tau)\left[\frac{Y_{D\tau}^L\widetilde{Y}_D^A}{\widetilde{Y}_D^L Y_D^A}-\ln\left(\frac{Y_{D\tau}^L\widetilde{Y}_D^A}{\widetilde{Y}_D^L Y_D^A}\right)\right]d\tau\\
&- \frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\int_0^{S_6}\Pi_6(\tau)\left[\frac{Y_{Z\tau}^L\widetilde{Y}_Z^A}{\widetilde{Y}_Z^L Y_Z^A}-\ln\left(\frac{Y_{Z\tau}^L\widetilde{Y}_Z^A}{\widetilde{Y}_Z^L Y_Z^A}\right)\right]d\tau\\
&- \frac{\beta_D}{F_7}\widetilde{X}\widetilde{V}_D\int_0^{S_7}\Pi_7(\tau)\left[\frac{Y_{D\tau}^A\widetilde{V}_D}{\widetilde{Y}_D^A V_D}-1-\ln\left(\frac{Y_{D\tau}^A\widetilde{V}_D}{\widetilde{Y}_D^A V_D}\right)\right]d\tau\\
&- \frac{\beta_Z}{F_8}\widetilde{X}\widetilde{V}_Z\int_0^{S_8}\Pi_8(\tau)\left[\frac{Y_{Z\tau}^A\widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}-1-\ln\left(\frac{Y_{Z\tau}^A\widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right)\right]d\tau\\
&+ \frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\ln\left(\frac{\widetilde{X}}{X}\right)+\frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\ln\left(\frac{\widetilde{X}}{X}\right)\\
&+ \frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\ln\left(\frac{Y_D^L\widetilde{V}_D}{\widetilde{Y}_D^L V_D}\right)+\frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\ln\left(\frac{Y_Z^L\widetilde{V}_Z}{\widetilde{Y}_Z^L V_Z}\right)\\
&+ \frac{\theta_D(\eta_D+b_D)F_2}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\ln\left(\frac{\widetilde{X}}{X}\right)+\frac{\theta_Z(\eta_Z+b_Z)F_5}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\ln\left(\frac{\widetilde{X}}{X}\right)\\
&+ \frac{\theta_D(\eta_D+b_D)F_2}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\ln\left(\frac{Y_D^A\widetilde{V}_D}{\widetilde{Y}_D^A V_D}\right)+\frac{\theta_Z(\eta_Z+b_Z)F_5}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\ln\left(\frac{Y_Z^A\widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right)\\
&+ \frac{\eta_D(1-\theta_D)F_1F_3}{\sigma_D}\beta_D\widetilde{X}\widetilde{V}_D\ln\left(\frac{\widetilde{Y}_D^L Y_D^A}{Y_D^L\widetilde{Y}_D^A}\right)+\frac{\eta_Z(1-\theta_Z)F_4F_6}{\sigma_Z}\beta_Z\widetilde{X}\widetilde{V}_Z\ln\left(\frac{\widetilde{Y}_Z^L Y_Z^A}{Y_Z^L\widetilde{Y}_Z^A}\right)\\
&+ \beta_D\widetilde{X}\widetilde{V}_D\ln\left(\frac{\widetilde{Y}_D^A V_D}{Y_D^A\widetilde{V}_D}\right)+\beta_Z\widetilde{X}\widetilde{V}_Z\ln\left(\frac{\widetilde{Y}_Z^A V_Z}{Y_Z^A\widetilde{V}_Z}\right).
\end{aligned}
$$

Thus,

$$
\begin{aligned}
\frac{d\Theta_3^L}{dt} = &-\frac{d(X-\widetilde{X})^2}{X}-\frac{\delta_D\psi_D(\eta_D+b_D)}{\rho_D\sigma_D}\frac{(U_D-\widetilde{U}_D)^2}{U_D}-\frac{\delta_Z\psi_Z(\eta_Z+b_Z)}{\rho_Z\sigma_Z}\frac{(U_Z-\widetilde{U}_Z)^2}{U_Z}\\
&+\frac{\delta_D(\eta_D+b_D)}{\sigma_D}\widetilde{Y}_D^A\frac{(U_D-\widetilde{U}_D)^2}{U_D}+\frac{\delta_Z(\eta_Z+b_Z)}{\sigma_Z}\widetilde{Y}_Z^A\frac{(U_Z-\widetilde{U}_Z)^2}{U_Z}-\beta_D\widetilde{X}\widetilde{V}_D\mathcal{L}\left(\frac{\widetilde{X}}{X}\right)
\end{aligned}
$$

$$
\begin{aligned}
&- \beta_Z \widetilde{X}\widetilde{V}_Z \mathcal{L}\left(\frac{\widetilde{X}}{X}\right) - \frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D \widetilde{X}\widetilde{V}_D \int_0^{S_1} \Pi_1(\tau)\mathcal{L}\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^L}{\widetilde{X}\widetilde{V}_D Y_D^L}\right)d\tau \\
&- \frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \int_0^{S_4} \Pi_4(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L}\right)d\tau - \frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D \widetilde{X}\widetilde{V}_D \\
&\times \int_0^{S_2} \Pi_2(\tau)\mathcal{L}\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^A}{\widetilde{X}\widetilde{V}_D Y_D^A}\right)d\tau - \frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \int_0^{S_5} \Pi_5(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A}\right)d\tau \\
&- \frac{\eta_D(1-\theta_D)F_1}{\sigma_D}\beta_D \widetilde{X}\widetilde{V}_D \int_0^{S_3} \Pi_3(\tau)\mathcal{L}\left(\frac{Y_{D\tau}^L \widetilde{Y}_D^A}{\widetilde{Y}_D^L Y_D^A}\right)d\tau - \frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \\
&\times \int_0^{S_6} \Pi_6(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^L \widetilde{Y}_Z^A}{\widetilde{Y}_Z^L Y_Z^A}\right)d\tau - \frac{\beta_D}{F_7}\widetilde{X}\widetilde{V}_D \int_0^{S_7} \Pi_7(\tau)\mathcal{L}\left(\frac{Y_{D\tau}^A \widetilde{V}_D}{\widetilde{Y}_D^A V_D}\right)d\tau \\
&- \frac{\beta_Z}{F_8}\widetilde{X}\widetilde{V}_Z \int_0^{S_8} \Pi_8(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^A \widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right)d\tau.
\end{aligned}
$$

From the equilibrium conditions, we have $\widetilde{Y}_D^A - \frac{\psi_D}{\rho_D} = -\frac{\varphi_D}{\rho_D \widetilde{U}_D}$ and $\widetilde{Y}_Z^A - \frac{\psi_Z}{\rho_Z} = -\frac{\varphi_Z}{\rho_Z \widetilde{U}_Z}$. It follows that

$$
\begin{aligned}
\frac{d\Theta_3^L}{dt} = &- \frac{d(X-\widetilde{X})^2}{X} - \frac{\delta_D \varphi_D(\eta_D+b_D)}{\rho_D \sigma_D}\frac{(U_D-\widetilde{U}_D)^2}{\widetilde{U}_D U_D} - \frac{\delta_Z \varphi_Z(\eta_Z+b_Z)}{\rho_Z \sigma_Z}\frac{(U_Z-\widetilde{U}_Z)^2}{\widetilde{U}_Z U_Z} \\
&- \beta_D \widetilde{X}\widetilde{V}_D \mathcal{L}\left(\frac{\widetilde{X}}{X}\right) - \beta_Z \widetilde{X}\widetilde{V}_Z \mathcal{L}\left(\frac{\widetilde{X}}{X}\right) - \frac{\eta_D(1-\theta_D)F_3}{\sigma_D}\beta_D \widetilde{X}\widetilde{V}_D \int_0^{S_1} \Pi_1(\tau)\mathcal{L}\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^L}{\widetilde{X}\widetilde{V}_D Y_D^L}\right)d\tau \\
&- \frac{\eta_Z(1-\theta_Z)F_6}{\sigma_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \int_0^{S_4} \Pi_4(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L}\right)d\tau - \frac{\theta_D(\eta_D+b_D)}{\sigma_D}\beta_D \widetilde{X}\widetilde{V}_D \\
&\times \int_0^{S_2} \Pi_2(\tau)\mathcal{L}\left(\frac{X_\tau V_{D\tau}\widetilde{Y}_D^A}{\widetilde{X}\widetilde{V}_D Y_D^A}\right)d\tau - \frac{\theta_Z(\eta_Z+b_Z)}{\sigma_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \int_0^{S_5} \Pi_5(\tau)\mathcal{L}\left(\frac{X_\tau V_{Z\tau}\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A}\right)d\tau \\
&- \frac{\eta_D(1-\theta_D)F_1}{\sigma_D}\beta_D \widetilde{X}\widetilde{V}_D \int_0^{S_3} \Pi_3(\tau)\mathcal{L}\left(\frac{Y_{D\tau}^L \widetilde{Y}_D^A}{\widetilde{Y}_D^L Y_D^A}\right)d\tau - \frac{\eta_Z(1-\theta_Z)F_4}{\sigma_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \\
&\times \int_0^{S_6} \Pi_6(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^L \widetilde{Y}_Z^A}{\widetilde{Y}_Z^L Y_Z^A}\right)d\tau - \frac{\beta_D}{F_7}\widetilde{X}\widetilde{V}_D \int_0^{S_7} \Pi_7(\tau)\mathcal{L}\left(\frac{Y_{D\tau}^A \widetilde{V}_D}{\widetilde{Y}_D^A V_D}\right)d\tau \\
&- \frac{\beta_Z}{F_8}\widetilde{X}\widetilde{V}_Z \int_0^{S_8} \Pi_8(\tau)\mathcal{L}\left(\frac{Y_{Z\tau}^A \widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right)d\tau.
\end{aligned}
$$

So $\frac{d\Theta_3^L}{dt} \leq 0$, for all $\left(X, Y_D^L, Y_D^A, Y_Z^L, Y_Z^A, V_D, V_Z, U_D, U_Z\right) > 0$. Moreover, $\frac{d\Theta_3^L}{dt} = 0$ when $X = \widetilde{X}$, $Y_D^L = \widetilde{Y}_D^L$, $Y_D^A = \widetilde{Y}_D^A$, $Y_Z^L = \widetilde{Y}_Z^L$, $Y_Z^A = \widetilde{Y}_Z^A$, $V_D = \widetilde{V}_D$, $V_Z = \widetilde{V}_Z$, $U_D = \widetilde{U}_D$, and $U_Z = \widetilde{U}_Z$ for all t. The solutions of system in Eqs (2.1)–(2.9) converge to $\Upsilon_3' = \{\widetilde{EQ}\}$, and the L-LAS theorem implies that $\widetilde{EQ}$ is G.A.S when $R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$.

Table 2 provides an overview of the existence and global stability conditions for each equilibria of model in Eqs (2.1)–(2.9).

Table 2. Conditions of existence and global stability of equilibria of the model in Eqs (2.1)–(2.9).

Equilibrium	Existence condition	Stability condition
$EQ^0 = (X^0, 0, 0, 0, 0, 0, 0, U_D^0, U_Z^0)$	-	$R_D^L \leq 1$ and $R_Z^L \leq 1$
$EQ^* = (X^*, Y_D^{L*}, Y_D^{A*}, 0, 0, V_D^*, 0, U_D^*, U_Z^*)$	$R_D^L > 1$	$R_D^L > 1$ and $R_Z^{L,inv} \leq 1$
$\overline{EQ} = (\overline{X}, 0, 0, \overline{Y}_Z^L, \overline{Y}_Z^A, 0, 0, \overline{V}_Z, \overline{U}_D, \overline{U}_Z)$	$R_Z^L > 1$	$R_Z^L > 1$ and $R_D^{L,inv} \leq 1$
$\widetilde{EQ} = (\widetilde{X}, \widetilde{Y}_D^L, \widetilde{Y}_D^A, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{V}_D, \widetilde{V}_Z, \widetilde{U}_D, \widetilde{U}_Z)$	$R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$	$R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$

6. Co-infection model with antiviral treatment for blocking viral infections

Inhibiting the ability of viruses to infect uninfected cells represents one of the most biologically intuitive antiviral mechanisms. This can be achieved through pharmacological agents that block viral entry into host cells, thereby reducing the effective infection rate. Within the framework of within-host mathematical modeling, as proposed in [19], this mechanism is incorporated by introducing treatment controls that reduce infection transmission parameters. Accordingly, the baseline infection rates β_D and β_Z are scaled by the control variables u_D and u_Z, respectively, reflecting treatment efficacy in preventing viral entry. As a result, the original system in Eqs (2.1)–(2.9) is modified as follows:

$$\frac{dX}{dt} = \lambda - dX - (1-u_D)\beta_D X V_D - (1-u_Z)\beta_Z X V_Z, \tag{6.1}$$

$$\frac{dY_D^L}{dt} = (1-\theta_D)(1-u_D)\beta_D \int_0^{S_1} \Pi_1(\tau) X_\tau V_{D\tau}\, d\tau - (\eta_D + b_D) Y_D^L, \tag{6.2}$$

$$\frac{dY_D^A}{dt} = \theta_D(1-u_D)\beta_D \int_0^{S_2} \Pi_2(\tau) X_\tau V_{D\tau}\, d\tau + \eta_D \int_0^{S_3} \Pi_3(\tau) Y_{D\tau}^L\, d\tau - a_D Y_D^A - \delta_D Y_D^A U_D, \tag{6.3}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)(1-u_Z)\beta_Z \int_0^{S_4} \Pi_4(\tau) X_\tau V_{Z\tau}\, d\tau - (\eta_Z + b_Z) Y_Z^L, \tag{6.4}$$

$$\frac{dY_Z^A}{dt} = \theta_Z(1-u_Z)\beta_Z \int_0^{S_5} \Pi_5(\tau) X_\tau V_{Z\tau}\, d\tau + \eta_Z \int_0^{S_6} \Pi_6(\tau) Y_{Z\tau}^L\, d\tau - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z, \tag{6.5}$$

$$\frac{dV_D}{dt} = k_D \int_0^{S_7} \Pi_7(\tau) Y_{D\tau}^A\, d\tau - c_D V_D, \tag{6.6}$$

$$\frac{dV_Z}{dt} = k_Z \int_0^{S_8} \Pi_8(\tau) Y_{Z\tau}^A\, d\tau - c_Z V_Z, \tag{6.7}$$

$$\frac{dU_D}{dt} = \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D, \tag{6.8}$$

$$\frac{dU_Z}{dt} = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z, \tag{6.9}$$

where u_D and $u_Z \in [0, 1]$ represent the antiviral efficacies against DENV and ZIKV, respectively. The influence of antiviral treatment on the viral dynamics is reflected through the basic reproduction

numbers of system in Eqs (6.1)–(6.9), which are given by:

$$R_D^L(u_D) = \frac{k_D(1-u_D)\beta_D\lambda\psi_D F_7\left[(\eta_D+b_D)\theta_D F_2+\eta_D(1-\theta_D)F_1F_3\right]}{dc_D(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)},$$
$$R_Z^L(u_Z) = \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z F_8\left[(\eta_Z+b_Z)\theta_Z F_5+\eta_Z(1-\theta_Z)F_4F_6\right]}{dc_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}.$$

For fixed parameter values, $R_D^L(u_D)$ and $R_Z^L(u_Z)$ are strictly decreasing functions of the treatment intensities u_D and u_Z, respectively. This monotonic behavior directly reflects the effectiveness of antiviral therapy in blocking the viral infection of uninfected target cells. As treatment intensity increases, the effective infection rates decrease, leading to a reduced generation of newly latently infected cells $\left(Y_D^L, Y_Z^L\right)$ and productively infected cells $\left(Y_D^A, Y_Z^A\right)$. Consequently, the viral concentrations (V_D, V_Z) decline. Hence, this treatment strategy acts as an effective preventive mechanism for limiting viral spread and mitigating the severity of DENV–ZIKV co-infection.

The minimum treatment efficacies required to ensure $R_D^L \leq 1$and $R_Z^L \leq 1$ are given by:

$$u_D^{cr} = \max\left\{1-\frac{c_D d(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{k_D\beta_D\lambda\psi_D F_7\left[(\eta_D+b_D)\theta_D F_2+\eta_D(1-\theta_D)F_1F_3\right]}, 0\right\},$$
$$u_Z^{cr} = \max\left\{1-\frac{c_Z d(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{k_Z\beta_Z\lambda\psi_Z F_8\left[(\eta_Z+b_Z)\theta_Z F_5+\eta_Z(1-\theta_Z)F_4F_6\right]}, 0\right\}.$$

Corolary 1. If $u_D^{cr} \leq u_D \leq 1$ and $u_Z^{cr} \leq u_Z \leq 1$, then the disease-free equilibrium EQ^0 is G.A.S.

6.1. Effect of time delays

To examine the influence of distributed time delays on viral dynamics, we first consider the limiting case in which all intracellular delays are neglected. In this case, the system in Eqs (6.1)–(6.9) reduces to the following delay-free system:

$$\frac{dX}{dt} = \lambda - dX - (1-u_D)\beta_D X V_D - (1-u_Z)\beta_Z X V_Z, \tag{6.10}$$
$$\frac{dY_D^L}{dt} = (1-\theta_D)(1-u_D)\beta_D X V_D - (\eta_D+b_D)Y_D^L, \tag{6.11}$$
$$\frac{dY_D^A}{dt} = \theta_D(1-u_D)\beta_D X V_D + \eta_D Y_D^L - a_D Y_D^A - \delta_D Y_D^A U_D, \tag{6.12}$$
$$\frac{dY_Z^L}{dt} = (1-\theta_Z)(1-u_Z)\beta_Z X V_Z - (\eta_Z+b_Z)Y_Z^L, \tag{6.13}$$
$$\frac{dY_Z^A}{dt} = \theta_Z(1-u_Z)\beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z, \tag{6.14}$$
$$\frac{dV_D}{dt} = k_D Y_D^A - c_D V_D, \tag{6.15}$$
$$\frac{dV_Z}{dt} = k_Z Y_Z^A - c_Z V_Z, \tag{6.16}$$

$$\frac{dU_D}{dt} = \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D, \tag{6.17}$$

$$\frac{dU_Z}{dt} = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z. \tag{6.18}$$

The corresponding basic reproduction numbers for DENV and ZIKV are given by:

$$R_D^{L,\text{ no delay}}(u_D) = \frac{k_D(1-u_D)\beta_D\lambda\psi_D(\eta_D+b_D\theta_D)}{dc_D(a_D\psi_D+\delta_D\varphi_D)(\eta_D+b_D)}, \quad R_Z^{L,\text{ no delay}}(u_Z) = \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z(\eta_Z+b_Z\theta_Z)}{dc_Z(a_Z\psi_Z+\delta_Z\varphi_Z)(\eta_Z+b_Z)}.$$

The minimum antiviral treatment efficacies required to ensure $R_D^{L,\text{ no delay}} \leq 1$ and $R_Z^{L,\text{ no delay}} \leq 1$ are given by:

$$u_D^{cr,\text{ no delay}} = \max\left\{1 - \frac{dc_D(a_D\psi_D+\delta_D\varphi_D)(\eta_D+b_D)}{k_D\beta_D\lambda\psi_D(\eta_D+b_D\theta_D)}, 0\right\},$$
$$u_Z^{cr,\text{ no delay}} = \max\left\{1 - \frac{dc_Z(a_Z\psi_Z+\delta_Z\varphi_Z)(\eta_Z+b_Z)}{k_Z\beta_Z\lambda\psi_Z(\eta_Z+b_Z\theta_Z)}, 0\right\}.$$

Since $0 < F_i \leq 1$, it follows that

$$\begin{aligned} R_D^{L,\text{ with delay}}(u_D) &= \frac{k_D(1-u_D)\beta_D\lambda\psi_D F_7\left[(\eta_D+b_D)\theta_D F_2 + \eta_D(1-\theta_D)F_1F_3\right]}{dc_D(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)} \\ &\leq \frac{k_D(1-u_D)\beta_D\lambda\psi_D(\eta_D+b_D\theta_D)}{dc_D(a_D\psi_D+\delta_D\varphi_D)(\eta_D+b_D)} = R_D^{L,\text{ no delay}}(u_D), \\ R_Z^{L,\text{ with delay}}(u_Z) &= \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z F_8\left[(\eta_Z+b_Z)\theta_Z F_5 + \eta_Z(1-\theta_Z)F_4F_6\right]}{dc_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)} \\ &\leq \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z(\eta_Z+b_Z\theta_Z)}{dc_Z(a_Z\psi_Z+\delta_Z\varphi_Z)(\eta_Z+b_Z)} = R_Z^{L,\text{ no delay}}(u_Z). \end{aligned}$$

Therefore, neglecting intracellular time delays leads to an overestimation of the viral reproduction potential. Biologically, this occurs because the delay-free formulation implicitly assumes that transitions between intracellular stages occur instantaneously. In reality, infected cells require time to establish infection, latent cells require activation before becoming productively infected, and newly produced virions may require maturation before becoming fully infectious. These delayed biological processes effectively slow viral propagation and reduce the number of secondary infected cells generated by a single infected cell.

Consequently, the treatment thresholds satisfy

$$u_D^{cr,\text{ no delay}} \geq u_D^{cr,\text{ with delay}}, \qquad u_Z^{cr,\text{ no delay}} \geq u_Z^{cr,\text{ with delay}}.$$

This indicates that neglecting intracellular delays may overestimate the antiviral efficacy required to suppress infection.

6.2. Effect of latently infected cells

We next investigate the effect of neglecting latently infected cells. In the absence of latent compartments, the system in Eqs (6.10)–(6.18) reduces to

$$\frac{dX}{dt} = \lambda - dX - (1-u_D)\beta_D X V_D - (1-u_Z)\beta_Z X V_Z,$$

$$\frac{dY_D^A}{dt} = (1-u_D)\beta_D X V_D - a_D Y_D^A - \delta_D Y_D^A U_D,$$
$$\frac{dY_Z^A}{dt} = (1-u_Z)\beta_Z X V_Z - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z,$$
$$\frac{dV_D}{dt} = k_D Y_D^A - c_D V_D,$$
$$\frac{dV_Z}{dt} = k_Z Y_Z^A - c_Z V_Z,$$
$$\frac{dU_D}{dt} = \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D,$$
$$\frac{dU_Z}{dt} = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z.$$

The corresponding basic reproduction numbers become

$$R_D^{\text{without latent}}(u_D) = \frac{k_D(1-u_D)\beta_D\lambda\psi_D}{dc_D(a_D\psi_D + \delta_D\varphi_D)}, \quad R_Z^{\text{without latent}}(u_Z) = \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z}{dc_Z(a_Z\psi_Z + \delta_Z\varphi_Z)}.$$

The corresponding minimum treatment efficacies are:

$$u_D^{cr,\text{ without latent}} = \max\left\{1 - \frac{dc_D(a_D\psi_D + \delta_D\varphi_D)}{k_D\beta_D\lambda\psi_D}, 0\right\}, \quad u_Z^{cr,\text{ without latent}} = \max\left\{1 - \frac{dc_Z(a_Z\psi_Z + \delta_Z\varphi_Z)}{k_Z\beta_Z\lambda\psi_Z}, 0\right\}.$$

Since $0 < \theta_D < 1$ and $0 < \theta_Z < 1$, then $\frac{\eta_D + b_D\theta_D}{\eta_D + b_D} < 1$ and $\frac{\eta_Z + b_Z\theta_Z}{\eta_Z + b_Z} < 1$, and so we get

$$R_D^{\text{with latent}}(u_D) = \frac{k_D(1-u_D)\beta_D\lambda\psi_D(\eta_D + b_D\theta_D)}{dc_D(a_D\psi_D + \delta_D\varphi_D)(\eta_D + b_D)} < \frac{k_D(1-u_D)\beta_D\lambda\psi_D}{dc_D(a_D\psi_D + \delta_D\varphi_D)} = R_D^{\text{without latent}}(u_D),$$
$$R_Z^{\text{with latent}}(u_Z) = \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z(\eta_Z + b_Z\theta_Z)}{dc_Z(a_Z\psi_Z + \delta_Z\varphi_Z)(\eta_Z + b_Z)} < \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z}{dc_Z(a_Z\psi_Z + \delta_Z\varphi_Z)} = R_Z^{\text{without latent}}(u_Z).$$

Thus, neglecting latently infected cells also leads to an overestimation of the viral reproduction numbers. Biologically, the latent compartment acts as a temporal bottleneck in intracellular viral progression. Following viral entry, not all infected cells immediately become productively infectious; rather, a proportion enters a latent state and requires activation before initiating viral production. Consequently, latency delays viral amplification and reduces the effective rate of infection spread. Ignoring this stage implicitly assumes immediate viral productivity, thereby artificially accelerating infection dynamics and inflating the estimated viral fitness. As a result,

$$u_D^{cr,\text{ without latent}} \geq u_D^{cr,\text{ with latent}}, \qquad u_Z^{cr,\text{ without latent}} \geq u_Z^{cr,\text{ with latent}}.$$

This finding suggests that models neglecting latency may overestimate the level of antiviral efficacy required for viral elimination.

7. Numerical simulations

In this section, we present numerical simulations of the system in Eqs (2.1)–(2.9) aimed at illustrating and supporting the theoretical results established in Theorems 1–4. In particular, the simulations are designed to examine the threshold dynamics of the model by selecting parameter regimes corresponding to the theoretical conditions governing the existence and stability of the equilibria. Numerical experiments are conducted under different scenarios determined by the reproduction and invasion reproduction numbers, including cases where (R_D^L) and (R_Z^L) are below or above unity, as well as situations in which $(R_D^{L,inv})$ and $(R_Z^{L,inv})$ determine competitive exclusion or coexistence. This enables numerical confirmation of the predicted equilibrium transitions and global asymptotic stability results. Moreover, variations in key parameters, particularly the infection rates (β_D), (β_Z), antiviral treatment intensities (u_D), (u_Z), and intracellular delay parameters (τ_i), are considered to investigate their influence on viral persistence, treatment outcomes, and stability thresholds. Due to the absence of reliable clinical datasets for DENV–ZIKV co-infection, the parameter values employed in the numerical simulations are either adopted from studies on DENV or ZIKV mono-infections or selected within biologically plausible ranges. Accordingly, the simulations are intended to illustrate the qualitative dynamics of the model rather than to provide data-driven parameter estimation or calibration. To this end, the distributed time-delay model in Eqs (2.1)–(2.9) is transformed to a discrete-delay system through the use of a particular class of probability density functions, namely the Dirac delta function $D(\cdot)$. Following [64], we define

$$f_i(\tau) = D(\tau - \tau_i), i = 1, 2, \cdots, 8.$$

In case $S_i \to \infty, i = 1, 2, \cdots, 8$, we have

$$\int_0^\infty f_i(\tau)d\tau = 1 \text{ and } F_i = \int_0^\infty D(\tau - \tau_i)\, e^{-n_i\tau}d\tau = e^{-n_i\tau_i}.$$

Then,

$$\int_0^\infty D(\tau-\tau_1)e^{-n_1\tau}X_\tau V_{D\tau}d\tau = e^{-n_1\tau_1}X_{\tau_1}V_{D\tau_1}, \quad \int_0^\infty D(\tau-\tau_2)e^{-n_2\tau}X_\tau V_{D\tau}d\tau = e^{-n_2\tau_2}X_{\tau_2}V_{D\tau_2},$$
$$\int_0^\infty D(\tau-\tau_3)e^{-n_3\tau}Y^L_{D\tau}d\tau = e^{-n_3\tau_3}Y^L_{D\tau_3}, \quad \int_0^\infty D(\tau-\tau_4)e^{-n_4\tau}X_\tau V_{Z\tau}d\tau = e^{-n_4\tau_4}X_{\tau_4}V_{Z\tau_4},$$
$$\int_0^\infty D(\tau-\tau_5)e^{-n_5\tau}X_\tau V_{Z\tau}d\tau = e^{-n_5\tau_5}X_{\tau_5}V_{Z\tau_5}, \quad \int_0^\infty D(\tau-\tau_6)e^{-n_6\tau}Y^L_{Z\tau}d\tau = e^{-n_6\tau_6}Y^L_{Z\tau_6},$$
$$\int_0^\infty D(\tau-\tau_7)e^{-n_7\tau}Y^A_{D\tau}d\tau = e^{-n_7\tau_7}Y^A_{D\tau_7}, \quad \int_0^\infty D(\tau-\tau_8)e^{-n_8\tau}Y^A_{Z\tau}d\tau = e^{-n_8\tau_8}Y^A_{Z\tau_8}.$$

Hence, the model in Eqs (2.1)–(2.9) can be written as:

$$\begin{aligned}
\frac{dX}{dt} &= \lambda - dX - \beta_D X V_D - \beta_Z X V_Z,\\
\frac{dY_D^L}{dt} &= (1-\theta_D)\beta_D e^{-n_1\tau_1}X_{\tau_1}V_{D\tau_1} - (\eta_D + b_D)Y_D^L,\\
\frac{dY_D^A}{dt} &= \theta_D\beta_D e^{-n_2\tau_2}X_{\tau_2}V_{D\tau_2} + \eta_D e^{-n_3\tau_3}Y^L_{D\tau_3} - a_D Y_D^A - \delta_D Y_D^A U_D,
\end{aligned}$$

$$
\begin{aligned}
\frac{dY_Z^L}{dt} &= (1-\theta_Z)\beta_Z e^{-n_4\tau_4} X_{\tau_4} V_{Z\tau_4} - (\eta_Z + b_Z) Y_Z^L, \\
\frac{dY_Z^A}{dt} &= \theta_Z \beta_Z e^{-n_5\tau_5} X_{\tau_5} V_{Z\tau_5} + \eta_Z e^{-n_6\tau_6} Y_{Z\tau_6}^L - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z, \\
\frac{dV_D}{dt} &= k_D e^{-n_7\tau_7} Y_{D\tau_7}^A - c_D V_D, \quad \frac{dV_Z}{dt} = k_Z e^{-n_8\tau_8} Y_{Z\tau_8}^A - c_Z V_Z, \\
\frac{dU_D}{dt} &= \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D, \quad \frac{dU_Z}{dt} = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z.
\end{aligned} \tag{7.1}
$$

The threshold parameters of the model in Eq (7.1) are provided as:

$$
\begin{aligned}
R_D^L &= \frac{k_D \beta_D \lambda \psi_D \sigma_D e^{-n_7\tau_7}}{dc_D(\eta_D + b_D)(a_D\psi_D + \delta_D\varphi_D)}, \quad R_Z^L = \frac{k_Z \beta_Z \lambda \psi_Z \sigma_Z e^{-n_8\tau_8}}{dc_Z(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}, \\
R_D^{L,inv} &= \frac{k_D \beta_D \lambda \psi_D \sigma_D e^{-n_7\tau_7}}{dc_D(a_D\psi_D + \delta_D\varphi_D)(\eta_D + b_D)\left(1 + \frac{k_Z\beta_Z e^{-n_8\tau_8}}{dc_Z}\overline{Y}_Z^A\right)}, \\
R_Z^{L,inv} &= \frac{k_Z \beta_Z \lambda \psi_Z \sigma_Z e^{-n_8\tau_8}}{dc_Z(a_Z\psi_Z + \delta_Z\varphi_Z)(\eta_Z + b_Z)\left(1 + \frac{k_D\beta_D e^{-n_7\tau_7}}{dc_D}Y_D^{A*}\right)},
\end{aligned}
$$

where σ_D and σ_Z become $\sigma_D = (\eta_D + b_D)\theta_D e^{-n_2\tau_2} + \eta_D(1-\theta_D)e^{-(n_1\tau_1 + n_3\tau_3)}$ and $\sigma_Z = (\eta_Z + b_Z)\theta_Z e^{-n_5\tau_5} + \eta_Z(1-\theta_Z)e^{-(n_4\tau_4 + n_6\tau_6)}$.

7.1. Stability of equilibria for the model in Eq (7.1)

By using the dde23 solver in MATLAB, we solve numerically the system of DDEs in Eq (7.1) numerically. The values of parameters of model in Eq (7.1) are given in Table 1. Here, we fix τ_i for $\tau_i = 0.1$, $i = 1, 2, ..., 8$. To analyze the global behavior of the system, ten distinct sets of initial conditions, inspired by the study of [65], are considered:

$$
\begin{aligned}
X(\phi) &= 40 + 4\sin(\phi) - 3k, \quad Y_D^L(\phi) = 10 + 0.1\sin(\phi) + 2k, \\
Y_D^A(\phi) &= 5 + 0.3\sin(\phi) + 0.9k, \quad Y_Z^L(\phi) = 10 + 0.2\sin(\phi) + 2k, \\
Y_Z^A(\phi) &= 5 + 0.2\sin(\phi) + 0.9k, \quad V_D(\phi) = 20 + 0.4\sin(\phi) + 7k, \\
V_Z(\phi) &= 20 + 0.5\sin(\phi) + 7k, \quad U_D(\phi) = 110 + 8\sin(\phi) - 10k, \\
U_Z(\phi) &= 150 + 10\sin(\phi) - 15k, \quad \phi \in [-0.1, 0], \quad k = 1, 2, ..., 10.
\end{aligned}
$$

These initial conditions are selected to examine whether the system trajectories converge to one of the steady states regardless of the starting values. The sinusoidal terms are introduced to represent heterogeneous and time-varying histories over the delay interval rather than constant initial profiles, thereby testing the robustness of the model dynamics under substantially different initial perturbations. Numerical simulations indicate that the qualitative asymptotic behavior remains unchanged and that the solutions converge to the equilibrium predicted by the global stability analysis, demonstrating that the stability conclusions are independent of the specific form of the initial conditions.

By varying the values of the parameters β_D and β_Z, parameters, the four following scenarios arise as:

Scenario 1 (Stability of EQ^0): When the incidence rates are low, $\beta_D = 0.001$ and $\beta_Z = 0.001$, the reproduction numbers satisfy $R_D^L = 0.4738 < 1$ and $R_Z^L = 0.5639 < 1$. Under the conditions

listed in Table 2, all solution trajectories converge to the infection-free equilibrium $EQ^0 = (71.43, 0, 0, 0, 0, 0, 0, 60, 62.5)$ as shown in Figure 2. This verifies the global asymptotic stability of EQ^0 in accordance with Theorem 1. Biologically, this outcome indicates complete elimination of both viruses and infected cells, while uninfected target cells return to their normal level.

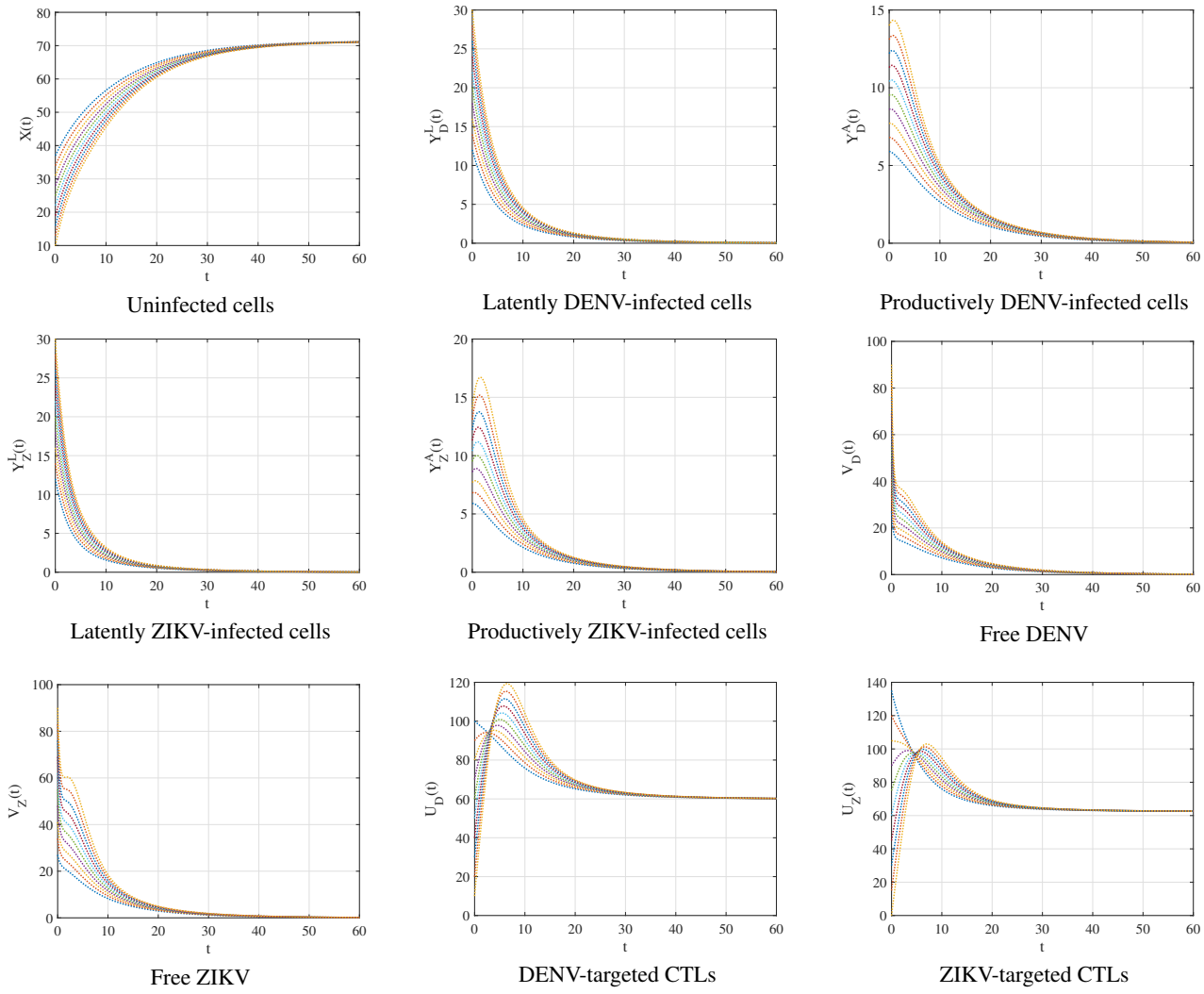

Figure 2. All trajectories of the system in Eq (7.1) starting from different initial states converge to the disease-free equilibrium $EQ^0 = (71.43, 0, 0, 0, 0, 0, 0, 60, 62.5)$ under the conditions $R_D^L \leq 1$ and $R_Z^L \leq 1$.

Scenario 2 (Stability of EQ^*): We choose parameter values $\beta_D = 0.004$ and $\beta_Z = 0.001$, and we obtain $R_D^L = 1.8953 > 1$ and $R_Z^{L,inv} = 0.5639 < 1$. The feasibility conditions in Table 2, therefore ensure the existence of the DENV mono-infection equilibrium $EQ^* = (46.41, 9.24, 7.26, 0, 0, 18.87, 0, 106.28, 62.50)$. As illustrated in Figure 3, trajectories from different initial histories converge to EQ^*, confirming its global asymptotic stability and agreeing with Theorem 2. From a biological standpoint, DENV persists, whereas ZIKV cannot successfully invade; any introduction of ZIKV decays over time, while DENV maintains a stable endemic presence.

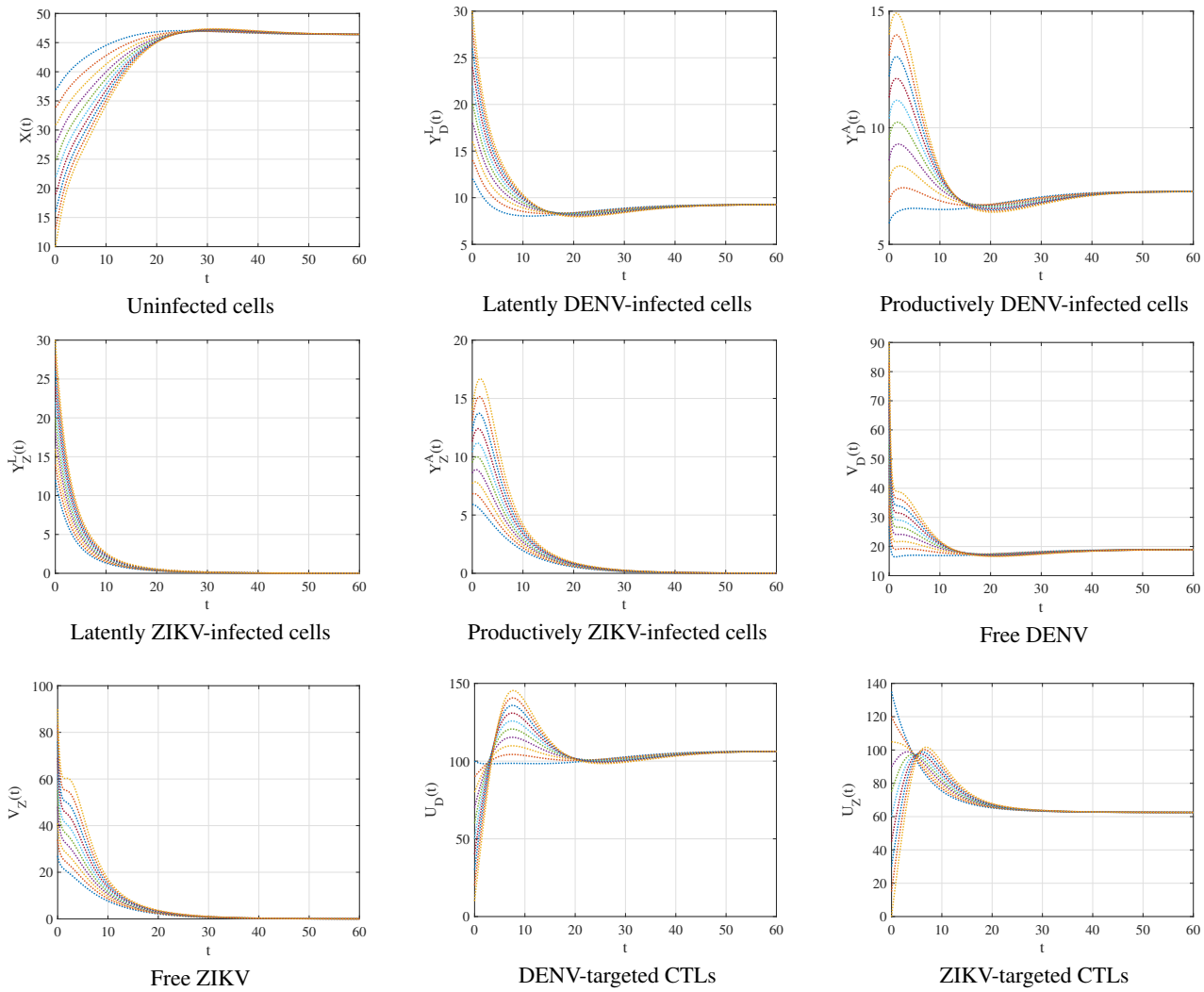

Figure 3. All trajectories of the system in Eq (7.1) starting from different initial states converge to the DENV mono-infection equilibrium $EQ^* = (46.41, 9.24, 7.26, 0, 0, 18.87, 0, 106.28, 62.50)$ under the conditions $R_D^L > 1$ and $R_Z^{L,inv} \leq 1$.

Scenario 3 (Stability of $\overline{EQ}$): With parameter values $\beta_D = 0.001$ and $\beta_Z = 0.004$, the reproduction numbers are calculated as $R_Z^L = 2.2557 > 1$ and $R_D^{L,inv} = 0.4738 < 1$. Under these conditions in Table 2, the system admits the ZIKV mono-infection equilibrium $\overline{EQ} = (40.37, 0, 0, 8.68, 7.44, 0, 26.92, 60, 99.51)$. Figure 4 shows that trajectories starting from different initial conditions converge toward this equilibrium $\overline{EQ}$, which is in full agreement with the analytical results established in Theorem 3. Biologically, this scenario reflects sustained ZIKV infection with unsuccessful DENV invasion, as DENV-related compartments decline to zero while ZIKV persists.

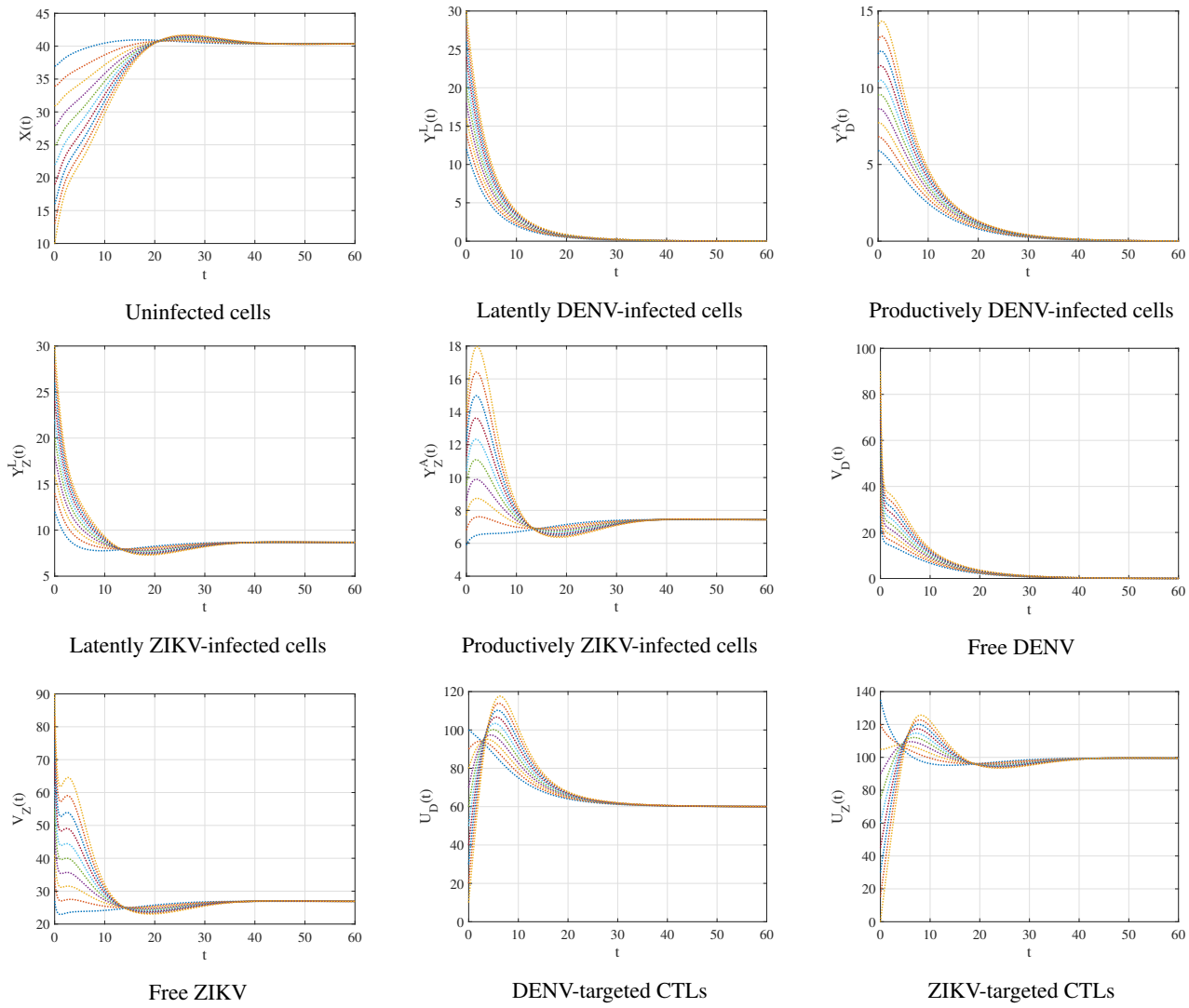

Figure 4. All trajectories of the system in Eq (7.1) starting from different initial states converge to the ZIKV mono-infection equilibrium $\overline{EQ} = (40.37, 0, 0, 8.68, 7.44, 0, 26.92, 60, 99.51)$ under the conditions $R_Z^L > 1$ and $R_D^{L,inv} \leq 1$.

Scenario 4 (Stability of $\widetilde{EQ}$): We select parameter values $\beta_D = 0.004$ and $\beta_Z = 0.004$, and we obtain $R_D^{L,inv} = 1.8953 > 1$ and $R_Z^{L,inv} = 2.2556 > 1$. Under these conditions summarized in Table 2, the system admits the DENV–ZIKV co-infection equilibrium $\widetilde{EQ} = (39.07, 1.95, 1.82, 7.57, 6.70, 4.73, 24.25, 67.35, 93.99)$, which is G.A.S, agreeing with Theorem 4. Figure 5 shows that trajectories starting from different initial conditions converge toward the equilibrium point $\widetilde{EQ}$. Both viruses approach a coexistence state. Biologically, this outcome corresponds to long-term coexistence of DENV and ZIKV, indicating that neither virus can be cleared by the modeled immune response under these parameter values.

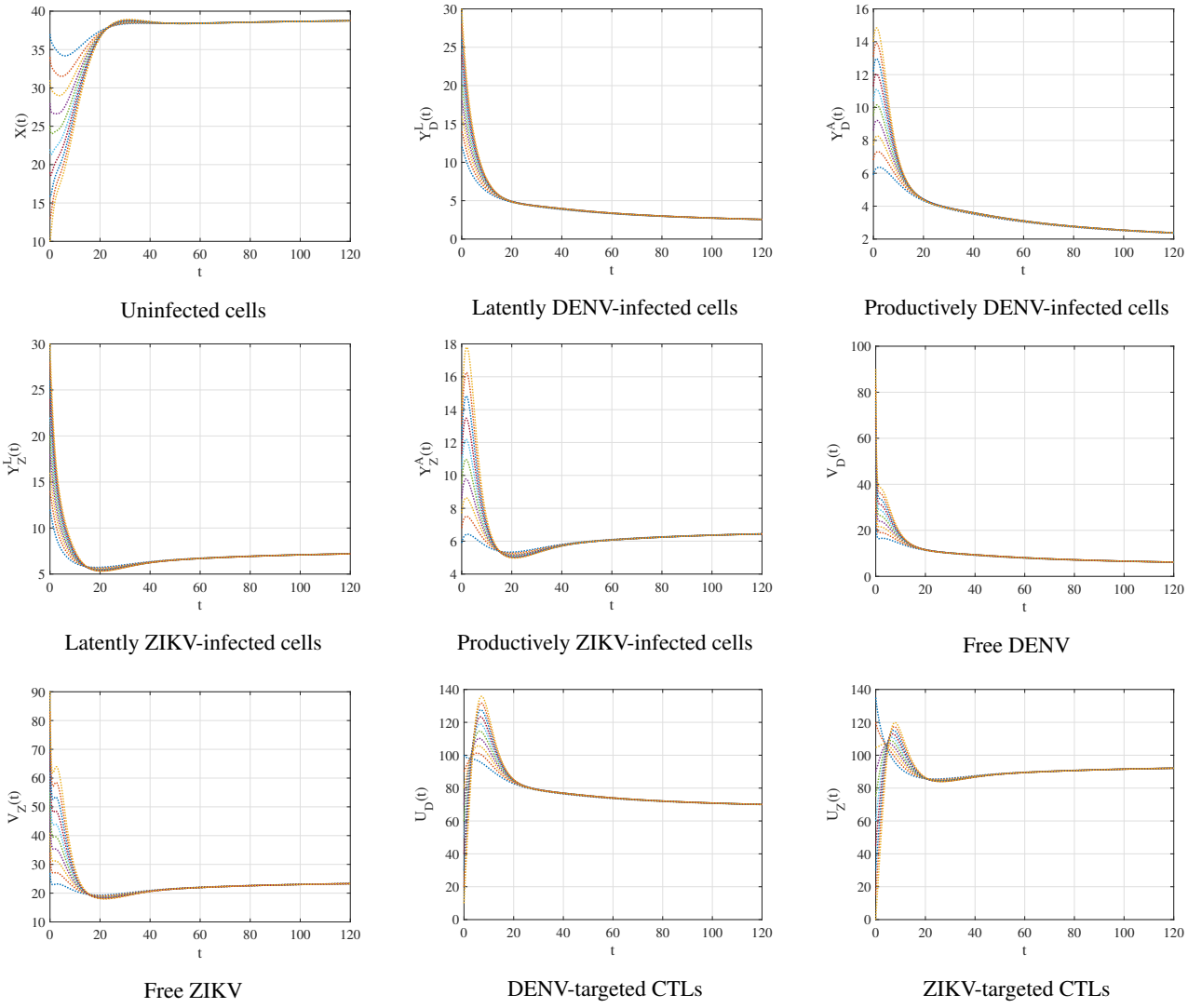

Figure 5. All trajectories of the system in Eq (7.1) starting from different initial states converge to the DENV–ZIKV co-infection equilibrium $\widetilde{EQ} = (39.07, 1.95, 1.82, 7.57, 6.70, 4.73, 24.25, 67.35, 93.99)$ under the conditions $R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$.

7.2. Model simulation under antiviral treatment for blocking viral infections

To investigate the impact of antiviral therapies on the within-host co-dynamics of DENV and ZIKV, we extend the system in Eq (7.1), by incorporating antiviral treatment that blocks viral infection of healthy target cells. The resulting model is given by

$$\frac{dX}{dt} = \lambda - dX - (1-u_D)\beta_D X V_D - \beta_Z(1-u_Z)XV_Z, \tag{7.2}$$

$$\frac{dY_D^L}{dt} = (1-\theta_D)(1-u_D)\beta_D e^{-n_1\tau_1}X_{\tau_1}V_{D\tau_1} - (\eta_D + b_D)Y_D^L, \tag{7.3}$$

$$\frac{dY_D^A}{dt} = \theta_D(1-u_D)\beta_D e^{-n_2\tau_2}X_{\tau_2}V_{D\tau_2} + \eta_D e^{-n_3\tau_3}Y_{D\tau_3}^L - a_D Y_D^A - \delta_D Y_D^A U_D, \tag{7.4}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z(1-u_Z)e^{-n_4\tau_4}X_{\tau_4}V_{Z\tau_4} - (\eta_Z + b_Z)Y_Z^L, \tag{7.5}$$

$$\frac{dY_Z^A}{dt} = \theta_Z(1-u_Z)\beta_Z e^{-n_5\tau_5}X_{\tau_5}V_{Z\tau_5} + \eta_Z e^{-n_6\tau_6}Y_{Z\tau_6}^L - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z, \tag{7.6}$$

$$\frac{dV_D}{dt} = k_D e^{-n_7\tau_7}Y_{D\tau_7}^A - c_D V_D, \tag{7.7}$$

$$\frac{dV_Z}{dt} = k_Z e^{-n_8\tau_8}Y_{Z\tau_8}^A - c_Z V_Z, \tag{7.8}$$

$$\frac{dU_D}{dt} = \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D, \tag{7.9}$$

$$\frac{dU_Z}{dt} = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z. \tag{7.10}$$

The basic reproduction numbers of the model in Eqs (7.2)–(7.10) are given by

$$R_D^L(u_D) = \frac{k_D(1-u_D)\beta_D\lambda\psi_D\sigma_D e^{-n_7\tau_7}}{dc_D(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}, \quad R_Z^L(u_Z) = \frac{k_Z(1-u_Z)\beta_Z\lambda\psi_Z\sigma_Z e^{-n_8\tau_8}}{dc_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}.$$

Both reproduction numbers are strictly decreasing functions of the treatment intensities u_D and u_Z, highlighting the inhibitory effect of antiviral therapy on viral transmission within the host. To guarantee $R_D^L(u_D) \le 1$ and $R_Z^L(u_Z) \le 1$, the treatment intensities must satisfy

$$u_D^{cr} \le u_D \le 1 \ \text{ where } u_D^{cr} = \max\left\{1 - \frac{c_D d(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}{k_D\beta_D\lambda\psi_D\sigma_D e^{-n_7\tau_7}}, 0\right\},$$

$$u_Z^{cr} \le u_Z \le 1 \ \text{ where } u_Z^{cr} = \max\left\{1 - \frac{c_Z d(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}{k_Z\beta_Z\lambda\psi_Z\sigma_Z e^{-n_8\tau_8}}, 0\right\}.$$

Substituting the parameter values in Scenario 4 by setting $\beta_D = \beta_Z = 0.004$ yields

$$u_D^{cr} \approx 0.472375, \ \ u_Z^{cr} \approx 0.556668.$$

Consequently, we have

(i) If $0.472375 \le u_D \le 1$ and $0.556668 \le u_Z \le 1$, then $R_D^L(u_D) \le 1$ and $R_Z^L(u_Z) \le 1$, and EQ^0 is G.A.S.

(ii) If $0 \le u_D < 0.472375$ and/or $0 \le u_Z < 0.556668$, then $R_D^L(u_D) > 1$ and/or $R_Z^L(u_Z) > 1$, causing EQ^0 to lose stability and another equilibrium to become globally asymptotically stable.

To evaluate treatment efficacy, the control parameters u_D and u_Z, representing the antiviral treatment intensities against DENV and ZIKV, respectively, are varied, as listed in Table 3. The system in Eqs (7.2)–(7.10) is simulated using these efficacy levels together with the following initial conditions:

$$\begin{aligned} X(\phi) &= 37 + 5\sin(\phi), \quad Y_D^L(\phi) = 8 + 0.1\sin(\phi), \\ Y_D^A(\phi) &= 12 + 0.1\sin(\phi), \quad Y_Z^L(\phi) = 8 + 0.2\sin(\phi), \\ Y_Z^A(\phi) &= 11 + 0.3\sin(\phi), \quad V_D(\phi) = 34 + 0.5\sin(\phi), \\ V_Z(\phi) &= 30 + 0.2\sin(\phi), \quad U_D(\phi) = 90 + 0.1\sin(\phi), \\ U_Z(\phi) &= 110 + 0.1\sin(\phi), \quad \phi \in [-0.1, 0]. \end{aligned} \tag{7.11}$$

Table 3. Influence of the antiviral treatment efficacies u_Z and u_D on the associated reproduction numbers R_D^L and R_Z^L.

Case	u_D	u_Z	R_D^L	R_Z^L
DE-1	0.0	0.0	1.8953	2.2556
DE-2	0.2	0.2	1.5162	1.8045
DE-3	0.4	0.4	1.1372	1.3534
DE-4	0.472375	0.556668	1	1
DE-5	0.8	0.8	0.3791	0.4511

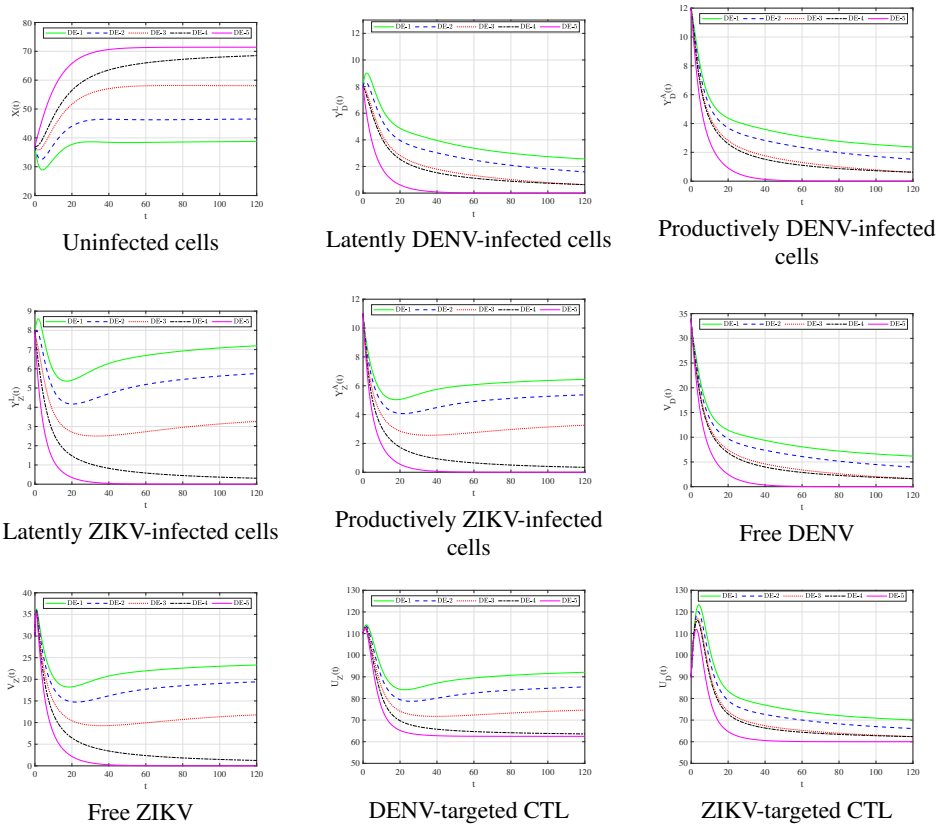

Figure 6. Solutions of the system in Eqs (7.2)–(7.10) under antiviral treatment.

Figure 6 shows that increasing the treatment intensities u_D and u_Z leads to a pronounced reduction in free virus concentrations (V_D, V_Z). This decline limits the generation of newly infected cells, while enabling the population of uninfected target cells to recover. Moreover, the reproduction numbers R_D^L and R_Z^L decrease monotonically with increasing treatment efficacy in Table 3 and cross the critical threshold of unity at approximately $u_D = 0.472375$ and $u_Z = 0.556668$. Beyond this level (e.g., $u_D = u_Z = 0.8$), both reproduction numbers remain below one, confirming that sufficiently strong inhibition of viral entry leads to within-host clearance of both DENV and ZIKV.

7.3. Sensitivity analysis

In biological systems, sensitivity analysis is employed to investigate the relationship between model parameters and system outputs, thereby enhancing the understanding of model behavior and identifying the key parameters that most strongly influence the outcomes. Several approaches have been developed to quantify the biological response to variations in model parameters, including direct differentiation, Latin hypercube sampling, and system linearization followed by the solutions of the resulting equations [66].

For the model in Eq (7.1), we adopt a derivative-based sensitivity analysis, which can be computed analytically by evaluating the partial derivatives of the model outputs with respect to the parameters. In particular, we focus on the sensitivity of R_D^L and R_Z^L, as these quantities play a central role in determining the stability of EQ^0. The normalized forward sensitivity index is generally given by

$$\Lambda_\alpha^{R_s^L} = \frac{\partial R_s^L}{\partial \alpha} \cdot \frac{\alpha}{R_s^L}, \quad s \in \{D, Z\}, \tag{7.12}$$

where α is a parameter. The sensitivity analyses of R_D^L and R_Z^L are carried out as follows:

7.3.1. Sensitivity analysis of R_D^L

The normalized forward sensitivity indices of R_D^L, which quantify the influence of DENV-related parameters on within-host viral dynamics, are computed using Eq (7.12). The resulting sensitivity indices are reported in Table 4 and illustrated in Figure 7.

Table 4. Sensitivity indices of R_D^L.

Parameters	Value of $\Lambda_\alpha^{R_D^L}$	Parameters	Value of $\Lambda_\alpha^{R_D^L}$
λ	1	θ_D	0.3314
d	−1	η_D	0.2730
β_D	1	n_1	−0.0468
c_D	−1	n_2	−0.0532
k_D	1	n_3	−0.0468
b_D	−0.2730	n_7	−0.1
a_D	−0.7	τ_1	−0.0468
δ_D	−0.3	τ_2	−0.0532
φ_D	−0.3	τ_3	−0.0468
ψ_D	0.3	τ_7	−0.1

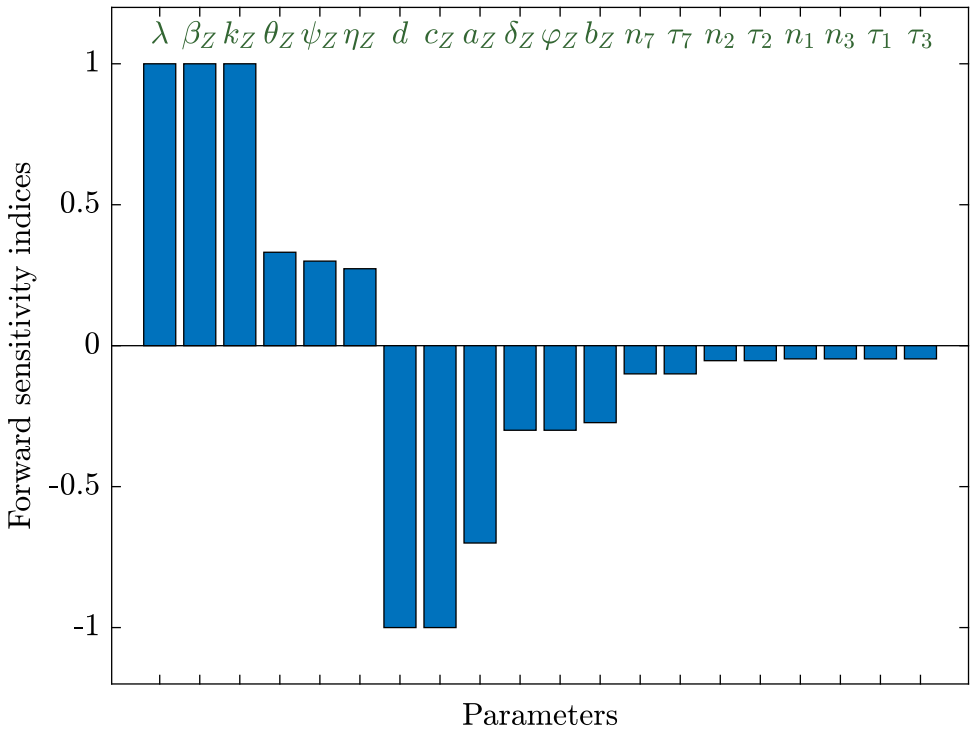

Figure 7. Forward sensitivity analysis of the parameters on R_D^L.

From the signs of the indices, we note the following observations:

- **Positive sensitivity indices** are associated with the parameters λ, β_D, k_D, ψ_D, η_D, and θ_D, indicating that increases in these parameters lead to an increase in R_D^L. Hence, they facilitate the proliferation and persistence of DENV within the host. Among them, λ, β_D, and k_D exhibit the largest positive sensitivity indices, reflecting their dominant role in viral propagation. In contrast, ψ_D, θ_D, and η_D, exert comparatively weaker positive effects. For example, a 10% increase (or decrease) in β_D produces a corresponding 10% increase (or decrease) in R_D^L, while a 10% change in η_D results in only a 2.73% change in R_D^L.
- **Negative sensitivity indices** are observed for the parameters d, a_D, c_D, δ_D, b_D, φ_D, n_1, n_2, n_3, n_7, τ_1, τ_2, τ_3, and τ_7, implying that increases in these parameters reduce the value of R_D^L. Consequently, these parameters play an inhibitory role in controlling DENV infection. For instance, the sensitivity index of b_D is -0.273, meaning that a 10% increase in b_D leads to an approximate 2.73% reduction in R_D^L. Among all negatively contributing parameters, d and c_D exert the strongest suppressive effects on viral dynamics.

7.3.2. Sensitivity analysis of R_Z^L

Using Eq (7.12), the normalized forward sensitivity indices of R_Z^L, which characterize the impact of model parameters on the within-host progression of ZIKV infection, are calculated. The numerical results are summarized in Table 5 and illustrated in Figure 8.

Table 5. Sensitivity indices of R_Z^L.

Parameters	Value of $\Lambda_\alpha^{R_Z^L}$	Parameters	Value of $\Lambda_\alpha^{R_Z^L}$
λ	1	θ_Z	0.1489
d	−1	η_Z	0.2628
β_Z	1	n_4	−0.0615
c_Z	−1	n_5	−0.0385
k_Z	1	n_6	−0.0615
b_Z	−0.2628	n_8	−0.1
a_Z	−0.5358	τ_4	−0.0615
δ_Z	−0.4642	τ_5	−0.0385
φ_Z	−0.4642	τ_6	−0.0615
ψ_Z	0.4642	τ_8	−0.1

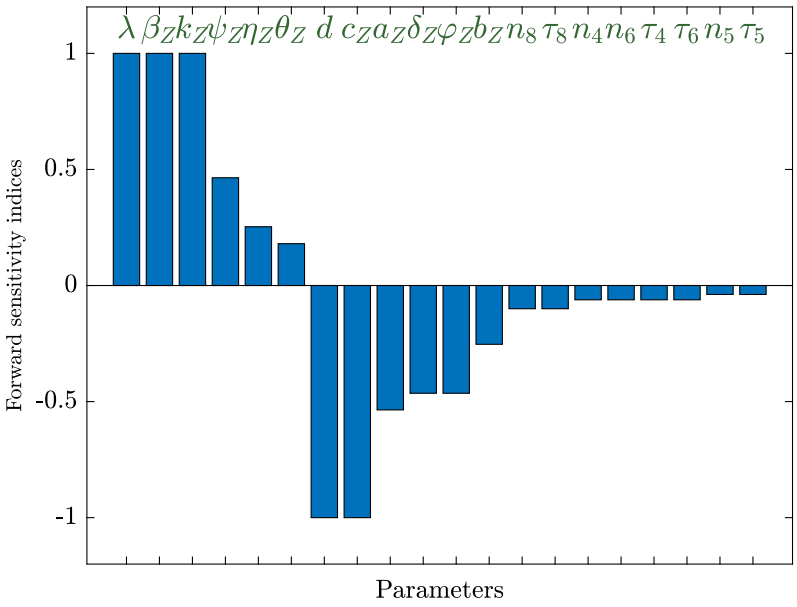

Figure 8. Forward sensitivity analysis of the parameters on R_Z^L.

Based on the signs and magnitudes of these indices, the following observations are made:

- **Positive sensitivity indices** correspond to the parameters $\lambda, \beta_Z, k_Z, \psi_Z, \eta_Z$, and θ_Z, indicating that increases in these parameters enhance R_Z^L and thus promote ZIKV amplification within the host. Notably, λ, β_Z, and k_Z display the highest positive sensitivity indices, underscoring their critical role in viral persistence. In contrast, ψ_Z, η_Z, and θ_Z contribute more modestly. As an illustration, a 10% increase (or decrease) in k_Z leads to an approximate 10% increase (or decrease) in R_Z^L, whereas a 10% variation in η_Z results in an approximate 2.63 % change in R_Z^L.
- **Negative sensitivity indices** are associated with the parameters d, a_Z, c_Z, δ_Z, b_Z, φ_Z, n_4, n_5, n_6, n_8, τ_4, τ_5, τ_6, and τ_8, indicating that increasing these parameters suppresses the value of R_Z^L

and consequently limits ZIKV progression. For example, the sensitivity index of a_Z is -0.5358, implying that a 10% increase (or decrease) in a_Z yields an approximate 5.35% decrease (or increase) in R_Z^L. Among all inhibitory parameters, d and c_Z exhibit the most pronounced negative influence, followed by a_Z, δ_Z, b_Z, φ_Z, n_4, n_5, n_6, n_8, τ_4, τ_5, τ_6, and τ_8, which consistently exert weaker yet stabilizing effects.

The present sensitivity analysis is local in nature and is intended to identify the dominant parameters governing the threshold dynamics of DENV–ZIKV co-infection. While the derivative-based approach provides useful insight into parameter influence near baseline values, a more comprehensive global sensitivity analysis and uncertainty quantification framework may further clarify parameter interactions and robustness of the predicted dynamics. Such investigations constitute an important direction for future work.

7.4. Impact of time delays on DENV–ZIKV co-dynamics

Among the delay parameters governing the DENV–ZIKV within-host co-infection dynamics, numerical investigations indicate that the basic reproduction numbers R_D^L and R_Z^L are particularly sensitive to variations in the delay parameters τ_7 and τ_8, respectively; these delays correspond to the maturation periods associated with newly released DENV and ZIKV virions, respectively. Owing to their dominant influence, our analysis focuses on examining how changes in τ_7 and τ_8 affect the stability properties of the disease-free equilibrium EQ^0.

To isolate the effects of these delays, the parameters $\beta_D = 0.004$, $\beta_Z = 0.004$, and $\tau_i = 0.1$ for $i = 1, 2, \ldots, 6$ are fixed. The impact of incorporating the delays τ_7 and τ_8 on the global stability of EQ^0 is then investigated. Since the expressions of the reproduction numbers R_D^L and R_Z^L given in Eq (7.13) depend explicitly on τ_7 and τ_8, any variation in these parameters directly modifies the stability characteristics of the disease-free equilibrium. In particular, increasing τ_7 and τ_8 leads to a reduction in the values of R_D^L and R_Z^L, which is favorable for stabilizing the system (see Table 6).

Table 6. The variation of R_D^L and R_Z^L with respect to the delay parameters.

Case	τ_7	τ_8	R_D^L	R_Z^L
T.D-1	0.2	0.2	1.7149	2.0410
T.D-2	0.4	0.4	1.4041	1.6710
T.D-3	0.7394	0.9134	1	1
T.D-4	1.4	1.4	0.5165	0.6147
T.D-5	1.6	1.6	0.4229	0.5033

The system in Eq (7.1) is solved numerically under the initial conditions in Eq (7.11). To determine the critical delay thresholds governing the stability of EQ^0, the reproduction numbers are expressed explicitly as functions of τ_7 and τ_8:

$$\begin{aligned} R_D^L(\tau_7) &= \frac{k_D\beta_D\lambda\psi_D\sigma_D e^{-n_7\tau_7}}{dc_D(\eta_D + b_D)(a_D\psi_D + \delta_D\varphi_D)}, \\ R_Z^L(\tau_8) &= \frac{k_Z\beta_Z\lambda\psi_Z\sigma_Z e^{-n_8\tau_8}}{dc_Z(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}. \end{aligned} \tag{7.13}$$

To ensure that $R_D^L(\tau_7) \leq 1$ and $R_Z^L(\tau_8) \leq 1$, the following threshold conditions must be satisfied:

$$\tau_7 \geq \tau_7^{cr} = \max\left\{0, \frac{1}{n_7}\ln\left(\frac{k_D\beta_D\lambda\psi_D\sigma_D}{dc_D(\eta_D + b_D)(a_D\psi_D + \delta_D\varphi_D)}\right)\right\},$$

$$\tau_8 \geq \tau_8^{cr} = \max\left\{0, \frac{1}{n_8}\ln\left(\frac{k_Z\beta_Z\lambda\psi_Z\sigma_Z}{dc_Z(\eta_Z + b_Z)(a_Z\psi_Z + \delta_Z\varphi_Z)}\right)\right\}.$$

Substituting the parameter values yields the critical thresholds

$$\tau_7^{cr} \approx 0.73937, \qquad \tau_8^{cr} \approx 0.91344.$$

Accordingly, the following stability scenarios arise:

(i) If $\tau_7 \geq 0.73937$ and $\tau_8 \geq 0.91344$, then $R_D^L(\tau_7) \leq 1$, $R_Z^L(\tau_8) \leq 1$, and the disease-free equilibrium EQ^0 is G.A.S.

(ii) If $\tau_7 < 0.73937$ and/or $\tau_8 < 0.91344$, then $R_D^L(\tau_7) > 1$ and/or $R_Z^L(\tau_8) > 1$, and the equilibrium EQ^0 loses stability, in which case another equilibrium becomes globally asymptotically stable.

Table 6 reports the computed values of $R_D^L(\tau_7)$ and $R_Z^L(\tau_8)$ for several representative delay scenarios. As the delays τ_7 and τ_8 increase, both reproduction numbers decrease monotonically, indicating enhanced system stability. This trend is further confirmed by the numerical simulations shown in Figure 9.

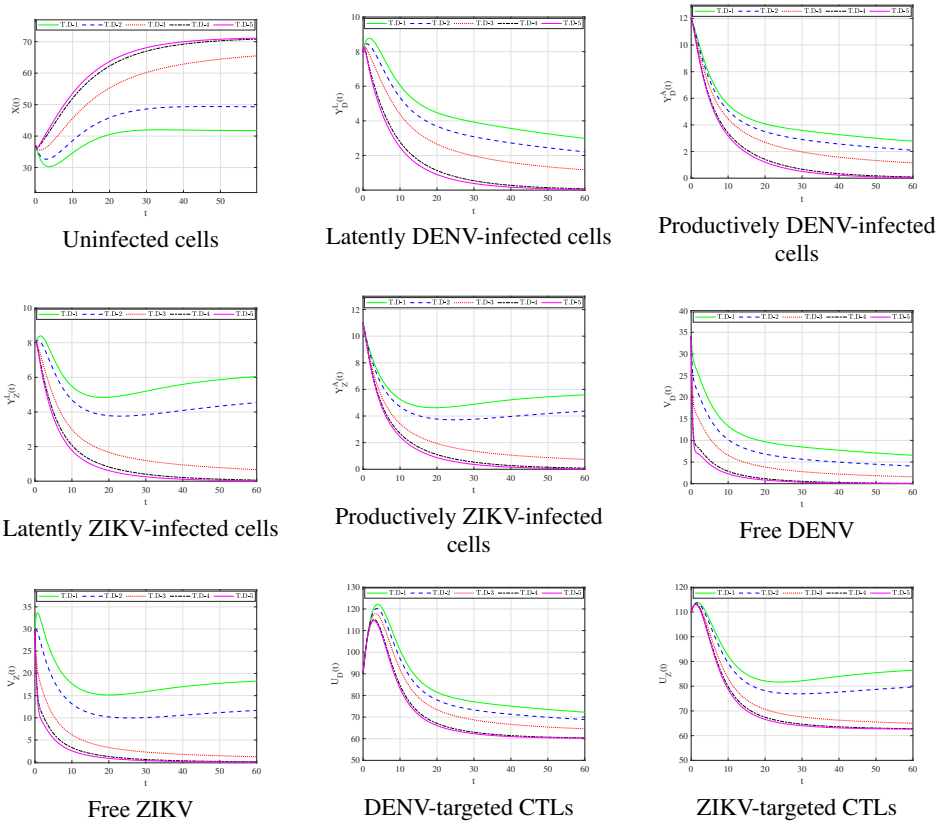

Figure 9. Solutions of the system in Eq (7.1) under the effect of three different time delays.

The simulations demonstrate that incorporating larger time delays results in a substantial increase in the population of uninfected cells, accompanied by marked reductions in latently and productively infected cells and viral loads. Biologically, prolonged intracellular delays slow viral replication processes, producing an effect analogous to antiviral treatment. Consequently, incorporating biologically realistic time delays provides valuable insight into potential therapeutic strategies that enhance infection control and promote host recovery.

Moreover, as viral loads decline due to extended delay periods, there is a gradual increase in uninfected cell concentrations over time.

8. Conclusions

In this study, we developed and rigorously analyzed a within-host dynamical model describing DENV–ZIKV co-infection under CTL-mediated immune regulation and multiple distributed intracellular delays. The model explicitly differentiates latent and productively infected cell compartments, enabling a biologically refined representation of intracellular viral progression and immune–virus interaction dynamics.

The basic reproduction numbers of the individual viral subsystems, denoted by R_D^L and R_Z^L, were derived using the next-generation operator framework. It was established that the overall basic reproduction number of the coupled co-infection system satisfies $R_0^L = \max\{R_D^L, R_Z^L\}$, which indicates that the virus with the greater replication and transmission capability within the host dominates the early-stage infection dynamics and possesses a competitive advantage during the initial phase of infection. Furthermore, invasion reproduction numbers $R_D^{L,inv}$ and $R_Z^{L,inv}$ were obtained to characterize the competitive ability of one virus to establish infection in a host environment where the other virus has already reached its endemic equilibrium.

These four threshold quantities, R_D^L, R_Z^L, $R_D^{L,inv}$ and $R_Z^{L,inv}$, were shown to completely determine the existence, and global asymptotic stability of the four biologically feasible equilibria: the disease-free state (EQ^0), DENV mono-infection (EQ^*), ZIKV mono-infection ($\overline{EQ}$), and DENV–ZIKV co-infection ($\widetilde{EQ}$). The global threshold behavior of the system was rigorously established using Lyapunov functional techniques adapted to distributed-delay systems.

8.1. Key findings

- EQ^0 always exists. EQ^* exists whenever ($R_D^L > 1$), while ($\overline{EQ}$) exists whenever ($R_Z^L > 1$). The coexistence equilibrium ($\widetilde{EQ}$) exists whenever ($R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$).

- EQ^0 is G.A.S when $R_0^L \leq 1$ implying that the infection will disappear regardless of the initial conditions, and the system returns to a healthy state. If $R_D^L > 1$ and $R_Z^{L,inv} \leq 1$, the system converges to EQ^*. In this case, DENV establishes persistent infection sustained by its reproduction potential, whereas ZIKV fails to invade due to an unfavorable effective reproduction threshold in the DENV-established immune environment. Similarly, when $R_Z^L > 1$ and $R_D^{L,inv} \leq 1$, then $\overline{EQ}$ becomes G.A.S. Here, CTL dynamics and viral competition prevent DENV from successfully invading the ZIKV-dominated host environment. In contrast, if $R_D^{L,inv} > 1$ and $R_Z^{L,inv} > 1$, then $\widetilde{EQ}$ is G.A.S. In this regime, each virus can successfully invade and persist despite the presence of the other, leading to long-term co-infection maintained through a balance

between viral replication and CTL-mediated immune pressure. Numerical simulations conducted under variations of the infection rates β_D and β_Z confirmed the global stability properties of all four equilibrium states.

- The model was extended to incorporate antiviral control parameters u_D and u_Z, which reduce viral entry, modifying the infection rates to $(1 - u_D)\beta_D$ and $(1 - u_Z)\beta_Z$, where $u_D, u_Z \in [0, 1]$. Under this modification, the effective reproduction numbers become functions of the control levels. It was shown that EQ^0 becomes G.A.S whenever the controlled reproduction numbers satisfy $R_D^L(u_D) \leq 1$ and $R_Z^L(u_Z) \leq 1$. Thus, sufficiently large treatment efficacy levels drive both effective reproduction numbers below unity, leading to elimination of DENV and ZIKV from the host. Numerical simulations confirmed that sufficiently strong antiviral intervention reduces viral concentration and restores global stability of the disease-free equilibrium.

- Sensitivity analysis revealed that the recruitment rate λ, infection rates β_D and β_Z, viral production rates k_D, and k_Z, natural death rate d and viral clearance rates c_D and c_Z exert the strongest influence on system dynamics.

- Examination of intracellular delay effects revealed that longer delay periods decrease (R_D^L) and (R_Z^L), producing an effect analogous to antiviral therapy. Hence, extending intracellular delays may represent a viable mechanism for reducing reproduction thresholds below one and achieving viral elimination. Moreover, comparison between the delayed and delay-free formulations showed that neglecting intracellular time delays leads to an overestimation of viral reproduction numbers and the minimum antiviral efficacy required for infection control.

- The role of latently infected cells was further examined by comparing the full model with a reduced formulation lacking latent compartments. The results demonstrated that the inclusion of latent infection stages decreases (R_D^L) and (R_Z^L), whereas neglecting latency leads to an overestimation of viral reproduction potential and antiviral treatment thresholds.

8.2. Limitations and future work

A limitation of this framework is the use of a bilinear CTL proliferation term, which provides a simplified representation of immune activation and does not explicitly account for saturation effects, antigen-presentation delays, or immune exhaustion. Furthermore, the sensitivity analysis performed in this study is local in nature.

Another limitation arises from the lack of reliable clinical co-infection data for DENV–ZIKV systems. Consequently, the numerical simulations are not calibrated using patient-specific observations; instead, parameter values are adopted from related mono-infection studies or selected within biologically reasonable ranges to illustrate the qualitative behavior of the model.

The framework also assumes independent DENV- and ZIKV-specific CTL responses. Since DENV and ZIKV are antigenically related flaviviruses, cross-reactive CTL responses may influence immune competition and cross-protection during co-infection. In future studies, researchers may incorporate CTL cross immunity by enabling DENV-specific CTLs to partially target ZIKV-infected cells and vice versa through additional immune interaction terms. However, such an extension would substantially increase model complexity and require additional biological assumptions and parameter estimation.

In future work, we will focus on obtaining sufficiently rich real-world or in vivo co-infection data to enable reliable parameter estimations and full model validations, thereby enabling a more rigorous assessment of the model's predictive capability. Additional extensions may incorporate nonlinear immune activation mechanisms, global sensitivity analysis, and parameter uncertainty quantification to further evaluate the robustness of the predicted DENV–ZIKV co-infection dynamics.

Mathematical virology and epidemiological models with diffusion have received considerable attention in recent years [67, 68]. This model may also be extended to a delayed PDE framework by incorporating the spatial diffusion of cells and virus particles. This extension will be explored in future work.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

The authors declare there is no conflict of interest.

Author contributions

Conceptualization, AE, ZA and EA; Methodology, AE; Formal analysis, AE and ZA; Investigation, AE; Resources, EA; Writing—original draft preparation, ZA; Writing—review and editing, AE and EA. All authors have read and agreed to the published version of the manuscript.

Appendix

A: Basic reproduction number

The basic reproduction number represents the expected number of newly infected cells generated by a single infected cell over its infectious lifespan, assuming that the entire population of target cells is initially uninfected. This threshold quantity is evaluated at the Disease-free equilibrium state.

i. Determination of the basic reproduction number for DENV single infection

To derive the DENV-only subsystem, all ZIKV-related variables are removed by setting $Y_Z^L = Y_Z^A = V_Z = 0$ in system in Eq (2.1)–(2.9). The resulting reduced system is given by:

$$\frac{dX}{dt} = \lambda - dX - \beta_D X V_D - \beta_Z X V_Z, \tag{A.1}$$

$$\frac{dY_D^L}{dt} = (1-\theta_D)\beta_D \int_0^{S_1} f_1(\tau) e^{-n_1\tau} X_\tau V_{D\tau}\, d\tau - (\eta_D + b_D) Y_D^L, \tag{A.2}$$

$$\frac{dY_D^A}{dt} = \theta_D \beta_D \int_0^{S_2} f_2(\tau) e^{-n_2\tau} X_\tau V_{D\tau}\, d\tau + \eta_D \int_0^{S_3} f_3(\tau) e^{-n_3\tau} Y_D^L d\tau - a_D Y_D^A - \delta_D Y_D^A U_D, \tag{A.3}$$

$$\frac{dV_D}{dt} = k_D \int_0^{S_7} f_7(\tau) e^{-n_7\tau} Y_{D\tau}^A\, d\tau - c_D V_D, \tag{A.4}$$

$$\frac{dU_D}{dt} = \varphi_D + \rho_D Y_D^A U_D - \psi_D U_D, \tag{A.5}$$

$$\frac{dU_Z}{dt} = \varphi_Z - \psi_Z U_Z. \tag{A.6}$$

The disease-free equilibrium (DFE) of the system in Eqs (A.1)–(A.6) is $EQ^0 = (X^0, 0, 0, 0, U_D^0, U_Z^0)$, where $X^0 = \frac{\lambda}{d}$, $U_D^0 = \frac{\varphi_D}{\psi_D}$, and $U_Z^0 = \frac{\varphi_Z}{\psi_Z}$.

Using the next-generation matrix approach, the basic reproduction number for DENV, denoted by R_D^L, is obtained as the spectral radius $\rho(\mathbb{F}_D \mathbb{V}_D^{-1})$, where $\mathbb{F}_D$ corresponds to new infection terms and $\mathbb{V}_D$ contains all remaining transition terms.

Define

$$\mathcal{F}_D = \begin{bmatrix} (1-\theta_D)\beta_D \int_0^{S_1} \Pi_1(\tau) X_\tau V_{D\tau}\, d\tau \\ \theta_D \beta_D \int_0^{S_2} \Pi_2(\tau) X_\tau V_{D\tau}\, d\tau \\ 0 \end{bmatrix}, \quad \mathcal{V}_D = \begin{bmatrix} (\eta_D + b_D) Y_D^L \\ -\eta_D \int_0^{S_3} \Pi_3(\tau) Y_D^L d\tau + a_D Y_D^A + \delta_D Y_D^A U_D \\ -\int_0^{S_7} \Pi_7(\tau) Y_{D\tau}^A\, d\tau + c_D V_D \end{bmatrix}.$$

Linearizing at the DFE yields the Jacobian matrices

$$\mathbb{F}_D = \begin{bmatrix} 0 & 0 & (1-\theta_D)\beta_D F_1 \frac{\lambda}{d} \\ 0 & 0 & \theta_D \beta_D F_2 \frac{\lambda}{d} \\ 0 & 0 & 0 \end{bmatrix}, \quad \mathbb{V}_D = \begin{bmatrix} \eta_D + b_D & 0 & 0 \\ -\eta_D F_3 & a_D + \delta_D \frac{\varphi_D}{\psi_D} & 0 \\ 0 & -k_D F_7 & c_D \end{bmatrix}.$$

Therefore,

$$R_D^L = \rho(\mathbb{F}_D \mathbb{V}_D^{-1}) = \frac{k_D \beta_D \lambda \psi_D F_7 \sigma_D}{d c_D (\eta_D + b_D)(a_D \psi_D + \delta_D \varphi_D)},$$

where

$$\sigma_D = (\eta_D + b_D)\theta_D e^{-n_2 \tau_2} + \eta_D (1-\theta_D) e^{-(n_1 \tau_1 + n_3 \tau_3)}.$$

ii. Determination of the basic reproduction number for ZIKV single infection

Following the same procedure, the ZIKV-only subsystem is obtained by setting $Y_D^L = Y_D^A = V_D = 0$ in the system in Eqs (2.1)–(2.9):

$$\frac{dX}{dt} = \lambda - dX - \beta_D X V_D - \beta_Z X V_Z, \tag{A.7}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z \int_0^{S_4} f_4(\tau) e^{-n_4 \tau} X_\tau V_{Z\tau}\, d\tau - (\eta_Z + b_Z) Y_Z^L, \tag{A.8}$$

$$\frac{dY_Z^A}{dt} = \theta_Z \beta_Z \int_0^{S_5} f_5(\tau) e^{-n_5 \tau} X_\tau V_{Z\tau}\, d\tau + \eta_Z \int_0^{S_6} f_6(\tau) e^{-n_6 \tau} Y_{Z\tau}^L d\tau - a_Z Y_Z^A - \delta_Z Y_Z^A U_Z, \tag{A.9}$$

$$\frac{dV_Z}{dt} = k_Z \int_0^{S_8} f_8(\tau) e^{-n_8 \tau} Y_{Z\tau}^A\, d\tau - c_Z V_Z, \tag{A.10}$$

$$\frac{dU_D}{dt} = \varphi_D - \psi_D U_D, \tag{A.11}$$

$$\frac{dU_Z}{dt} = \varphi_Z + \rho_Z Y_Z^A U_Z - \psi_Z U_Z. \tag{A.12}$$

Applying the next-generation matrix method again,

$$R_Z^L = \rho(\mathbb{F}_Z\mathbb{V}_Z^{-1}) = \frac{k_Z\beta_Z\lambda\psi_Z F_8\sigma_Z}{dc_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)},$$

where

$$\sigma_Z = (\eta_Z+b_Z)\theta_Z e^{-n_5\tau_5} + \eta_Z(1-\theta_Z)e^{-(n_4\tau_4+n_6\tau_6)}.$$

iii. Computation of the basic reproduction number for DENV/ZIKV co-infection

In a similar way, we can calculate the basic reproduction number for DENV–ZIKV co-infection model in Eqs (2.1)–(2.9), as $R_0^L = \rho(\mathbb{F}_0\mathbb{V}_0^{-1})$, where

$$\mathbb{F}_0 = \begin{bmatrix} 0 & 0 & 0 & 0 & (1-\theta_D)\beta_D F_1 X^0 & 0 \\ 0 & 0 & 0 & 0 & \theta_D\beta_D F_2 X^0 & 0 \\ 0 & 0 & 0 & 0 & 0 & (1-\theta_Z)\beta_Z F_4 X^0 \\ 0 & 0 & 0 & 0 & 0 & \theta_Z\beta_Z F_5 X^0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \text{ and}$$

$$\mathbb{V}_0 = \begin{bmatrix} \eta_D+b_D & 0 & 0 & 0 & 0 & 0 \\ -\eta_D F_3 & a_D+\delta_D U_D^0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \eta_Z+b_Z & 0 & 0 & 0 \\ 0 & 0 & -\eta_Z F_6 & a_Z+\delta_Z U_Z^0 & 0 & 0 \\ 0 & -k_D F_7 & 0 & 0 & c_D & 0 \\ 0 & 0 & 0 & -k_Z F_8 & 0 & c_Z \end{bmatrix}.$$

Then, the next generation matrix at the Disease-free equilibrium, denoted as $\mathbb{F}_0\mathbb{V}_0^{-1}$, is obtained by multiplying the infection matrix $\mathbb{F}_0$ with the inverse of the transition matrix $\mathbb{V}_0^{-1}$. Therefore, the basic reproductive number for the co-infection model is:

$$R_0^L = \rho(\mathbb{F}_0\mathbb{V}_0^{-1}) = \max\left\{\frac{k_D\beta_D\lambda\psi_D F_7\sigma_D}{dc_D(\eta_D+b_D)(a_D\psi_D+\delta_D\varphi_D)}, \frac{k_Z\beta_Z\lambda\psi_Z F_8\sigma_Z}{dc_Z(\eta_Z+b_Z)(a_Z\psi_Z+\delta_Z\varphi_Z)}\right\} = \max\{R_D^L, R_Z^L\}.$$

B: The invasion reproduction numbers

In between-host dynamics, the invasion reproduction number quantifies the ability of a new disease to invade a population in which another disease is already at an endemic equilibrium [69, 70]. In within-host viral dynamics, it measures the ability of a new virus to invade a host in which another virus has already established an infected equilibrium [71].

i. Invasion of DENV into a ZIKV-resident host

Assume that ZIKV is resident at the ZIKV mono-infection equilibrium $\overline{EQ} = (\overline{X}, 0, 0, \overline{Y}_Z^L, \overline{Y}_Z^A, 0, \overline{V}_Z, \overline{U}_D, \overline{U}_Z)$, where

$$\overline{X} = \frac{\lambda c_Z}{dc_Z + \beta_Z k_Z F_8 \overline{Y}_Z^A},\ \overline{Y}_D^L = 0,\ \overline{Y}_Z^L = \frac{(1-\theta_Z)\beta_Z k_Z F_4 F_8 \lambda \overline{Y}_Z^A}{(\eta_Z+b_Z)(dc_Z+\beta_Z k_Z F_8 \overline{Y}_Z^A)},$$

$$\overline{V}_D = 0,\ \overline{V}_Z = \frac{k_Z F_8}{c_Z}\overline{Y}_Z^A,\ \overline{U}_D = \frac{\varphi_D}{\psi_D} > 0 \text{ and } \overline{U}_Z = \frac{\varphi_Z}{\psi_Z - \rho_Z \overline{Y}_Z^A} \text{ where } \overline{Y}_Z \in \left(0, \frac{\psi_Z}{\rho_Z}\right).$$

The invasion reproduction number of DENV is derived by considering the system in Eqs (A.1)–(A.6) and evaluating the Jacobian matrices of $\mathcal{F}_D$ and $\mathcal{V}_D$ at the equilibrium $\overline{EQ}$, yielding

$$\mathbb{F}_D^{L,inv} = \begin{bmatrix} 0 & 0 & (1-\theta_D)\beta_D F_1 \overline{X} \\ 0 & 0 & \theta_D \beta_D F_2 \overline{X} \\ 0 & 0 & 0 \end{bmatrix}, \mathbb{V}_D^{L,inv} = \begin{bmatrix} \eta_D + b_D & 0 & 0 \\ -\eta_D F_3 & a_D + \delta_D \overline{U}_D & 0 \\ 0 & -k_D F_7 & c_D \end{bmatrix}.$$

Thus, the invasion reproduction number of DENV is given by

$$R_D^{L,inv} = \rho\left(\mathbb{F}_D^{inv}\mathbb{V}_D^{inv-1}\right) = \frac{k_D\beta_D F_7 \sigma_D \overline{X}}{c_D(a_D + \delta_D \overline{U}_D)(\eta_D + b_D)} = \frac{k_D\beta_D \lambda \psi_D F_7 \sigma_D}{dc_D(a_D\psi_D + \delta_D\varphi_D)(\eta_D + b_D)\left(1 + \frac{k_Z\beta_Z F_8}{dc_Z}\overline{Y}_Z^A\right)}.$$

ii. Invasion of ZIKV into a DENV-resident host

Assume that DENV is a resident at the DENV mono-infection equilibrium $EQ^* = (X^*, Y_D^{L*}, Y_D^{A*}, 0, 0, V_D^*, 0, U_D^*, U_Z^*)$, where

$$\begin{aligned} X^* &= \frac{\lambda c_D}{dc_D + \beta_D k_D F_7 Y_D^{A*}},\ Y_D^{L*} = \frac{(1-\theta_D)\beta_D k_D F_1 F_7 \lambda Y_D^{A*}}{(\eta_D + b_D)(dc_D + \beta_D k_D F_7 Y_D^{A*})}, \\ Y_Z^{L*} &= 0,\ Y_Z^{A*} = 0, V_D^* = \frac{k_D F_7}{c_D} Y_D^{A*},\ V_Z^* = 0, \\ U_D^* &= \frac{\varphi_D}{\psi_D - \rho_D Y_D^{A*}} \text{ and } U_Z^* = \frac{\varphi_Z}{\psi_Z}. \end{aligned}$$

Consider Eqs (A.7)–(A.12). The corresponding next-generation matrices for ZIKV invading a DENV-resident host are given by

$$\mathbb{F}_Z^{inv} = \begin{bmatrix} 0 & 0 & (1-\theta_Z)\beta_Z F_4 X^* \\ 0 & 0 & \theta_Z \beta_Z F_5 X^* \\ 0 & 0 & 0 \end{bmatrix}, \mathbb{V}_Z^{inv} = \begin{bmatrix} \eta_Z + b_Z & 0 & 0 \\ -\eta_Z F_6 & a_Z + \delta_Z U_Z^* & 0 \\ 0 & -k_Z F_8 & c_Z \end{bmatrix}.$$

Hence, the invasion reproductive number of ZIKV is

$$R_Z^{L,inv} = \rho\left(\mathbb{F}_Z^{inv}\mathbb{V}_Z^{inv-1}\right) = \frac{k_Z\beta_Z F_8 \sigma_Z X^*}{c_Z(a_Z + \delta_Z U_Z^*)(\eta_Z + b_Z)} = \frac{k_Z\beta_Z \lambda \psi_Z F_8 \sigma_Z}{dc_Z(a_Z\psi_Z + \delta_Z\varphi_Z)(\eta_Z + b_Z)\left(1 + \frac{k_D\beta_D F_7}{dc_D} Y_D^{A*}\right)}.$$

References

1. K. Bessey, M. Mavis, J. Rebaza, J. Zhang, Global stability analysis of a general model of Zika virus, *Nonauton. Dyn. Syst.*, **6** (2019), 18–34. https://doi.org/10.1515/msds-2019-0002
2. World Health Organization, *Dengue and Severe Dengue*, 2025. Available from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

3. N. Haider, M. N. Hasan, J. Onyango, M. Billah, S. Khan, D. Papakonstantinou, et al., Global dengue epidemic worsens with record 14 million cases and 9,000 deaths reported in 2024, *Int. J. Infect. Dis.*, **158** (2025), 107940. https://doi.org/10.1016/j.ijid.2025.107940

4. I. B. Rabe, S. L. Hills, J. M. Haussig, A. T. Walker, T. Dos Santos, J. L. San Martin, et al., A review of the recent epidemiology of Zika virus infection, *Am. J. Trop. Med. Hyg.*, **112** (2025), 1026–1035. https://doi.org/10.4269/ajtmh.24-0420

5. D. D. Chaplin, Overview of the immune response, *J. Allergy Clin. Immunol.*, **125** (2010), S3–S23. https://doi.org/10.1016/j.jaci.2009.12.980

6. A. Iwasaki, R. Medzhitov, Control of adaptive immunity by the innate immune system, *Nat. Immunol.*, **16** (2015), 343–353. https://doi.org/10.1038/ni.3123

7. L. Rivino, M. Q. Lim, $CD4^+$ and $CD8^+$ T-cell immunity to dengue—Lessons for the study of Zika virus, *Immunology*, **150** (2017), 146–154. https://doi.org/10.1111/imm.12681

8. J. Wen, W. W. Tang, N. Sheets, J. Ellison, A. Sette, K. Kim, et al., Identification of Zika virus epitopes reveals immunodominant and protective roles for $CD8^+$ T cells, *Nat. Microbiol.*, **2** (2017), 17036. https://doi.org/10.1038/nmicrobiol.2017.36

9. C. Kribs, D. Greenhalgh, Impact of tetravalent dengue vaccination with screening, ADE and altered infectivity on single-serotype dengue and Zika transmission, *J. Math. Biol.*, **86** (2023), 85. https://doi.org/10.1007/s00285-023-01915-7

10. W. G. Valiant, Y. J. S. Huang, D. L. Vanlandingham, S. Higgs, M. G. Lewis, J. J. Mattapallil, Zika convalescent macaques display delayed induction of anamnestic cross-neutralizing antibody responses after dengue infection, *Emerg. Microbes Infect.*, **7** (2018), 1–11. https://doi.org/10.1038/s41426-018-0132-z

11. M. Mercado-Reyes, J. Acosta-Reyes, E. Navarro-Lechuga, S. Corchuelo, A. Rico, E. Parra, et al., Dengue, chikungunya and zika virus coinfection: Results of the national surveillance during the zika epidemic in Colombia, *Epidemiol. Infect.*, **147** (2019), e77. https://doi.org/10.1017/S095026881800359X

12. M. Y. Carrillo-Hernandez, J. Ruiz-Saenz, L. J. Villamizar, S. Y. Gomez-Rangel, M. Martinez-Gutierrez, Co-circulation and simultaneous co-infection of dengue, chikungunya and zika viruses in patients with febrile syndrome at the Colombian-Venezuelan border, *BMC Infect. Dis.*, **18** (2018), 61. https://doi.org/10.1186/s12879-018-2976-1

13. R. Ben-Shachar, K. Koelle, Minimal within-host dengue models highlight the specific roles of the immune response in primary and secondary dengue infections, *J. R. Soc. Interface*, **12** (2015), 20140886. https://doi.org/10.1098/rsif.2014.0886

14. R. Nikin-Beers, S. M. Ciupe, Modelling original antigenic sin in dengue viral infection, *Math. Med. Biol.*, **35** (2018), 257–272. https://doi.org/10.1093/imammb/dqx002

15. C. E. Osuna, S. Y. Lim, C. Deleage, B. D. Griffin, D. Stein, L. T. Schroeder, et al., Zika viral dynamics and shedding in rhesus and cynomolgus macaques, *Nat. Med.*, **22** (2016), 1448–1455. https://doi.org/10.1038/nm.4206

16. K. Best, J. Guedj, V. Madelain, X. De Lamballerie, S. Y. Lim, C. E. Osuna, et al., Zika plasma viral dynamics in nonhuman primates provides insights into early infection and antiviral strategies, *Proc. Natl. Acad. Sci. USA*, **114** (2017), 8847–8852. https://doi.org/10.1073/pnas.1704011114

17. K. Best, A. S. Perelson, Mathematical modeling of within-host Zika virus dynamics, *Immunol. Rev.*, **285** (2018), 81–96. https://doi.org/10.1111/imr.12687

18. R. Nikin-Beers, S. M. Ciupe, The role of antibody in enhancing dengue virus infection, *Math. Biosci.*, **263** (2015), 83–92. https://doi.org/10.1016/j.mbs.2015.02.004

19. N. Tuncer, M. Martcheva, Determining reliable parameter estimates for within-host and within-vector models of Zika virus, *J. Biol. Dyn.*, **15** (2021), 430–454. https://doi.org/10.1080/17513758.2021.1970261

20. K. Best, D. H. Barouch, J. Guedj, R. M. Ribeiro, A. S. Perelson, Zika virus dynamics: Effects of inoculum dose, the innate immune response and viral interference, *PLoS Comput. Biol.*, **17** (2021), e1008564. https://doi.org/10.1371/journal.pcbi.1008564

21. N. Nuraini, H. Tasman, E. Soewono, K. A. Sidarto, A within-host dengue infection model with immune response, *Math. Comput. Model.*, **49** (2009), 1148–1155. https://doi.org/10.1016/j.mcm.2008.06.016

22. S. D. Perera, S. S. N. Perera, Impact of innate and cell mediated immune responses on dengue virus dynamics, *Int. J. Pure Appl. Math.*, **118** (2018), 353–360. Available from: https://acadpubl.eu/jsi/2018-118-6/articles/6/39.pdf.

23. S. D. Perera, S. S. N. Perera, Simulation model for dynamics of dengue with innate and humoral immune responses, *Comput. Math. Methods Med.*, **2018** (2018), 8798057. https://doi.org/10.1155/2018/8798057

24. S. D. Perera, S. S. N. Perera, Mathematical modeling and analysis of innate and humoral immune responses to dengue infections, *Int. J. Biomath.*, **12** (2019), 1950077. https://doi.org/10.1142/S1793524519500773

25. H. Ansari, M. Hesaaraki, A within-host dengue infection model with immune response and Beddington—DeAngelis incidence rate, *Appl. Math.*, **3** (2012), 177–184. https://doi.org/10.4236/am.2012.32028

26. J. J. Thibodeaux, D. Nunez, A. Rivera, A generalized within-host model of dengue infection with a non-constant monocyte production rate, *J. Biol. Dyn.*, **14** (2020), 143–161. https://doi.org/10.1080/17513758.2020.1733678

27. Q. Liu, D. Jiang, T. Hayat, A. Alsaedi, Stationary distribution of a stochastic within-host dengue infection model with immune response and regime switching, *Phys. A*, **526** (2019), 121057. https://doi.org/10.1016/j.physa.2019.121057

28. B. Modak, P. Muthu, Stochastic approach to a delayed in-host model of DENV transmission, *Phys. Scr.*, **99** (2024), 075006. https://doi.org/10.1088/1402-4896/ad4ea6

29. S. K. Sasmal, Y. Dong, Y. Takeuchi, Mathematical modeling on T-cell mediated adaptive immunity in primary dengue infections, *J. Theor. Biol.*, **429** (2017), 229–240. https://doi.org/10.1016/j.jtbi.2017.06.035

30. A. Mishra, S. Gakkhar, A micro-epidemic model for primary dengue infection, *Commun. Nonlinear Sci. Numer. Simul.*, **47** (2017), 426–437. https://doi.org/10.1016/j.cnsns.2016.12.001

31. M. Cerón Gómez, H. M. Yang, Mathematical model of the immune response to dengue virus, *J. Appl. Math. Comput.*, **63** (2020), 455–478. https://doi.org/10.1007/s12190-020-01325-8

32. S. K. Sasmal, Y. Takeuchi, S. Nakaoka, T-cell mediated adaptive immunity and antibody-dependent enhancement in secondary dengue infection, *J. Theor. Biol.*, **470** (2019), 50–63. https://doi.org/10.1016/j.jtbi.2019.03.010

33. M. Borisov, G. Dimitriu, P. Rashkov, Modelling the host immune response to mature and immature dengue viruses, *Bull. Math. Biol.*, **81** (2019), 4951–4976. https://doi.org/10.1007/s11538-019-00664-3

34. F. de A. Camargo, M. Adimy, L. Esteva, C. Métayer, C. P. Ferreira, Modeling the relationship between antibody-dependent enhancement and disease severity in secondary dengue infection, *Bull. Math. Biol.*, **83** (2021), 85. https://doi.org/10.1007/s11538-021-00919-y

35. M. A. Alshaikh, E. Elnahary, A. M. Elaiw, Stability of a secondary dengue viral infection model with multi-target cells, *Alexandria Eng. J.*, **61** (2022), 7075–7087. https://doi.org/10.1016/j.aej.2021.12.050

36. A. A. Raezah, Dynamical analysis of secondary dengue viral infection with multiple target cells and diffusion by mathematical model, *Discrete Dyn. Nat. Soc.*, **2022** (2022), 2106910. https://doi.org/10.1155/2022/2106910

37. F. Alves Rubio, H. M. Yang, A mathematical model to describe antibody-dependent enhancement and assess the effect of limiting cloning for plasma cells in heterologous secondary dengue infection, *Math. Med. Biol.*, **39** (2022), 169–196. https://doi.org/10.1093/imammb/dqab021

38. S. Rashid, F. Jarad, S. A. El-Marouf, S. K. Elagan, Global dynamics of deterministic-stochastic dengue infection model including multi specific receptors via crossover effects, *AIMS Math.*, **8** (2023), 6466–6503. https://doi.org/10.3934/math.2023327

39. T. P. Gujarati, G. Ambika, Virus antibody dynamics in primary and secondary dengue infections, *J. Math. Biol.*, **69** (2014), 1773–1800. https://doi.org/10.1007/s00285-013-0749-4

40. R. O. Aldubiban, A. M. Elaiw, E. A. Almohaimeed, A. D. Hobiny, Global properties of secondary DENV infection models with pre-existing CTL immunity and discrete/distributed delays, *Int. J. Anal. Appl.*, **23** (2025), 88. https://doi.org/10.28924/2291-8639-23-2025-88

41. S. A. Jose, R. Raja, B. I. Omede, R. P. Agarwal, J. Alzabut, J. Cao, et al., Mathematical modeling on co-infection: Transmission dynamics of Zika virus and dengue fever, *Nonlinear Dyn.*, **111** (2023), 4879–4914. https://doi.org/10.1007/s11071-022-08063-5

42. N. O. Iheonu, U. K. Nwajeri, A. Omame, A non-integer order model for Zika and dengue co-dynamics with cross-enhancement, *Healthcare Anal.*, **4** (2023), 100276. https://doi.org/10.1016/j.health.2023.100276

43. C. M. Kribs, P. Mays, Impact of ADE and dengue vaccination with screening on cost and disease burden for homoserotypic dengue and Zika, *Bull. Math. Biol.*, **87** (2025), 62. https://doi.org/10.1007/s11538-025-01440-2

44. B. Tang, Y. Xiao, B. Sander, M. A. Kulkarni, Radam-Lac Research Team, J. Wu, Modelling the impact of antibody-dependent enhancement on disease severity of Zika virus and dengue virus sequential and co-infection, *R. Soc. Open Sci.*, **7** (2020), 191749. https://doi.org/10.1098/rsos.191749

45. A. M. Elaiw, Z. Y. Alkhudhari, A. D. Hobiny, Within-host dynamics, stability, and treatment approaches for Dengue–Zika virus co-infection with CTL immunity, *Adv. Contin. Discrete Models*, 2026. https://doi.org/10.1186/s13662-026-04105-z

46. Y. Kuang, *Delay Differential Equations with Applications in Population Dynamics*, Academic Press, Boston, 1993. Available from: https://shop.elsevier.com/books/delay-differential-equations/kuang/978-0-12-427610-9.

47. J. K. Hale, S. M. Verduyn Lunel, *Introduction to Functional Differential Equations*, Springer-Verlag, New York, 1993. https://doi.org/10.1007/978-1-4612-4342-7

48. A. M. Elaiw, G. S. Alsaadi, A. D. Hobiny, Global co-dynamics of viral infections with saturated incidence, *AIMS Math.*, **9** (2024), 13770–13818. https://doi.org/10.3934/math.2024671

49. W. Li, L. Yang, J. Cao, Threshold dynamics of a degenerated diffusive incubation period host—Pathogen model with saturation incidence rate, *Appl. Math. Lett.*, **160** (2025), 109312. https://doi.org/10.1016/j.aml.2024.109312

50. Z. Xu, H. Zhang, D. Yang, D. Wei, J. Demongeot, Q. Zeng, The mathematical modeling of the host-virus interaction in dengue virus infection: A quantitative study, *Viruses*, **16** (2024), 216. https://doi.org/10.3390/v16020216

51. A. E. S. Almocera, V. K. Nguyen, E. A. Hernandez-Vargas, Multiscale model within-host and between-host for viral infectious diseases, *J. Math. Biol.*, **77** (2018), 1035–1057. https://doi.org/10.1007/s00285-018-1241-y

52. S. A. Gourley, Y. Kuang, J. D. Nagy, Dynamics of a delay differential equation model of hepatitis B virus infection, *J. Biol. Dyn.*, **2** (2008), 140–153. https://doi.org/10.1080/17513750701769873

53. L. Min, Y. Su, Y. Kuang, Mathematical analysis of a basic virus infection model with application to HBV infection, *Rocky Mt. J. Math.*, **38** (2008), 1573–1585. https://doi.org/10.1216/RMJ-2008-38-5-1573

54. S. Han, C. Lei, X. Zhang, Qualitative analysis on a diffusive SIRS epidemic model with standard incidence infection mechanism, *Z. Angew. Math. Phys.*, **71** (2020), 190. https://doi.org/10.1007/s00033-020-01418-1

55. Y. Pan, S. Zhu, J. Wang, Asymptotic profiles of a diffusive SIRS epidemic model with standard incidence mechanism and a logistic source, *Z. Angew. Math. Phys.*, **73** (2022), 36. https://doi.org/10.1007/s00033-021-01667-8

56. H. Sage, H. M. Dobrovolny, Exploring the effect of density dependent infection rate in a within-host viral infection model, *Math. Biosci. Eng.*, **23** (2026), 1687–1707. https://doi.org/10.3934/mbe.2026061

57. H. Zhao, L. Jin, S. L. Wu, Spreading speed for a delayed epidemic model incorporating Beddington—DeAngelis incidence rate, *Appl. Math. Lett.*, **179** (2026), 109969. https://doi.org/10.1016/j.aml.2026.109969

58. G. Huang, Y. Takeuchi, W. Ma, Lyapunov functionals for delay differential equations model of viral infections, *SIAM J. Appl. Math.*, **70** (2010), 2693–2708. https://doi.org/10.1137/090780821

59. P. T. Karaji, N. Nyamoradi, Analysis of a fractional SIR model with general incidence function, *Appl. Math. Lett.*, **108** (2020), 106499. https://doi.org/10.1016/j.aml.2020.106499

60. X. Yang, L. Chen, J. Chen, Permanence and positive periodic solution for the single-species nonautonomous delay diffusive models, *Comput. Math. Appl.*, **32** (1996), 109–116. https://doi.org/10.1016/0898-1221(96)00129-0

61. P. Van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.*, **180** (2002), 29–48. https://doi.org/10.1016/S0025-5564(02)00108-6

62. P. Dubey, U. S. Dubey, B. Dubey, Modeling the dynamics of viral-host interaction during treatment of productively infected cells and free virus involving total immune response, *Nonlinear Anal. Model. Control*, **26** (2021), 678–701. https://doi.org/10.15388/namc.2021.26.21434

63. A. Korobeinikov, Global properties of basic virus dynamics models, *Bull. Math. Biol.*, **66** (2004), 879–883. https://doi.org/10.1016/j.bulm.2004.02.001

64. H. Shu, L. Wang, J. Watmough, Global stability of a nonlinear viral infection model with infinitely distributed intracellular delays and CTL immune responses, *SIAM J. Appl. Math.*, **73** (2013), 1280–1302. https://doi.org/10.1137/120896463

65. B. Song, Y. Zhang, Y. Sang, L. Zhang, Stability and Hopf bifurcation on an immunity delayed HBV/HCV model with intra- and extra-hepatic coinfection and saturation incidence, *Nonlinear Dyn.*, **111** (2023), 14485–14511. https://doi.org/10.1007/s11071-023-08580-x

66. S. Marino, I. B. Hogue, C. J. Ray, D. E. Kirschner, A methodology for performing global uncertainty and sensitivity analysis in systems biology, *J. Theor. Biol.*, **254** (2008), 178–196. https://doi.org/10.1016/j.jtbi.2008.04.011

67. W. Li, Y. Zhang, J. Ji, L. Huang, Dynamics of a diffusion epidemic SIRI system in heterogeneous environment, *Z. Angew. Math. Phys.*, **74** (2023), 104. https://doi.org/10.1007/s00033-023-02002-z

68. N. Bellomo, N. Outada, J. Soler, Y. Tao, M. Winkler, Chemotaxis and cross-diffusion models in complex environments: Models and analytic problems toward a multiscale vision, *Math. Models Methods Appl. Sci.*, **32** (2022), 713–792. https://doi.org/10.1142/S0218202522500166

69. N. Hussaini, J. M. Lubuma, K. Barley, A. B. Gumel, Mathematical analysis of a model for AVL-HIV co-endemicity, *Math. Biosci.*, **271** (2016), 80–95. https://doi.org/10.1016/j.mbs.2015.10.008

70. C. Mitchell, C. Kribs, Invasion reproductive numbers for periodic epidemic models, *Infect. Dis. Model.*, **4** (2019), 124–141. https://doi.org/10.1016/j.idm.2019.04.002

71. R. Ding, L. Zhang, H. L. Li, Y. Luo, Z. Teng, Global dynamics on a class of HIV and Mycobacterium tuberculosis co-infection model within body, *Int. J. Biomath.*, 2025, 2550016. https://doi.org/10.1142/S1793524525500160

AIMS Press