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Global stability of a delayed SARS-CoV-2 reactivation model with logistic growth, antibody immunity and general incidence rate

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Abstract Mathematical models have been considered as a robust tool to support biological and medical studies of the coronavirus disease 2019 (COVID-19). This new disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This paper develop a within-host SARS-CoV-2 dynamics model with logistic growth for healthy epithelial cells, humoral (antibody) immune response and general SARS-CoV-2-target incidence rate. The model is incorporated with four mixed (distributed/discrete) time delays, delay in the formation of latent infected epithelial cells, delay in the formation of active infected epithelial cells, delay in the activation of latent infected epithelial cells, and maturation delay of new SARS-CoV-2 particles. The model is formulated as a system of delay differential equations (DDEs). We establish that the model’s solutions are non-negative and ultimately bounded. We deduce that the model has three equilibria and their existence and stability are perfectly determined by two threshold parameters. We prove the global stability of the model’s equilibria by utilizing the Lyapunov method and applying the LaSalle’s invariance principle. To support and illustrate our theoretical findings we present numerical simulations for the model with a special form of the general incidence rate function. The effect of time delays on the SARS-CoV-2 dynamics is addressed. We observe that increasing time delays values can have the same impact as drug therapies in suppressing viral progression.

1. Introduction

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which causes the new coronavirus disease 2019 (COVID-19), has become a global pandemic. World Health Organization (WHO) reported in the
COVID-19 weekly epidemiological update of 20 February 2022 that, over 422 million confirmed cases and over 5.8 million deaths worldwide [1]. SARS-CoV-2 can be transmitted from infected human to healthy one either through direct contact or droplet infection. The transmission of SARS-CoV-2 can be reduced by implementing preventive measures such as hand washing, using of face masks, physical and social distancing, disinfection of surfaces and getting COVID-19 vaccine. Fortunately, WHO approved the following COVID-19 vaccines: Moderna, Oxford/AstraZeneca, Sinovac, Janssen (Johnson & Johnson), Pfizer/BioNTech, Sinpharm (Beijing), Serum Institute of India, Novavax and Bharat Biotech [2]. Beside vaccination, scientists and researchers are working hard to create new effective drugs for COVID-19 patients.

SARS-CoV-2 attacks the healthy epithelial cells which founded in lungs, nasal and trachea/bronchial tissues [3]. The epithelial cells become infected and start producing new SARS-CoV-2 particles which again begin infecting other healthy epithelial cells. When the human body is infected with viruses the immune system start rapidly with innate immune response such as macrophage cells and natural killer cells. After that, adaptive immune response is activated which mainly depends on B Lymphocytes and Cytotoxic T Lymphocytes (CTLs). CTLs kill the viral-infected cells (CTL immune response), while B cells produce antibodies to neutralize viruses (humoral or antibody immune response) [4].

1.1. Mathematical models of within-host SARS-CoV-2 dynamics

Mathematical modeling of within host viral infection allows one to quantify and understand the biological mechanisms of the viral dynamics. By fitting mathematical models to real data, one can estimate the parameters which quantify the interactions between the virus, host cells and immune system as well as the influence of drug therapies and vaccination. Mathematical models can be useful for making predictions about disease progression and drug therapies outcomes [5]. Finally, models can be helped to determine the suitable time of antiviral treatment initiation [6]. In the following, we introduce some mathematical models for within-host SARS-CoV-2 infection (see also the review paper [7]).

1.1.1. Model with constant regeneration of target cells

Following the basic within-host viral infection model presented in [8], Li et al. [9] formulated the following within host SARS-CoV-2 model:

\[
\begin{align*}
\dot{T}(t) &= d_T(T(0) - T(t)) - \xi V(t)T(t), \\
\dot{I}(t) &= \xi V(t)T(t) - d_I I(t), \\
\dot{V}(t) &= \omega I(t) - d_V V(t),
\end{align*}
\]

where \(T(t), I(t)\) and \(V(t)\) represent the concentrations of healthy epithelial cells, active infected cells and SARS-CoV-2 particles at time \(t\), respectively. The healthy epithelial cells are regenerated at a constant rate \(d_T T(0)\) where \(T(0)\) is the concentration of healthy epithelial cells without virus. The parameters \(d_T, d_I\) and \(d_V\) are the death rate constants of healthy epithelial cells, active infected cells and SARS-CoV-2 particles, respectively. \(\xi\) is the virus-target incidence rate constant. The term \(\omega I(t)\) is the rate at which active infected cells generate SARS-CoV-2 particles. The model’s parameters were estimated by using Chest radiograph score data in [9]. Sadrba and Layton [10] formulated a within-host SARS-CoV-2 infection model with constant regeneration of target cells to simulate the effect of three drug therapies, Remdesivir, an alternative (hypothetical) therapy and transfusion therapy convalescent plasma. It was suggested that therapies are more effective when they applied early, one or two days post symptoms onset [10]. Du and Yuan [11] proposed a within-host model of SARS-CoV-2 infection with constant regeneration of target cells. They studied the influence of the interaction between adaptive and innate immune responses on the viral load’s peak in patients with COVID-19. They showed that, temporarily suppress the adaptive immune response to avoid interfering with the innate immune response, it may allow the innate immunity to get rid of the SARS-CoV-2 more efficiently.

1.1.2. SARS-CoV-2 infection models with latency

It was observed experimentally that there exists a time lag between initial infection of a target cell and the emission of new SARS-CoV-2 particles [12]. Therefore, some SARS-CoV-2 infection models were formulated using ordinary differential equations (ODEs) by splitting the infected cells into two populations, latent infected cells and active (productive) infected cells (see e.g. [10–18]). Latent infected cells contain viruses but do not release them until they are activated. SARS-CoV-2 infection model with target cell-limited and latent infected cells was developed in [14] as:

\[
\begin{align*}
\dot{T}(t) &= -\xi V(t)T(t), \\
\dot{L}(t) &= \xi V(t)T(t) - \alpha L(t), \\
\dot{I}(t) &= \alpha L(t) - d_I I(t), \\
\dot{V}(t) &= \omega I(t) - d_V V(t),
\end{align*}
\]

where \(L(t)\) is the concentration of latent infected cells. The term \(\alpha L(t)\) represents the activation rate of latent infected cells. Ke et al. [15] developed some mathematical models for within-host dynamics of SARS-CoV-2 and fitted them to real data. They supported a quantitative framework for concluding the influence of vaccines and therapies on the infectiousness of COVID-19 patients and for assessing rapid testing strategies. Based on model (2), Pinky and Dobrovolny [16] developed a mathematical model for SARS-CoV-2 and other respiratory viruses coinfection within a host. It was reported that SARS-CoV-2 progression can be suppressed by other viruses when the infections occur at the same time. Gonzalvez et al. [6] modified model (2) by including the absorption effect. The last equation of model (2) was modified as:

\[
\dot{V}(t) = \omega I(t) - d_V V(t) - \xi V(t)T(t).
\]

The model was fitted using real data. The results showed that, less drug efficacy is required to reduce the peak viral load when the treatment is starting before the symptom onset. Wang et al. [17] introduced a within-host SARS-CoV-2 dynamics model with two types of target cells (pneumocytes and lymphocytes). They fitted their model and model (2) with real data of COVID-19 patients and non-human primates. The results showed that model with two target cells significantly improves the fit. The effect of antiviral drugs or anti-inflammatory treatments combined with interferon on the viral load and recovery time were studied.
1.1.3. SARS-CoV-2 infection models with immune response

Danchin et al. [19] developed the following SARS-CoV-2 infection model by incorporating the influence of antibody immunity:

\[
\begin{aligned}
\dot{T}(t) &= d_A (T(0) - T(t)) - (\xi + \xi_{ADE}) A(t) V(t), \\
\dot{I}(t) &= (\xi + \xi_{ADE}) A(t) V(t) - \delta I(t), \\
\dot{V}(t) &= a I(t) - d_V V(t) - u A(t) V(t), \\
\dot{A}(t) &= q A(t) V(t) - d_A A(t),
\end{aligned}
\]

where \( A(t) \) represents the concentration of antibodies, \( uAV \) is the neutralization rate of SARS-CoV-2 particles and \( qAV \) is the recruited rate of antibodies. Parameter \( \xi_{ADE} \) represents the rate of antibody-dependent enhancement (ADE) infection route. \( \delta \) is the death rate constant of antibodies. In this model, latent infected cells were not considered.

CTL immune response was included in the SARS-CoV-2 infection model in [20–26]. Mondal et al. [27] developed and analyzed a five-dimensional SARS-CoV-2 dynamics model which includes both CTL and antibody immunities. Ghosh [28] formulated a model that describes the SARS-CoV-2 dynamics with both innate and adaptive immune responses. The model was fitted with real data and the effect of different antiviral drugs was addressed.

Studying the dynamical behavior of within-host SARS-CoV-2 infection models is one of the powerful tools that can provide researchers with better understanding about the dynamics of the virus and how the immune system control and clear the virus. Moreover, optimal control theory can be utilized to specify optimal treatment strategies for COVID-19 infected patients. Nait et al. [29] studied the mathematical analysis of model (1). They proved both local and global stability of the two equilibria of the model. Abuin et al. [30] studied the mathematical analysis of model (2) without considering the latent infected cells. The effect of the antiviral Pharmacodynamic therapy which reduces the production of infectious SARS-CoV-2 particles was studied using control theory. Almoccet et al. [31] studied the stability analysis of a two-dimensional SARS-CoV-2 infection model with effector cells. It was mentioned that SARS-CoV-2 may replicate fast enough to overcome the response of the effector cells and cause infection. Hattaf and Yousfi [20] developed a SARS-CoV-2 dynamics model with cell-to-cell mode and CTL immune response. The global stability of the three equilibria of the model was studied. Chatterjee and Al Basir [26] studied a SARS-CoV-2 infection model with treatment and CTL immune response. Elaiw et al. [32] developed and proved the global stability of a SARS-CoV-2/cancer coinfection model with two immune responses: cancer-specific CTL immune response and SARS-CoV-2-specific antibody. Mathematical modeling and analysis of SARS-CoV-2/HIV coinfection dynamics were studied in [33]. Chhetri et al. [34] formulated and analyzed SARS-CoV-2 dynamics model under the impact of immunomodulating and antiviral drug therapies. Optimal drug interventions were determined. It was suggested that the combination of immunomodulating and antiviral drug therapies is most effective.

Fractional differential equations (FDEs) were used in studying the SARS-CoV-2 dynamics between hosts [21–24] and within-host [25–35]. Ghanbari [25] extended the model presented in [20] by using fractional derivatives. In [35], fractional differential equations were used in formulating within-host SARS-CoV-2 model with non-lytic and lytic immune responses. Two types of antiviral drugs were included as control inputs, one for blocking the infection and the other for inhibiting the viral production. Optimal antiviral drugs were determined by solving the fractional optimal control problem. In [36], the SARS-CoV-2 model with CTL immunity was given by FDEs. Different forms of the proliferation rate of CTLs were considered.

In most of the above-mentioned works, the proliferation of the healthy target cells was not considered. Fatehi et al. [13] and Fadai et al. [37] developed SARS-CoV-2 dynamics models by assuming that the healthy epithelial cells follow logistic growth in the absence of the virus, but they did not study the mathematical analysis of these models. Moreover, the virus-target incidence rate is given by bilinear form \( \xi VT \) which may not be completely characterize the incidence between healthy epithelial cells and SARS-CoV-2 particles. If the number of viruses is too high, so that exposure of a target cell is practically certain, then the incidence rate may respond more slowly than linear to the further increase in the number of the viruses [38]. In the literature of viral infection modelling, many incidence rate forms were proposed such as saturated incidence \( \frac{TV}{1+V} \) [39], Beddington-DeAngelis incidence \( \frac{TV}{1+V(1+c)} \) [40], Crowley-Martin incidence \( \frac{TV}{1+V(1+c)} \) [41], Hill-type incidence \( \frac{TV}{1+V^p} \) [42], and nonlinear incidence rate function \( \Omega(T, V) \) [43,44].

The models presented in [10–18] assumed that one infected, the cell immediately becomes a latent infected cell. Further, these models neglected the time for the latent infected cells to be activated [45]. Furthermore, the maturation time of the new viruses was not considered. To incorporate these time lags we need to formulate the SARS-CoV-2 dynamics using delay differential equations (DDEs). DDEs models can characterize the effect time delay on the dynamical behavior of the virus. DDEs were used to describe the within-host dynamics of several human viruses such as: HIV [46], HTLV [47], HBV [48] and HCV [49].

The objective of the present work is to develop and analyze a within host SARS-CoV-2 infection model by including: (i) logistic growth term for the healthy epithelial cells, (ii) general SARS-CoV-2-target incidence rate (iii) latent and active infected epithelial cells, (iv) antibody immunity, (v) four time delays, the time from the SARS-CoV-2 particles contact the healthy epithelial cells to become latent/active infected cells, the reactivation time of latent infected cells, and the maturation time of new virions. The basic properties and global dynamics of the model are studied. To support the theoretical results we performed some numerical simulations by choosing a special form of the general incidence rate function. The effect of time delay on the dynamics of SARS-CoV-2 is addressed.

Our proposed model can be useful to develop coinfection dynamics model with more aggressive variants of SARS-CoV-2 like Alpha, Beta, Gamma, Delta, Lambda, and Omicron.

2. Model development

This section introduces a brief description of the model under consideration. The model takes the form
The healthy epithelial cells are regenerated at rate \( \ell \) and proliferate at a logistic growth rate \( rT \left( 1 - \frac{T(t)}{T_{\text{max}}} \right) \), where \( r \) is the rate of growth and \( T_{\text{max}} \) is the maximum capacity of healthy epithelial cells in the human body. \( \Omega(T,V) \) is a general function which represents the incidence rate. Parameter \( \eta \in (0,1) \) is the fraction of the healthy epithelial cells that enters the latent state. Parameter \( d_i \) denotes the death rate constant of latent infected cells. The factor \( f(\psi)e^{-\eta\psi} \) denotes the probability that healthy epithelial cells touched by SARS-CoV-2 particles at time instant \( t - \tau \) survived \( \psi \) time units and become latent infected cells at time \( t \). The factor \( g(\psi)e^{-\eta\psi} \) is the probability that healthy epithelial cells touched by SARS-CoV-2 particles at time instant \( t - \tau \) survived \( \psi \) time units and become active infected cells at time \( t \). Here, \( \psi \) is a random variable generated from probability distribution functions \( f(\psi) \) and \( g(\psi) \) over the intervals \([0, \tau_1]\) and \([0, \tau_2]\), respectively. \( \tau_1 \) and \( \tau_2 \) are the upper limits of the delay periods. \( \tau_1 \) is the period of time during which latent infected cells are activated to produce active infected cells. \( \tau_2 \) is the time it takes from the newly released viruses to be mature and then infectious. Factors \( e^{-\eta\psi_1} \) and \( e^{-\eta\psi_2} \) are the survival rates of latent infected and viruses during their delay periods \([t - \tau_1, t]\) and \([t - \tau_2, t]\), respectively.

The functions \( f(\psi) : [0, \tau_1] \to (0,\infty) \) and \( g(\psi) : [0, \tau_2] \to (0,\infty) \) are the distribution functions which satisfy the following conditions:

1. \( f(\psi) > 0 \), \( g(\psi) > 0 \),
2. \( \int_0^{\tau_1} f(\psi) e^{-\psi} d\psi = 1 \), \( \int_0^{\tau_2} g(\psi) e^{-\psi} d\psi = 1 \),
3. \( \int_0^{\tau_1} f(\psi) e^{-\psi} d\psi < \infty \), \( \int_0^{\tau_2} g(\psi) e^{-\psi} d\psi < \infty \), \( n_1, n_2 > 0 \).

Let
\[
F = \int_0^{\tau_1} f(\psi) e^{-\eta\psi} d\psi \quad \text{and} \quad G = \int_0^{\tau_2} g(\psi) e^{-\eta\psi} d\psi. \]

Hence \( 0 < F, G \leq 1 \).

Function \( \Omega(T,V) \) is continuously differentiable and satisfy the following conditions:

- **Condition (C1)** \( \Omega(T,V) > 0 \), \( \Omega(0,V) = \Omega(T,0) = 0 \) for all \( T > 0 \) and \( V > 0 \).
- **Condition (C2)** \( \frac{\partial \Omega(T,V)}{\partial T} > 0 \), \( \frac{\partial \Omega(T,V)}{\partial V} > 0 \) and \( \frac{\partial \Omega(T,0)}{\partial T} > 0 \) for all \( T > 0 \) and \( V > 0 \).
- **Condition (C3)** \( \frac{\partial \Omega(T,V)}{\partial T} \) is decreasing w.r.t \( V \) for all \( V > 0 \).
- **Condition (C4)** \( \frac{\partial \Omega(T,V)}{\partial V} \) is decreasing w.r.t \( V \) for all \( V > 0 \).

The initial conditions of system (3)-(7) are:
\[
T(x) = \varphi_1(x), \quad L(x) = \varphi_2(x), \quad I(x) = \varphi_3(x), \quad V(x) = \varphi_4(x), \quad A(x) = \varphi_5(x), \quad \varphi_i(x) \geq 0, \quad x \in [-\kappa,0], \quad i = 1,2,\ldots,5, \tag{8}
\]
where \( \kappa = \max\{\tau_1, \tau_2, \tau_3, \tau_4\} \) and \( \varphi_i \in \mathcal{C}([-\kappa,0], \mathbb{R}_{\geq 0}) \), \( i = 1,2,\ldots,5 \), and \( \mathcal{C} \) is the Banach space of continuous functions mapping the interval \([-\kappa,0] \) to \( \mathbb{R}_{\geq 0} \) with
\[
\|\varphi_i\| = \sup_{-\kappa \leq x \leq 0} |\varphi_i(x)| \quad \text{for} \quad \varphi_i \in \mathcal{C}. \]

The fundamental theory of functional differential equations [50] guarantees the uniqueness of the model’s solution.

### 3. Basic properties of the model

This section proves the non-negativity and boundedness of solutions. Moreover, it lists all equilibria and deduces the conditions of their existence.

**Theorem 1.** Let \((T(t), L(t), I(t), V(t), A(t))'\) be arbitrary solution of system (3)-(7) with initial conditions (8). Then, \((T(t), L(t), I(t), V(t), A(t))'\) are non-negative on \([0, +\infty)\) and ultimately bounded.

**Proof.** System (3)-(7) can be given in the matrix form \( B(t) = H(B(t)) \), where \( B = (T, L, I, V, A) ', H = (H_1, H_2, H_3, H_4, H_5)' \), and
\[
H(B(t)) = \begin{pmatrix}
H_1(B(t)) \\
H_2(B(t)) \\
H_3(B(t)) \\
H_4(B(t)) \\
H_5(B(t))
\end{pmatrix}
= \begin{pmatrix}
\ell - d_T T(t) + r T(t) \left( 1 - \frac{T(t)}{T_{\text{max}}} \right) - \Omega(T(t), V(t)) \\
\eta \int_0^{\tau_1} f(\psi)e^{-\eta\psi}\Omega(T(t) - \psi, V(t - \psi))d\psi - z L(t) - d_L L(t) \\
(1 - \eta) \int_0^{\tau_2} g(\psi)e^{-\eta\psi}\Omega(T(t) - \psi, V(t - \psi))d\psi + x e^{-\eta\psi} L(t - \tau_1) - d_i I(t) \\
q A(I(t)) - d_A A(t)
\end{pmatrix}
\]

We observe that the function \( H \) fulfills the following condition:
\[
H_i(B(t)) \bigg|_{B(t) \in \mathbb{R}_{\geq 0}^5} \geq 0, \quad i = 1,2,\ldots,5.
\]

Using Using Lemma 2 in [51], any solution of system (3)-(7) with initial (8) is such that \( B(t) \in \mathbb{R}_{\geq 0}^5 \) for all \( t \geq 0 \). Hence, \( \mathbb{R}_{\geq 0}^5 \) is positively invariant for the system (3)-(7).

Next, we prove the ultimate boundedness of the solutions. From Eq. (3), we have
\[
\dot{T}(t) = \ell - d_T T(t) + r T(t) \left( 1 - \frac{T(t)}{T_{\text{max}}} \right) - \Omega(T(t), V(t)), \tag{9}
\]
\[
\dot{V}(t) \leq \ell - d_T T(t) + r T(t) \left( 1 - \frac{T(t)}{T_{\text{max}}} \right).
\]
From the inequality (9) and the comparison principle, we obtain \( \lim_{t \to \infty} T(t) \leq T_0 \), where \( T_0 \) is the positive root of \( \ell - d_T T + r T \left( 1 - \frac{T}{T_{\text{max}}} \right) = 0 \), that is
\[
T_0 = \frac{T_{\text{max}}}{2r} \left[ r - d_T + \sqrt{(r - d_T)^2 + \frac{4\ell}{T_{\text{max}}}} \right]. \tag{10}
\]
Note that the net target cell proliferation rate \( r - d_T \) needs not to be positive [52], therefore we assume that \( d_T \geq r \). Now, we define
\[
W_i(t) = \int_0^{\tau_i} f(\psi)e^{-\eta\psi} T(t - \psi)d\psi + \frac{1}{\eta} L(t).
\]
Then, we get
Let us define $\Gamma(T) = -\frac{2r}{T_{\text{max}}} T^2 + rT + \ell$. Then to find the maximum value of $\Gamma(T)$, we find

$$
\Gamma'(T) = -\frac{4r}{T_{\text{max}}} T + r = 0 \Rightarrow T = \frac{T_{\text{max}}}{2},
$$

and

$$
\Gamma''(T) = -\frac{2r}{T_{\text{max}}^2} < 0.
$$

Then

$$
\Gamma\left(\frac{T_{\text{max}}}{2}\right) = -\frac{r}{T_{\text{max}}^2} \left(\frac{T_{\text{max}}}{2}\right)^2 + r \frac{T_{\text{max}}}{2} + \ell = 0 + \ell = \frac{T_{\text{max}}}{4} + \ell.
$$

Let $N_1 = \frac{T_{\text{max}}^2 + 4 \ell}{4} > 0$ and $q_1 = \min\{d_1, s \} + \frac{\ell}{s}$, then

$$
\hat{W}_1(t) \leq FN_1 - q_1 W_1(t) \leq N_1 - q_1 W_1(t).
$$

Therefore, $\limsup_{t \to \infty} W_1(t) \leq \frac{N_1}{q_1}$. Since $T(t) \geq 0$ and $L(t) \geq 0$, then $\limsup_{t \to \infty} L(t) \leq \frac{N_1}{q_1} = p_1$. To prove the ultimate boundedness of $I(t)$, we define

$$
W_2(t) = \int_0^{T(t)} g(\psi)e^{\eta \psi} T(t - \psi) d\psi + \frac{1}{1 - \eta} f(t).
$$

Then, we obtain

$$
W_2(t) = \int_0^{T(t)} g(\psi)e^{\eta \psi} T(t - \psi) d\psi + \frac{1}{1 - \eta} f(t) = \int_0^{T(t)} g(\psi)e^{\eta \psi} \left[ -dT_0 T(t - \psi) + dt_0 (T(t - \psi) - \frac{T_{\text{max}}}{2}) \right] d\psi
$$

where $q_2 = \min\{d_1, d_t\}$. Hence, $\limsup_{t \to \infty} W_2(t) \leq \frac{\eta q_2}{T_{\text{max}}} = p_2$. Since $V(t), A(t) \geq 0$, hence $\limsup_{t \to \infty} V(t) \leq p_3$, and $\limsup_{t \to \infty} A(t) \leq \frac{\eta p_3}{d_t}$. The above analysis proves that $T(t), L(t), I(t), V(t)$ and $A(t)$ are ultimately bounded. □

### 3.1. Equilibria

This subsection computes all equilibria of model (3)–(7) and the threshold parameters that guarantee the existence of these equilibria. Let $EQ = (T, L, I, V, A)$ be any equilibrium of system (3)–(7) fulfilling the following system of nonlinear equations:

\begin{align}
0 &= \frac{dL}{dt} + T \left(1 - \frac{T}{T_{\text{max}}} \right) - \Omega(T, V), \\
0 &= \eta \Omega(T, V) - (\alpha + d_1) L, \\
0 &= (1 - \eta) G \Omega(T, V) + 2e^{-\alpha T} - d_t L, \\
0 &= \omega e^{-\alpha T} I - d_t V - u AV, \\
0 &= qAV - d_A A.
\end{align}

Eq. (15) has two solutions, $A = 0$ and $V = \frac{d_1}{q}$. When $A = 0$, then from Eq. (14) we get

$$
I = \frac{d_v}{\omega e^{-\alpha t}} V.
$$

From Eq. (12), we have

$$
\Omega(T, V) = \frac{\alpha + d_1}{\eta F} L, 
$$

and from Eqs. (13), (16) and (17), we obtain

$$
L = \frac{d_d d_v \eta F}{\omega e^{-\alpha t} [2\eta e^{-\alpha t} F + (1 - \eta)(\alpha + d_1)G]} V.
$$

Now, from Eqs. (11), (17) and (18), we get

$$
T = \frac{T_{\text{max}}}{2r} \left[ (r - d_t) + \sqrt{(r - d_t)^2 + 4r \left( \ell - \frac{d_d d_v}{\omega e^{-\alpha t} \rho} \right) V} \right],
$$

where $\rho = \frac{\eta q_2}{s d_t} F + (1 - \eta)G$. Let

$$
\Phi(V) = \frac{T_{\text{max}}}{2r} \left[ (r - d_t) + \sqrt{(r - d_t)^2 + 4r \left( \ell - \frac{d_d d_v}{\omega e^{-\alpha t} \rho} \right) V} \right],
$$

Therefore, we can write $T$ as $T = \Phi(V)$. Note that $\Phi(0) = \frac{T_{\text{max}}}{2r} \left[ (r - d_t) + \sqrt{(r - d_t)^2 + \frac{4r \ell}{T_{\text{max}}}} \right] = T_0$. From Eqs. (12) and (18), we have

$$
\Omega(\Phi(V), V) - \frac{d_d d_v}{\omega e^{-\alpha t} \rho} V = 0.
$$

Note that $V = 0$ is a solution of Eq. (20). Then, from Eqs. (16), (18) and (19), we have

$$
T = T_0, L = 0 \text{ and } I = 0.
$$

Then, we obtain the healthy equilibrium $EQ_0 = (T_0, 0, 0, 0, 0)$. If $V \neq 0$ let
there exists a unique infected equilibrium with antibody immunity

From Eq. (14) we find $A_2$ as:

$$A_2 = \frac{dr}{u} \left[ \frac{\rho e^{-\alpha_1} \Omega(T, V_2)}{d_d V_2} - 1 \right].$$

Thus, if $\frac{\rho e^{-\alpha_1} \Omega(T, V_2)}{d_d V_2} > 1$ then $A_2 > 0$. Now we define:

$$\mathcal{R}_1 = \frac{\rho e^{-\alpha_1} \Omega(T, V_2)}{d_d V_2}.$$

Hence, $A_2$ can be rewritten as $A_2 = \frac{dr}{u} (\mathcal{R}_1 - 1)$. As a result, there exists an infected equilibrium with antibody immunity $EQ_2 = (T_2, L_2, I_2, V_2)$ if $\mathcal{R}_1 > 1$.

Clearly from Conditions (C2) and (C4), we obtain

$$\mathcal{R}_1 = \frac{\rho e^{-\alpha_1} \Omega(T, V_2)}{d_d V_2} \leq \lim_{V \to 0} \frac{\Omega(T, V)}{V}.$$

\[\mathcal{R}_1 \leq \frac{\rho e^{-\alpha_1} \Omega(T, V_2)}{d_d V_2} \leq \frac{\rho e^{-\alpha_1} \Omega(T, 0)}{d_d V_2} = \mathcal{R}_0.\]

**Lemma 1.** Let Conditions (C1)-(C4) be satisfied then the system has:

(i) one equilibrium $EQ_0$ when $\mathcal{R}_0 \leq 1$,
(ii) two equilibria $EQ_0$ and $EQ_1$ when $\mathcal{R}_1 \leq 1 < \mathcal{R}_0$,
(iii) three equilibria $EQ_0, EQ_1$ and $EQ_2$ when $\mathcal{R}_1 > 1$.

4. Global stability

To establish the global asymptotic stability of the model’s equilibria we construct Lyapunov functionals and use LaSalle’s invariance principle following the method presented [53–55]. Denote $(T, L, I, V, A) = (T(t), L(t), I(t), V(t), A(t))$ and define a function $\mathcal{V}_1 = \mathcal{V}_1 (T, L, I, V, A), i = 0, 1, 2$. Let $M_i$ be the largest invariant subset of $M_i = \{(T, L, I, V, A) \mid \frac{dT}{dt} = 0 \}, i = 0, 1, 2$.

**Theorem 2.** Suppose that Conditions (C1)-(C4) are valid and $\mathcal{R}_0 \leq 1$, then the equilibrium $EQ_0$ is globally asymptotically stable (GAS).

**Proof.** Define a Lyapunov function $\mathcal{V}_0(T, L, I, V, A)$ as

$$\mathcal{V}_0 = \rho \left[ T - T_0 - \int_{T_0}^T \frac{\Omega(T, V)}{\Omega(T, V)} \left( \frac{d_d V_2}{T_{\text{max}}} \right) dt \right] + \frac{\rho e^{-\alpha_1} L}{d_d + 1} + \frac{\rho e^{-\alpha_1} A}{d_d + 1} + \mathcal{V}_0(t),$$

where

$$\mathcal{V}_0(t) = \frac{\rho e^{-\alpha_1} \int_{t_0}^t f(\phi) e^{-\alpha_1} \left[ \int_{t_0}^\phi \Omega(T, V) \right] d\phi + (1 - \eta) \int_{t_0}^t g(\phi) e^{-\alpha_1} \left[ \int_{t_0}^\phi \Omega(T, V) \right] d\phi + \frac{\rho e^{-\alpha_1} L(\phi) d\phi + d_d \int_{t_0}^\phi f(\phi) d\phi}{d_d + 1}.$$

$\mathcal{R}(x) = x - 1 - \ln x, x > 0$.

Clearly, $\mathcal{V}_0(T, L, I, V, A) > 0$ for all $T, L, I, V, A > 0$ and $\mathcal{V}_0(T_0, 0, 0, 0, 0) = 0$. The derivative of $\mathcal{V}_0(t)$ is computed as:
Global stability of a delayed SARS-CoV-2 reactivation model

\[
\frac{\partial \Omega(T, V)}{\partial V} \leq \lim_{\tau \to 0} \left( \Omega(T, V) \right) \frac{\partial \Omega(T, 0)}{\partial V},
\]

then

\[
\frac{dT_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]

\[
+ \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]

hence

\[
\frac{dT_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) + \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]

\[
\left( \frac{\partial \Omega(T, 0)}{\partial V} - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) \right) (T - T_0) \geq 0,
\]

hence

\[
\left( 1 - \frac{\partial \Omega(T_0, V)}{\partial V} \right) \left( \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) \leq 0,
\]

and

\[
\left( d_T - r + \frac{rT_0}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) \leq 0,
\]

then

\[
\frac{dT_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) + \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]

\[
+ \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) + \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]

\[
+ \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) + \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]

\[
+ \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) + \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]

\[
+ \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T) + \frac{dV_0}{dt} \leq \rho \left( d_T - r + \frac{rT_0}{T_{\text{max}}} \right) \left( 1 - \frac{\partial \Omega(T_0, 0)}{\partial V} \right) (T_0 - T)
\]
At the equilibrium, we have \( \ell = d_T T_0 - r T_0 \left( 1 - \frac{T_1}{T_{\text{max}}} \right) \), which implies that \( d_T - r + \frac{T_1}{T_{\text{max}}} > 0 \). It follows that \( \frac{d_T}{dV} \leq 0 \) when \( \mathcal{R}_0 \leq 1 \). Moreover, \( \frac{dV}{dT} = 0 \) when \( T = T_0, V = 0 \) and \( A = 0 \). The solutions of system (3)-(7) converge to \( \mathcal{E}_0 \), which has elements with \( T = T_0 \) and \( V = A = 0 \). Hence, \( V = 0 \) and from Eq. (6), we get

\[
0 = \dot{V} = o e^{-\nu t} i(t - \tau) \Rightarrow I = 0 \Rightarrow \dot{I} = 0.
\]

From Eq. (5), we get

\[
0 = \dot{I} = ze^{-\nu t} L(t - \tau) \Rightarrow L = 0.
\]

It follows that \( \mathcal{E}_0 = \{EQ_0\} \) and by LIP [56], we get that \( EQ_0 \) is GAS when \( \mathcal{R}_0 \leq 1 \). \( \square \)

**Remark 1.** From Conditions (C2) and (C4), we obtain

\[
\left( \frac{\Omega(T, V)}{V} - \frac{\Omega(T, V_i)}{V_i} \right) \left( \frac{\Omega(T, V) - \Omega(T, V_i)}{V_i} \right) \leq 0,
\]

which gives

\[
\left( \frac{\Omega(T, V)}{V} V \right) \left( \frac{\Omega(T, V_i)}{V_i} \right) \leq 0 \text{ for all } T, V > 0, \quad i = 1, 2.
\]

(21)

**Lemma 2.** Suppose that Conditions (C1)-(C4) are satisfied, \( \mathcal{R}_0 > 1 \) and \( d_T - r + \frac{T_1}{T_{\text{max}}} > 0 \). Then \( T_1, T_2, V_1, V_2 \) exist satisfying

\[
\text{sgn}(T_2 - T_1) = \text{sgn}(V_1 - V_2) = \text{sgn}(\mathcal{R}_1 - 1).
\]

**Proof.** If follows from Condition (C2) that:

\[
(\Omega(T, V_i) - \Omega(T, V))(T_2 - T_1) > 0,
\]

(22)

\[
(\Omega(T, V_i) - \Omega(T, V))(V_2 - V_1) > 0, \quad i = 1, 2,
\]

(23)

for \( T_1, T_2, V_1, V_2 > 0 \). Using inequality (21) with \( i = 1, T = T_1 \) and \( V = V_2 \) we get

\[
\Omega(T_1, V_1) V_1 - \Omega(T_1, V_1) V_2)(\Omega(T_1, V_2) - \Omega(T_1, V_1)) \leq 0,
\]

(24)

It follows from inequality (23) that,

\[
(\Omega(T_1, V_1) V_1 - \Omega(T_1, V_1) V_2)(\Omega(T_1, V_2) - \Omega(T_1, V_1)) > 0.
\]

(25)

First, we claim \( \text{sgn}(T_2 - T_1) = \text{sgn}(V_1 - V_2) \). Assume this is not true, i.e., \( \text{sgn}(T_2 - T_1) = \text{sgn}(V_2 - V_1) \). From the conditions of the equilibria \( EQ_1 \) and \( EQ_2 \), we obtain

\[
\left[ \ell - d_T T_2 + r T_2 \left( 1 - \frac{T_2}{T_{\text{max}}} \right) \right] - \left[ \ell - d_T T_1 + r T_1 \left( 1 - \frac{T_1}{T_{\text{max}}} \right) \right] = \Omega(T_2, V_2) - \Omega(T_1, V_1)
\]

\[
(T_1 - T_2) \left[ d_T - r + \frac{T_1 + T_2}{T_{\text{max}}} \right] = (\Omega(T_2, V_2) - \Omega(T_1, V_2)) + (\Omega(T_1, V_2) - \Omega(T_1, V_1)).
\]

Since \( d_T - r + \frac{T_1 + T_2}{T_{\text{max}}} > 0 \) then \( d_T - r + \frac{U(T_1, V_1)}{T_{\text{max}}} > 0 \). Therefore, from inequalities (22) and (23), we obtain

\[
\text{sgn}(T_1 - T_2) = \text{sgn}(T_2 - T_1),
\]

which leads to a contradiction and hence \( \text{sgn}(T_2 - T_1) = \text{sgn}(V_1 - V_2) \). The equilibrium conditions for \( EQ_1 \) gives \( \frac{\partial \omega e^{-\nu t} i(t - \tau)}{dV} = 1 \), then

\[
\mathcal{R}_1 - 1 = \frac{\partial \omega e^{-\nu t} (T_2, V_2)}{dV} = \frac{\partial \omega e^{-\nu t} (T_1, V_1)}{dV}
\]

\[
= \frac{\partial \omega e^{-\nu t}}{dV} \left[ \frac{1}{r_1} \left( \Omega(T_2, V_2) - \Omega(T_1, V_1) \right) \right].
\]

Thus, from inequality (21) and (25), we deduce that

\[
\text{sgn}(\mathcal{R}_1 - 1) = \text{sgn}(V_1 - V_2), \quad \square
\]

**Theorem 3.** Let Conditions (C1)-(C4) be hold true, \( \mathcal{R}_0 > 1 \) and \( d_T - r + \frac{T_1}{T_{\text{max}}} > 0 \) then the equilibrium \( EQ_1 \) is GAS.

**Proof.** Define

\[
\mathcal{H}_1 = \rho \left( T - T_1 - \int_T T_1 \frac{\Omega(T, V_i)}{V_i} dV_i \right) + \frac{\omega e^{-\nu t}}{dV} L_i \left( \frac{\Omega(T, V_i)}{V_i} \right)
\]

\[
+ I_i \left( \frac{\Omega(T, V_i)}{V_i} \right) + \omega e^{-\nu t} A + \mathcal{H}_1(t),
\]

where

\[
\mathcal{H}_1(t) = \frac{\omega e^{-\nu t}}{dV} \left( \Omega(T_1, V_1) \int_T T_1 \frac{\Omega(T, V_i)}{V_i} dV_i \right)
\]

\[
+ \left( 1 - \frac{1}{\eta} \right) \Omega(T_1, V_1) \int_T T_1 \frac{\Omega(T, V_i)}{V_i} dV_i \left( \frac{\Omega(T_2, V_2)}{T_{\text{max}}} \right) \frac{dV_i}{dV}
\]

\[
+ \frac{\omega e^{-\nu t}}{dV} \left( \Omega(T_1, V_1) \int_T T_1 \frac{\Omega(T, V_i)}{V_i} dV_i \right) \frac{dV_i}{dV}.
\]

It is seen that \( \mathcal{H}_1(T, L, I, V, A) = 0 \) for all \( T, L, I, V, A > 0 \) and \( \mathcal{H}_1(t, L, I, V, A) = 0 \). Then, \( \mathcal{H}_1(t) \) is given by

\[
\frac{\partial \omega e^{-\nu t}}{dV} = \rho \Omega(T, V) - \frac{\omega e^{-\nu t}}{dV} \left( \frac{\Omega(T, V)}{V} \right) + \left( 1 - \frac{1}{\eta} \right) \Omega(T_1, V_1) \int_T T_1 \frac{\Omega(T, V_i)}{V_i} dV_i \left( \frac{\Omega(T_2, V_2)}{T_{\text{max}}} \right) \frac{dV_i}{dV}
\]

\[
+ \frac{\omega e^{-\nu t}}{dV} \left( \Omega(T_1, V_1) \int_T T_1 \frac{\Omega(T, V_i)}{V_i} dV_i \right) \frac{dV_i}{dV}
\]

By using the derivatives in (3)-(7), we get
\[
\frac{d\psi}{dt} = \rho \left( 1 - \frac{\Omega(T, V)}{\Omega(T, V_t)} \right) \left[ \ell - d_T T + rT \left( 1 - \frac{T}{T_{\text{max}}} \right) - \Omega(T, V) \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} f(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} g(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} h(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} k(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} l(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} m(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} n(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} o(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} p(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} q(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} r(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} s(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} t(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} u(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} v(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} w(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} x(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ (1 - \eta) \int_0^{\psi} y(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right] \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \left[ \int_0^{\psi} z(\psi)e^{-\psi} \Omega(T(t - \psi), V(t - \psi))d\psi \right].
\]

(26)

Summing the terms of Eq. (26), we get

\[
\frac{d\psi}{dt} = \rho \left( 1 - \frac{\Omega(T, V)}{\Omega(T, V_t)} \right) \left[ \ell - d_T T + rT \left( 1 - \frac{T}{T_{\text{max}}} \right) \right] + \rho \Omega(T, V) \left( \frac{\Omega(T, V)}{\Omega(T, V_t)} \right) \\
- \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \int_0^{\psi} f(\psi)e^{-\psi} \frac{\Omega(T(t - \psi), V(t - \psi))}{L} d\psi + L e^{-\psi} L_1 \\
- (1 - \eta) \int_0^{\psi} g(\psi)e^{-\psi} \frac{\Omega(T(t - \psi), V(t - \psi))}{L} d\psi - L e^{-\psi} L_1 \left( \frac{T(t - \psi)}{T} \right) + d_T I_1 + \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} V \\
- d_T I_1 + \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} V_1 + \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} A - \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} A \\
+ \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} \Omega(T, V) \int_0^{\psi} g(\psi)e^{-\psi} \frac{\Omega(T(t - \psi), V(t - \psi))}{L} d\psi \\
+ (1 - \eta) \Omega(T, V) \int_0^{\psi} h(\psi)e^{-\psi} \frac{\Omega(T(t - \psi), V(t - \psi))}{L} d\psi + L e^{-\psi} L_1 \left( \frac{T(t - \psi)}{T} \right) \\
+ d_T I_1 \ln \left( \frac{L(t - \psi)}{L} \right).
\]

By using the equilibrium conditions at \( EQ_1 \):

\[
\ell = d_T T_1 - r T_1 \left( 1 - \frac{T}{T_{\text{max}}} \right) + \Omega(T_1, V_1), \\
L e^{-\psi} L_1 = \frac{\rho x_0^2 \psi}{(1 - \rho \psi)} F \Omega(T_1, V_1), \\
d_T I_1 = \rho \Omega(T_1, V_1), \\
\frac{\rho x_0^2 \psi}{(1 - \rho \psi)} V_1 = d_T I_1,
\]

we get,

\[
\ell - d_T T + rT \left( 1 - \frac{T}{T_{\text{max}}} \right) = (T_1 - T) \left( d_T - r + \frac{T}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}} \right) + \Omega(T_1, V_1).
\]

Hence

\[
(1 - \frac{\Omega(T, V)}{\Omega(T, V_t)}) \left( \ell - d_T T + rT \left( 1 - \frac{T}{T_{\text{max}}} \right) \right) \\
= (1 - \frac{\Omega(T, V)}{\Omega(T, V_t)}) \left( T_1 - T \right) \left( d_T - r + \frac{T}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}} + \Omega(T_1, V_1) \right) \\
= (d_T - r + \frac{T}{T_{\text{max}}} + \frac{rT}{T_{\text{max}}}) \left( 1 - \frac{\Omega(T, V)}{\Omega(T, V_t)} \right) (T_1 - T) \\
+ \Omega(T_1, V_1) \left( 1 - \frac{\Omega(T, V)}{\Omega(T, V_t)} \right).
\]

Condition (C2) implies that
\[
\left(1 - \frac{\Omega(T_1, V_1)}{\Omega(T, V_1)}\right)(T_1 - T) \leq 0.
\]

Then
\[
\left(\frac{d_T - r}{T_{\max}} + \frac{r_T}{T_{\max}}\right) \left(1 - \frac{\Omega(T_1, V_1)}{\Omega(T, V_1)}\right)(T_1 - T) \leq \left(\frac{d_T - r}{T_{\max}} + \frac{r_T}{T_{\max}}\right) \left(1 - \frac{\Omega(T_1, V_1)}{\Omega(T, V_1)}\right)(T_1 - T).
\]

By using the above relations, we get
\[
\begin{align*}
\frac{d^2T}{dt^2} & \leq \rho \left(\frac{d_T - r}{T_{\max}} + \frac{r_T}{T_{\max}}\right) \left(1 - \frac{\Omega(T, V)}{\Omega(T, V)}\right)(T_1 - T) + \rho \Omega(T_1, V_1) \\
& \quad - \rho \Omega(T_1, V_1) \frac{\Omega(T, V)}{\Omega(T, V)} + \rho \Omega(T_1, V_1) \frac{\Omega(T, V)}{\Omega(T, V)} - \rho \Omega(T, V) \frac{\Omega(T, V)}{\Omega(T, V)} \\
& \quad - \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) f_0 \int_{T_1}^{V_1} g(\psi) e^{-\eta_{T_{\max}}} \int_{T_{\max}}^{T_{\max}} g(\psi) e^{-\eta_{T_{\max}}} d\psi \\
& \quad + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) f_0 \int_{T_1}^{V_1} g(\psi) e^{-\eta_{T_{\max}}} \int_{T_{\max}}^{T_{\max}} g(\psi) e^{-\eta_{T_{\max}}} d\psi \\
& \quad + \left(1 - \eta\right) \Omega(T_1, V_1) G - \rho \Omega(T_1, V_1) \frac{\Omega(T, V)}{\Omega(T, V)} + \rho \Omega(T_1, V_1) \\
& \quad + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) f_0 \int_{T_1}^{V_1} g(\psi) e^{-\eta_{T_{\max}}} \int_{T_{\max}}^{T_{\max}} g(\psi) e^{-\eta_{T_{\max}}} d\psi \\
& \quad + \left(1 - \eta\right) \Omega(T_1, V_1) G \ln \left(\frac{\Omega(T, V)}{\Omega(T_1, V_1)}\right) \\
& \quad + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right) + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right) \\
& \quad + \left(1 - \eta\right) \Omega(T_1, V_1) G \ln \left(\frac{T_1}{T_1}\right) + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right) + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right).
\end{align*}
\]

By using th following equality:
\[
\ln \left(\frac{L(t - t_{\max})}{L(t - t_{\max})}\right) + \ln \left(\frac{I(t - t_{\max})}{I(t - t_{\max})}\right)
\]
\[
= \ln \left(\frac{I(t - t_{\max})}{I(t - t_{\max})}\right) + \ln \left(\frac{I(t - t_{\max})}{I(t - t_{\max})}\right) + \ln \left(\frac{\Omega(T, V_1)}{\Omega(T, V)}\right).
\]

and rearranging the R.H.S. of (27), we get
\[
\begin{align*}
\frac{d^2T}{dt^2} & \leq \rho \left(\frac{d_T - r}{T_{\max}} + \frac{r_T}{T_{\max}}\right) \left(1 - \frac{\Omega(T_1, V_1)}{\Omega(T_1, V_1)}\right)(T_1 - T) + \rho \Omega(T_1, V_1) \\
& \quad - \rho \Omega(T_1, V_1) \frac{\Omega(T_1, V_1)}{\Omega(T_1, V_1)} + \rho \Omega(T_1, V_1) \frac{\Omega(T_1, V_1)}{\Omega(T_1, V_1)} - \rho \Omega(T_1, V_1) \frac{\Omega(T_1, V_1)}{\Omega(T_1, V_1)} \\
& \quad - \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) f_0 \int_{T_1}^{V_1} g(\psi) e^{-\eta_{T_{\max}}} \int_{T_{\max}}^{T_{\max}} g(\psi) e^{-\eta_{T_{\max}}} d\psi \\
& \quad + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) f_0 \int_{T_1}^{V_1} g(\psi) e^{-\eta_{T_{\max}}} \int_{T_{\max}}^{T_{\max}} g(\psi) e^{-\eta_{T_{\max}}} d\psi \\
& \quad + \left(1 - \eta\right) \Omega(T_1, V_1) G - \rho \Omega(T_1, V_1) \frac{\Omega(T_1, V_1)}{\Omega(T_1, V_1)} + \rho \Omega(T_1, V_1) \\
& \quad + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) f_0 \int_{T_1}^{V_1} g(\psi) e^{-\eta_{T_{\max}}} \int_{T_{\max}}^{T_{\max}} g(\psi) e^{-\eta_{T_{\max}}} d\psi \\
& \quad + \left(1 - \eta\right) \Omega(T_1, V_1) G \ln \left(\frac{\Omega(T, V_1)}{\Omega(T_1, V_1)}\right) \\
& \quad + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right) + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right) \\
& \quad + \left(1 - \eta\right) \Omega(T_1, V_1) G \ln \left(\frac{T_1}{T_1}\right) + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right) + \frac{\rho \omega^{\eta_{T_{\max}}}}{\omega^{\eta_{T_{\max}}}} \Omega(T_1, V_1) F \ln \left(\frac{T_1}{T_1}\right).
\end{align*}
\]
\[
\frac{dT}{dt} \leq \rho \left( d_T - r + \frac{\Delta t}{\tau_{mix}} \right) (T_1 - T) + \rho \Omega(T_1, V_1) \left( \frac{\Delta t}{\tau_{mix}} \right) V_1 - \rho \Omega(T_1, V_1) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) (T_1 - T) \]

By simplifying \( \frac{dT}{dt} \) we get

\[
\frac{dT}{dt} \leq \rho \left( d_T - r + \frac{\Delta t}{\tau_{mix}} \right) (T_1 - T) + \rho \Omega(T_1, V_1) \left( \frac{\Delta t}{\tau_{mix}} \right) V_1 - \rho \Omega(T_1, V_1) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) (T_1 - T)
\]

When \( d_T - r + \frac{\Delta t}{\tau_{mix}} > 0 \) and from Conditions (C1)-(C4) and Remark 1, we get that, the first and second terms of Eq. (28) are non-positive. Lemma 2 implies that, if \( R_1 \leq 1 \), then \( V_1 \leq V_2 \). It follows that, \( \frac{dT}{dt} \leq 0 \) for all \( T, L, I, V, A > 0 \). Moreover, \( \frac{dT}{dt} \leq 0 \) when \( T = T_1, L = L_1, I = I_1, V = V_1 \) and \( A = 0 \). Therefore, \( M'_1 = \{E_2, A\} \) and then \( EQ_1 \) is GAS when \( R_1 \leq 1 < R_0 \) and \( d_T - r + \frac{\Delta t}{\tau_{mix}} > 0 \). \[ \square \]

Theorem 4. Let Conditions (C1)-(C4) be hold true, \( R_1 > 1 \) and \( d_T - r + \frac{\Delta t}{\tau_{mix}} > 0 \) then the equilibrium \( EQ_2 \) is GAS.

Proof. Define

\[
\varphi_2 = \rho \left( T - T_2 - \int_{T_1}^{T_2} \frac{\Delta t}{\tau_{mix}} \right) \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right) + \rho \Omega(T_2, V_2) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right)
\]

where

\[
\varphi_2(t) = \rho \left( T - T_2 - \int_{T_1}^{T_2} \frac{\Delta t}{\tau_{mix}} \right) \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right) + \rho \Omega(T_2, V_2) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right)
\]

We have \( \varphi_2(T, L, I, V, A) > 0 \) for all \( T, L, I, V, A > 0 \), and \( \varphi_2(T_2, L_2, V_2, A_2) = 0 \). Then, we have

\[
\rho \left( T - T_2 - \int_{T_1}^{T_2} \frac{\Delta t}{\tau_{mix}} \right) \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right) + \rho \Omega(T_2, V_2) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right)
\]

Summing the terms of Eq. (29), we get

\[
\rho \left( T - T_2 - \int_{T_1}^{T_2} \frac{\Delta t}{\tau_{mix}} \right) \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right) + \rho \Omega(T_2, V_2) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right)
\]

The equilibrium conditions at \( EQ_2 \) are given by:

\[
\ell = d_T T_2 - r T_2 \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) + \Omega(T_2, V_2),
\]

where

\[
\ell = \rho \left( T - T_2 - \int_{T_1}^{T_2} \frac{\Delta t}{\tau_{mix}} \right) \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right) + \rho \Omega(T_2, V_2) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) \left( \frac{\Delta t}{\tau_{mix}} \right) d\mu \left( \frac{\Delta t}{\tau_{mix}} \right)
\]

we get,

\[
\ell - d_T T + r T \left( 1 - \frac{\Delta t}{\tau_{mix}} \right) = \left( T_2 - T \right) \left( d_T - r + \frac{\Delta t}{\tau_{mix}} \right) + \Omega(T_2, V_2).
\]
Hence

\[
\left(1 - \frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right) \left(\ell - d_T T + r T \left(1 - \frac{1}{\bar{T}_T} \right)\right) = \left(1 - \frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right) \times \left((T - T) \left(d_T - r + \frac{\tau_T}{\bar{T}_T} + \frac{\tau_T}{\bar{T}_T}\right) + \Omega(T, V_2) \right)
\]

\[
= \left(\frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right) \left(1 - \frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right) \left((T - T) \left(d_T - r + \frac{\tau_T}{\bar{T}_T} + \frac{\tau_T}{\bar{T}_T}\right) + \Omega(T, V_2) \right). 
\]

Condition (C2) implies that

\[
\left(1 - \frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right)(T_2 - T) \leq 0.
\]

Then

\[
\left(\frac{d_T - r + \frac{\tau_T}{\bar{T}_T}}{\frac{\tau_T}{\bar{T}_T}} \right) \left(1 - \frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right)(T_2 - T) \leq \left(\frac{d_T - r + \frac{\tau_T}{\bar{T}_T}}{\frac{\tau_T}{\bar{T}_T}} \right) \left(1 - \frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right)(T_2 - T).
\]

By using the above relations, we get

\[
\frac{d\bar{T}_T}{dT} \leq \rho \left(\frac{d_T - r + \frac{\tau_T}{\bar{T}_T}}{\frac{\tau_T}{\bar{T}_T}} \right) \left(1 - \frac{\Omega(T, V_2)}{\Omega(T, V_2)} \right)(T_2 - T) + \rho \Omega(T, V_2)
\]

\[
-\rho \Omega(T, V_2) \frac{\Omega(T, V_2)}{\Omega(T, V_2)} + \rho \Omega(T, V_2) \frac{\Omega(T, V_2)}{\Omega(T, V_2)} - \rho \Omega(T, V_2) \frac{\Omega(T, V_2)}{\Omega(T, V_2)}
\]

\[
-\frac{\omega^{\tau_T}}{\tau_T} \Omega(T, V_2) \int_{\tau_T}^{\infty} \frac{T(\tau') \int_{\tau_T}^{\infty} \frac{T(\tau')}{\tau_T} d\tau'}{\tau_T} d\tau' + \frac{\omega^{\tau_T}}{\tau_T} \Omega(T, V_2) \int_{\tau_T}^{\infty} \frac{T(\tau') \int_{\tau_T}^{\infty} \frac{T(\tau')}{\tau_T} d\tau'}{\tau_T} d\tau'
\]

\[
+ \frac{\omega^{\tau_T}}{\tau_T} \Omega(T, V_2) \int_{\tau_T}^{\infty} \frac{T(\tau') \int_{\tau_T}^{\infty} \frac{T(\tau')}{\tau_T} d\tau'}{\tau_T} d\tau'
\]

\[
+ (1 - \eta) \Omega(T, V_2) \int_{\tau_T}^{\infty} \frac{T(\tau') \int_{\tau_T}^{\infty} \frac{T(\tau')}{\tau_T} d\tau'}{\tau_T} d\tau' + \frac{\omega^{\tau_T}}{\tau_T} \Omega(T, V_2) \int_{\tau_T}^{\infty} \frac{T(\tau') \int_{\tau_T}^{\infty} \frac{T(\tau')}{\tau_T} d\tau'}{\tau_T} d\tau'
\]

\[
+ (1 - \eta) \Omega(T, V_2) \int_{\tau_T}^{\infty} \frac{T(\tau') \int_{\tau_T}^{\infty} \frac{T(\tau')}{\tau_T} d\tau'}{\tau_T} d\tau' + (1 - \eta) \Omega(T, V_2) \int_{\tau_T}^{\infty} \frac{T(\tau') \int_{\tau_T}^{\infty} \frac{T(\tau')}{\tau_T} d\tau'}{\tau_T} d\tau'
\]

Now, using the following relations:

\[
\ln \left(\frac{\Omega(T, V_2) T(\tau')}{\Omega(T, V_2)} \right) + \ln \left(\frac{T(\tau')}{\tau_T} \right) = \ln \left(\frac{T(\tau')}{\tau_T} \right) + \ln \left(\frac{\Omega(T, V_2) T(\tau')}{\Omega(T, V_2)} \right)
\]

\[
+ \ln \left(\frac{\Omega(T, V_2) T(\tau')}{\Omega(T, V_2)} \right) + \ln \left(\frac{T(\tau')}{\tau_T} \right) = \ln \left(\frac{T(\tau')}{\tau_T} \right) + \ln \left(\frac{\Omega(T, V_2) T(\tau')}{\Omega(T, V_2)} \right)
\]

\[
+ \ln \left(\frac{\Omega(T, V_2) T(\tau')}{\Omega(T, V_2)} \right) + \ln \left(\frac{T(\tau')}{\tau_T} \right) = \ln \left(\frac{T(\tau')}{\tau_T} \right) + \ln \left(\frac{\Omega(T, V_2) T(\tau')}{\Omega(T, V_2)} \right)
\]
we get

\[
\frac{dT_c}{dt} \leq \rho \left( d_T - r + \frac{\alpha_T}{T_{max}} \right) \left( T_2 - T \right) + \rho \Omega(T_2, V_2)
\]

\[
-\rho \Omega(T_2, V_2) \frac{V}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} - \rho \Omega(T_2, V_2) \frac{V}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} - \rho \Omega(T_2, V_2) \frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}
\]

\[
-\mu \gamma_{T_2} \Omega(T_2, V_2) \int_0^\tau \delta(\psi) e^{-\eta \psi} \frac{\frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} d\psi + \mu \gamma_{T_2} \Omega(T_2, V_2) F
\]

\[
-\left( 1 - \eta \right) \Omega(T_2, V_2) \int_0^\tau \delta(\psi) e^{-\eta \psi} \frac{\frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} d\psi - \mu \gamma_{T_2} \Omega(T_2, V_2) F_{\frac{dV}{d\psi}}
\]

\[
+ \mu \gamma_{T_2} \Omega(T_2, V_2) F_{\frac{dV}{d\psi}} + \left( 1 - \eta \right) \Omega(T_2, V_2) G - \rho \Omega(T_2, V_2) \frac{V}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} + \rho \Omega(T_2, V_2)
\]

\[
+ \mu \gamma_{T_2} \Omega(T_2, V_2) \int_0^\tau \delta(\psi) e^{-\eta \psi} \frac{\frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} d\psi
\]

We have the following relation:

\[
\ln \left( \frac{L(t - \tau)}{\Omega(T, V)} \right) + \ln \left( \frac{dT}{d\psi} \right) = \ln \left( \frac{T_2(t - \tau)}{T_2} \right) + \ln \left( \frac{(\frac{dT}{d\psi})_T}{(\frac{dT}{d\psi})_T} \right) + \ln \left( \frac{(\frac{dV}{d\psi})_T}{(\frac{dV}{d\psi})_T} \right)
\]

and rearranging the R.H.S. of \( \frac{dT}{dt} \), we get

\[
\frac{dT}{dt} \leq \rho \left( d_T - r + \frac{\alpha_T}{T_{max}} \right) \left( T_2 - T \right)
\]

\[
+ \rho \Omega(T_2, V_2) \left( \frac{dV}{d\psi} + \frac{dV}{d\psi} \right) - \rho \Omega(T_2, V_2) \left( \frac{dV}{d\psi} + \frac{dV}{d\psi} \right) - \rho \Omega(T_2, V_2) \left( \frac{dV}{d\psi} + \frac{dV}{d\psi} \right)
\]

\[
- \mu \gamma_{T_2} \Omega(T_2, V_2) \int_0^\tau \delta(\psi) e^{-\eta \psi} \frac{\frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} d\psi + \mu \gamma_{T_2} \Omega(T_2, V_2) F
\]

\[
- \left( 1 - \eta \right) \Omega(T_2, V_2) \int_0^\tau \delta(\psi) e^{-\eta \psi} \frac{\frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} d\psi - \mu \gamma_{T_2} \Omega(T_2, V_2) F_{\frac{dV}{d\psi}}
\]

By simplifying \( \frac{dT}{dt} \), we get

\[
\frac{dT}{dt} \leq \rho \left( d_T - r + \frac{\alpha_T}{T_{max}} \right) \left( T_2 - T \right)
\]

\[
+ \rho \Omega(T_2, V_2) \left( \frac{dV}{d\psi} + \frac{dV}{d\psi} \right) - \rho \Omega(T_2, V_2) \left( \frac{dV}{d\psi} + \frac{dV}{d\psi} \right) - \rho \Omega(T_2, V_2) \left( \frac{dV}{d\psi} + \frac{dV}{d\psi} \right)
\]

\[
- \mu \gamma_{T_2} \Omega(T_2, V_2) \int_0^\tau \delta(\psi) e^{-\eta \psi} \frac{\frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} d\psi + \mu \gamma_{T_2} \Omega(T_2, V_2) F
\]

\[
- \left( 1 - \eta \right) \Omega(T_2, V_2) \int_0^\tau \delta(\psi) e^{-\eta \psi} \frac{\frac{T}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)}}{\left( \frac{dT}{d\psi} + \frac{dV}{d\psi} \right)} d\psi - \mu \gamma_{T_2} \Omega(T_2, V_2) F_{\frac{dV}{d\psi}}
\]

It follows that \( M'_2 = \{ EQ_2 \} \) and by LIP \( EQ_2 \) is GAS when \( \gamma_1 > 1 \) and \( d_T - r + \frac{\alpha_T}{T_{max}} > 0 \). \( \square \)

5. Numerical simulations

In this section, we present numerical simulations to illustrate the results of Theorems 2-4. In addition, we study the impact of time delays on the qualitative behavior of the system. We choose a Crowley-Martin incidence function:

\[
\Omega(T, V) = \frac{\zeta T V}{1 + \gamma T} \left( 1 + \xi V \right)
\]
where $\xi > 0$, $\gamma > 0$ and $\zeta \geq 0$. Clearly $\Omega(T, V)$ is continuously differentiable. In the following we verify Conditions (C1)-(C4).

- Verification of Condition (C1): Clearly, $\Omega(T, V) > 0$, $\Omega(0, V) = \Omega(T, 0) = 0$ for all $T > 0, V > 0$. Thus, Condition (C1) is satisfied.
- Verification of Condition (C2): We have
  
  $$
  \frac{d\Omega(T, V)}{dT} = \frac{\xi T}{(1 + \gamma T)(1 + \zeta V)} > 0,
  $$

  for all $T > 0, V > 0$, then Condition (C2) is satisfied.
- Verification of Condition (C3): We see that
  
  $$
  \frac{d}{dT} \left( \frac{\partial \Omega(T, 0)}{\partial V} \right) = \frac{\xi}{1 + \gamma T} > 0,
  $$

  for all $T > 0$, then Condition (C3) is satisfied.
- Verification of Condition (C4): We have
  
  $$
  \frac{\partial \Omega(T, V)}{\partial V} = \frac{-\zeta \xi T}{(1 + \gamma T)(1 + \zeta V)},
  $$

  $\Rightarrow \frac{\partial \Omega(T, V)}{\partial V} < 0$ for all $T, V > 0$.

  Then, Condition (C4) is also satisfied.

Let us take a particular form of the probability distributed functions as:

$$
 f(\psi) = \delta(\psi - \psi_1), \quad g(\psi) = \delta(\psi - \psi_2),
$$

where $\delta(\cdot)$ is the Dirac delta function. When $\tau_i \to \infty, i = 1, 2$, we have

$$
 \int_0^\infty f(\psi)d\psi = 1, \quad \int_0^\infty g(\psi)d\psi = 1.
$$

We have

$$
 \int_0^\infty \delta(\psi - \psi_1)e^{-\alpha t}\psi = e^{-\alpha \psi_1}, \quad i = 1, 2,
$$

Moreover,

$$
 \int_0^\infty \delta(\psi - \psi_1)e^{-\alpha t}\Omega(T(t - \psi), V(t - \psi))d\psi = e^{-\alpha \psi_1}\Omega(T(t - \psi_1), V(t - \psi_1)), \quad i = 1, 2.
$$

Hence, model (3)-(7) becomes:

$$
 T(t) = t - d_T t + r_T t \left( 1 - \frac{T(t)}{T_{\text{max}}} \right) - \frac{\xi \xi T V}{(1 + \gamma T)(1 + \zeta V)}, \quad (31)
$$

$$
 L(t) = r e^{-\alpha \psi_1} + \frac{\zeta \xi T(t - \psi_1) V(t - \psi_1)}{(1 + \gamma T(t - \psi_1))(1 + \zeta V(t - \psi_1))}, \quad (32)
$$

$$
 H(t) = (1 - \eta) e^{-\alpha \psi_1} + \frac{\xi \xi T(t - \psi_1) V(t - \psi_1)}{(1 + \gamma T(t - \psi_1))(1 + \zeta V(t - \psi_1))}
 + \xi \xi^2 L(t - \tau_i) - d_L L(t), \quad (33)
$$

$$
 \tilde{A}(t) = q A(t) V(t) - d_A A(t), \quad (34)
$$

$$
 A(t) = q A(t) V(t) - d_A A(t), \quad (35)
$$

The parameters $\alpha_B$ and $\beta_B$ of model (31)-(35) are given by:

$$
 \frac{d\alpha_B}{dt} = \frac{\alpha_B T e^{-\alpha t}}{2 + d_L} + \frac{\alpha_B T e^{-\alpha t}}{2 + d_L} + \frac{\alpha_B T e^{-\alpha t}}{2 + d_L} + \frac{\alpha_B T e^{-\alpha t}}{2 + d_L} + \frac{\alpha_B T e^{-\alpha t}}{2 + d_L}, \quad (36)
$$

To solve system (31)-(35) numerically we use the MATLAB solver dde23. Without loss of generality let us consider for simplicity that $\psi_1 = \psi_2 = \tau_1 = \tau_2 = \tau_3$. The values of the parameters of model (31)-(35) are chosen as $\ell = 0.11$, $r = 0.01$, $T_{\text{max}} = 12$, $\gamma = 0.001$, $\zeta = 0.001$, $\eta = 0.5$, $\alpha = 4.08$, $\omega = 0.3$, $u = 0.05$, $d_t = 0.01$, $d_L = 0.11$, $d_V = 0.11$, $d_A = 3.5$, $d_L = 0.31$, $n_1 = 0.11$, $n_2 = 0.11$, $n_3 = 1$, and $n_4 = 1$. The parameters $\tau, \xi, \eta$ and $q$ will be varied. We select three different sets of initial conditions for (31)-(35):

- **Initial** - 1: $(T(\tau), L(\tau), H(\tau), V(\tau), A(\tau)) = (8.1, 0.004, 0.3, 0.0027)$.
- **Initial** - 2: $(T(\tau), L(\tau), H(\tau), V(\tau), A(\tau)) = (7.8, 0.005, 0.04, 0.0258)$.
- **Initial** - 3: $(T(\tau), L(\tau), H(\tau), V(\tau), A(\tau)) = (7.5, 0.006, 0.5, 0.0039)$.

where $\tau \in [-\tau, 0]$.

### 5.1. Stability of equilibria

In this subsection we address the stability of the three equilibria with $\tau = 0.1$, $\xi$ and $q$ are varied.

- **Scenario 1 (Stability of $E_{Q_1}$):** $\xi = 0.2$ and $q = 0.5$. Using these values, we obtain $\alpha_B = 0.7075 < 1$ and $\beta_B = 0.2712 < 1$. According to Theorem 2, $E_{Q_1}$ is GAS and the SARS-CoV-2 is predicted to be removed from the body. From Fig. 1, we can see that the numerical results confirm the results of Theorem 2. We see that, the concentration of healthy epithelial cells is increased and reached its healthy value $T_0 = 10.9048$, while the concentrations of latent infected cells, active infected cells, SARS-CoV-2 particles and antibodies are extremely decaying and tend toward zero. In this situation, the virus particles will be eliminated from the body.

- **Scenario 2 (Stability of $E_{Q_2}$):** $\xi = 0.2$ and $q = 0.5$. Using these data, we compute $\alpha_B = 1.415 > 1$, $\beta_B = 1.5424 < 1$ and $d_t - r + \frac{r}{\nu_{\text{max}}} = 0.0074 > 0$. According to Theorem 3, $E_{Q_2}$ is GAS. Fig. 2 shows that there is an agreement between the numerical and results of Theorem 3. In addition, the solutions of the system converge to the equilibrium $E_{Q_2} = (7.682, 0.0063, 0.4494, 0.0349, 0)$. In such a case, SARS-CoV-2 exists but with an inactive antibody immune response.

- **Scenario 3 (Stability of $E_{Q_3}$):** $\xi = 0.2$ and $q = 1.2$. Using these data, we compute $\alpha_B = 1.415 > 1$, $\beta_B = 1.1323 > 1$ and $d_t - r + \frac{r}{\nu_{\text{max}}} = 0.0083 > 0$. According to Theorem 4, $E_{Q_3}$ is GAS. Fig. 3 shows that, both the numerical and theoretical results are compatible. Further, the solutions converge to the equilibrium $E_{Q_3} = (8.4576, 0.005, 0.3546, 0.025, 7.0089)$. In this situation, SARS-CoV-2 exists with active antibody immunity.

### 5.2. Influence of the time delays on the SARS-CoV-2 dynamics

In this subsection, we explore the impact of time delay parameter $\tau$ on the stability of the equilibrium. We note from Eq. (36)
Fig. 1  Dynamics of system (31)-(35) with three initial conditions when $\mathcal{R}_0 \leq 1$. (a) Healthy epithelial cell; (b) Latent infected cells; (c) Active infected cells; (d) SARS-CoV-2 particles; (e) Antibodies.
Fig. 2  Dynamics of system (31)–(35) with three initial conditions when \( R_1/C_2 > R_0 \) and \( d_T - r + \frac{d_T}{C_0 T_{max}} > 0 \). (a) Healthy epithelial cell; (b) Latent infected cells; (c) Active infected cells; (d) SARS-CoV-2 particles; (e) Antibodies.
that the parameter $\mathcal{R}_0$ relies on $\tau_1$ which causes a significant change in the stability of equilibria. To clarify this case, we fix $\zeta = 0.2$, $q = 1.2$ and vary $\tau$. Moreover, we consider the initial condition Initial-3. Fig. 4 shows the influence of time delay on the trajectories of the system. We notice that as time delay $\tau$ is increased the number of the healthy epithelial cells is increased, while the numbers of latent infected cells, active infected cells, SARS-CoV-2 particles and antibodies are decreased. Let us write $\mathcal{R}_0$ as:

$$
\mathcal{R}_0(\tau) = \frac{\omega e^{-\gamma \tau}}{d_\zeta d_\gamma} \frac{T_0}{(1 + \gamma T_0)} \left[ \frac{x \rho e^{-(n_1 + n_2)\tau}}{\alpha + d_\zeta} + (1 - \eta) e^{-n_2\tau} \right].$

Fig. 3  Dynamics of system (31)-(35) with three initial conditions when $\mathcal{R}_1 > 1$ and $dT > \frac{\alpha + d_\zeta}{\gamma T_0} > 0$. (a) Healthy epithelial cell; (b) Latent infected cells; (c) Active infected cells; (d) SARS-CoV-2 particles; (e) Antibodies.
Fig. 4  Dynamics of system (31)–(35) under the influence of the time delays $\tau$. (a) Healthy epithelial cell; (b) Latent infected cells; (c) Active infected cells; (d) SARS-CoV-2 particles; (e) Antibodies.
We can see that $\mathcal{R}_0$ is a decreasing function of $\tau$. Let $\tau_{cr}$ be such that $\mathcal{R}_0(\tau_{cr}) = 1$. Using the values of the parameters given above we get, $\tau_{cr} = 0.32387$. From Fig. 4 we can see the following scenarios:

(i) if $\tau \geq 0.32387$, then $\mathcal{R}_0 \leq 1$ and $EQ_0$ is GAS.
(ii) if $0 \leq \tau < 0.32387$, then $\mathcal{R}_0 > 1$ and one of the other equilibria is GAS. We see from the above argumentation that increasing time delays values can have the same impact as drug therapies.

6. Conclusion

In this article, we introduced a SARS-CoV-2 infection model with mixed distributed and discrete delays. The antibody immunity against viral infection was included. The virus-target incidence rate was given by a general function which generalized many incidence rate forms exist in the literature. We considered four time delays in the model: delay in the formation of latent infected cells, delay in the formation of active infected cells, delay in the activation of latent infected cells, maturation delay of new SARS-CoV-2 particles. We considered a logistic term for the healthy epithelial cells. We proved the nonnegativity and boundedness of the solutions. We calculated all equilibria and derived their existence conditions. The global stability of all equilibria of the model was investigated by constructing Lyapunov functions and LaSalle’s invariance principal. We obtained that the healthy equilibrium $EQ_0$ is GAS when $\mathcal{R}_0 \leq 1$. When $\mathcal{R}_1 \leq 1 < \mathcal{R}_0$ and $d_1 - r + \frac{rT_0}{\tau_{cr}} > 0$, the infected equilibrium without antibody immunity $EQ_1$ is GAS. When $\mathcal{R}_1 > 1$ and $d_1 - r + \frac{rT_0}{\tau_{cr}} > 0$ the infected equilibrium with antibody immunity $EQ_2$ is GAS. We performed the numerical simulations for the model and we showed that both theoretical and numerical results are consistent. We noted that the increase of delay length can give similar influence as drug therapies.

The model proposed in this paper can be developed by considering the diffusion of the virus particles [57,58] and studying the effect of CTL immune response on eliminating infected cells. Our model can also be expanded by constructing multiscale SARS-CoV-2 model [59,60]. The memory is an important characteristic of human immune system. It will be interesting to investigate the memory effect on the SARS-CoV-2 dynamics by using fractional derivative [61–63]. Modeling the effect of treatments on the SARS-CoV-2 dynamics is an important direction. In this case, the SARS-CoV-2 dynamics model can be considered as a nonlinear control system. Controlability and feedback stabilization of the fractional SARS-CoV-2 dynamics model with delay can be studied in future works [64,65].

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Coronavirus disease (COVID-19), weekly epidemiological update (16 January 2022), World Health Organization (WHO), 2022. Available online: https://www.who.int/emergencies/diseases/novel-coronavirus-2019-situation-reports.
[2] Coronavirus disease (COVID-19), Vaccine tracker, World Health Organization (WHO), 2021. Available online: https://covid19.trackvaccines.org/agency/who/.
[3] Z. Varga, A.J. Flammer, P. Steiger, M. Haberecker, R. Andermatt, A.S. Zinkernagel, et al, Endothelial cell infection and endotheliitis in COVID-19, Lancet 395 (2020) 1417–1418.
[4] M.C. Jung, G.R. Pape, Immunology of hepatitis B infection, Lancet Infectious Dis. 2 (1) (2002) 43–50.
[5] L. Canni, A.S. Perelson, Viral kinetic modeling: state of the art, J. Pharmacokin. Pharmacod. 41 (2014) 431–443.
[6] A. Gonçalves, J. Bertrand, R. Ke, E. Comets, X. De Lamballerie, D. Malvy, et al, Timing of antiviral treatment initiation is critical to reduce SARS-CoV-2 viral load, CPT: Pharmacometrics Syst. Pharmacol. 9 (9) (2020) 599–614.
[7] A.S. Perelson, R. Ke, Mechanistic modeling of SARS-CoV-2 and other infectious diseases and the effects of therapeutics, Clin. Pharmacol. Therapeutics 109 (4) (2021) 829–840.
[8] M.A. Nowak, C.R.M. Bangham, Population dynamics of immune responses to persistent viruses, Science 272 (1996) 74-79.
[9] C. Li, J. Xu, J. Liu, Y. Zhou, The within-host viral kinetics of SARS-CoV-2, Math. Biosci. Eng. 17 (4) (2020) 2853–2861.
[10] M. Sadria, A.T. Layton, Modeling within-host SARS-CoV-2 infection dynamics and potential treatments, Viruses 13 (6) (2021) 1141.
[11] S.Q. Du, W. Yuan, Mathematical modeling of interaction between innate and adaptive immune responses in COVID-19 and implications for viral pathogenesis, J. Med. Virol. 92 (9) (2020) 1615–1628.
[12] Y.M. Bar-On, A. Flamholz, R. Phillips, R. Milo, Science Forum: SARS-CoV-2 (COVID-19) by the numbers, elife 9 (2020) e57309.
[13] F. Fatehi, R.J. Bingham, E.C. Dykeman, P.G. Stockley, R. Twarock, Comparing antiviral strategies against COVID-19 via multiscale within-host modelling, R. Soc. Open Sci. 8 (2021) 210082.
[14] E.A. Hernandez-Vargas, J.X. Velasco-Hernandez, In-host mathematical modelling of COVID-19 in humans, Ann. Rev. Control 50 (2020) 448–456.
[15] R. Ke, C. Zitzmann, D.D. Ho, R.M. Ribeiro, A.S. Perelson, In vivo kinetics of SARS-CoV-2 infection and its relationship with a person’s infectiousness, Proc. Nat. Acad. Sci. 118 (49) (2021), e2111477118.
[16] L. Pinky, H.M. Dobrovolsky, SARS-CoV-2 coinfections: could influenza and the common cold be beneficial?, J Med. Virol. 92 (2020) 2623–2630.
[17] S. Wang, Y. Pan, Q. Wang, H. Miao, A.N. Brown, L. Rong, Modeling the viral dynamics of SARS-CoV-2 infection, Math. Biosci. 328 (2020) 108438.
[18] N. Neant, G. Lingas, Q. Le Hingrat, J. Ghosn, I. Engelmann, Q. Lepiller, A. Gaymard, V. Ferré, C. Hartard, J.-C. Plantier, et al, Modeling SARS-CoV-2 viral kinetics and association with mortality in hospitalized patients from the French COVID cohort, Proc. Nat. Acad. Sci. 118 (8) (2021), e2017962118.

[19] A. Danchin, O. Pagani-Aziz, G. Turinici, G. Yahioues, COVID-19 adaptive humoral immunity models: non-neutralizing versus antibody-disease enhancement scenarios, medRxiv (2020).

[20] K. Hattaf, N. Yousfi, Dynamics of SARS-CoV-2 infection model with two modes of transmission and immune response, Math. Biosci. Eng. 17 (5) (2020) 5326–5340.

[21] K. Logeswari, C. Ravichandran, K.S. Nisar, Mathematical model for spreading of COVID-19 virus with the Mittag-Leffler kernel, Numer. Methods Partial Differential Eqs. (2020), https://doi.org/10.1002/num.22652.

[22] O.J. Peter, A.S. Shaih, M.O. Ibrahim, K.S. Nisar, D. Baleanu, I. Khan, A.I. Abioye, Analysis and dynamics of fractional order mathematical model of COVID-19 in Nigeria using atangana-baleanu operator, Comput. Mater. Continua 66 (2) (2021) 1823–1848.

[23] S. Ahmad, A. Ullah, Q.M. Al-Mdallal, H. Khan, K. Shah, A. Khan, Fractional order mathematical modeling of COVID-19 transmission, Chaos Solitons Fract. 139 (2020) 105256.

[24] H. Singh, H.M. Srivastava, Z. Hammouch, K.S. Nisar, Numerical simulation and stability analysis for the fractional-order dynamics of COVID-19, Res. Phys. 20 (2021) 103722.

[25] B. Ghanbari, On fractional approaches to the dynamics of a SARS-CoV-2 infection model including singular and non-singular kernels, Res. Phys. 28 (2021) 104600.

[26] A.N. Chatterjee, F. Al Basir, A model for SARS-CoV-2 infection with treatment, Comput. Math. Methods Med. (2020) Article ID 1352982.

[27] J. Mondal, P. Samui, A.N. Chatterjee, Dynamical demeanour of SARS-CoV-2 virus undergoing immune response mechanism in COVID-19 pandemic, Eur. Phys. J. Spec. Top. (2022), https://doi.org/10.1140/epjs/s11734-022-00437-5.

[28] I. Ghosh, Within host dynamics of SARS-CoV-2 in humans: modeling immune responses and antiviral treatments, SN Comput. Sci. 2 (6) (2021) 482.

[29] B.J. Nath, K. Dehingia, V.N. Mishra, Y.-M. Chu, H.K. Sarmah, Mathematical analysis of a within-host model of SARS-CoV-2, Adv. Differen. Eqs. 2021 (2021) 113.

[30] P. Abuin, A. Anderson, A. Ferramosca, E.A. Hernandez-Vargas, A.H. Gonzalez, Characterization of SARS-CoV-2 dynamics in the host, Ann. Rev. Control 30 (2020) 457–468.

[31] A.E.S. Almoceraa, G. Quiroz, E.A. Hernandez-Vargas, Stability analysis in COVID-19 within-host model with immune response, Commun. Nonlinear Sci. Numer. Simul. 95 (2021) 105584.

[32] A.M. Elaiw, A.D. Hobiny, A.D. Al Agha, Global dynamics of SARS-CoV-2/cancer model with immune responses, Appl. Math. Comput. 408 (2021) 126364.

[33] A.M. Elaiw, A.D. Al Agha, S.A. Azoz, E. Ramadan, Global analysis of within-host SARS-CoV-2/HIV coinfection model with latency, Eur. Phys. J. Plus 137 (2) (2022) 174.

[34] B. Chhetri, V.M. Bhagat, D.K.K. Vamsi, V.S. Ananth, D.B. Prakash, R. Mandal, S. Muthusamy, C.B. Sanjevi, Within-host mathematical modeling on crucial inflammatory mediators and drug interventions in COVID-19 identifies combination therapy to be most effective and optimal, Alexandria Eng. J. 60 (2) (2021) 2491–2512.

[35] A.N. Chatterjee, F. Al Basir, M.A. Almuqrin, J. Mondal, I. Khan, SARS-CoV-2 infection with lytic and nonlytic immune responses: a fractional order optimal control theoretical study, Res. Phys. 26 (2021) 104260.

[36] J.P.S.M. de Carvalho, Immune response in SARS-CoV-2 epidemics: A fractional-order model, arXiv preprint arXiv:2103.09053 (2021).

[37] N.T. Fadai, R. Sachak-Patwa, H.M. Byrne, P.K. Maini, M. Bafadhel, D.V. Nicolau Jr, Infection, inflammation and intervention: mechanistic modelling of epithelial cells in COVID-19, J. Roy. Soc. Interface 18 (175) (2021) 20200950.

[38] A. Korobeinikov, Global asymptotic properties of virus dynamics models with dose-dependent parasite reproduction and virulence and non-linear incidence rate, Math. Med. Biol. J. IMA 26 (3) (2009) 255–269.

[39] X. Song, A. Neumann, Global stability and periodic solution of the viral dynamics, J. Math. Anal. Appl. 329 (2007) 281–297.

[40] G. Huang, W. Ma, Y. Takeuchi, Global properties for virus dynamics model with Beddington-DeAngelis functional response, Appl. Math. Lett. 22 (2009) 1690–1693.

[41] S. Xu, Global stability of the virus dynamics model with Crowley-Martin functional response, Electron. J. Qual. Theory Differ. Eqs. 2012 (9) (2012) 1–9.

[42] N. Bairagi, D. Adak, Global analysis of HIV-1 dynamics with Hill type infection rate and intracellular delay, Appl. Math. Model. 38 (21–22) (2014) 5047–5066.

[43] G. Huang, Y. Takeuchi, W. Ma, Lyapunov functions for delay differential equations model of viral infections, SIAM J. Appl. Math. 70 (7) (2010) 2693–2708.

[44] M.Y. Li, H. Shu, Impact of intracellular delays and target-cell dynamics on in vivo viral infections, SIAM J. Math. Appl. 70 (2010) 2434–2448.

[45] X. Zhou, L. Zhang, T. Zheng, H. Li, Z. Teng, Global stability for a delayed HIV reactivation model with latent infection and Beddington-DeAngelis incidence, Appl. Math. Lett. 117 (2021) 1–10.

[46] P.W. Nelson, J.D. Murray, A.S. Perelson, A model of HIV-1 pathogenesis that includes an intracellular delay, Math. Biosci. 163 (2) (2000) 201–215.

[47] X. Pan, Y. Chen, H. Shu, Rich dynamics in a delayed HTLV-I infection model: Stability switch, multiple stable cycles, and torus, J. Math. Anal. Appl. 479 (2) (2019) 2214–2235.

[48] S.A. Gourley, Y. Kuang, J.D. Nagy, Dynamics of a delay differential equation model of hepatitis B virus infection, J. Biol. Dyn. 2 (2) (2008) 140–153.

[49] F. Zhang, J. Li, C. Zheng, L. Wang, Dynamics of an HBV/HCV infection model with intracellular delay and cell proliferation, Commun. Nonlinear Sci. Numer. Simul. 42 (2017) 464–476.

[50] J.K. Hale, S.M. Verduyn Lunel, Introduction to Functional Differential Equations, Springer-Verlag, New York, 1993.

[51] X. Yang, S. Chen, J. Chen, Permanence and positive periodic solution for the single-species nonautonomous delay diffusive models, Comput. Math. Appl. 32 (4) (1996) 109–116.

[52] A.S. Perelson, D.E. Kirschner, R. De Boer, Dynamics of HIV infection of CD4+ T cells, Math. Biosci. 114 (1993) 81–125.

[53] A. Korobeinikov, Global properties of basic virus dynamics models, Bull. Math. Biol. 66 (4) (2004) 879–883.

[54] A. Korobeinikov, Global properties of infectious disease models with nonlinear incidence, Bull. Math. Biol. 69 (6) (2007) 1871–1886.

[55] A.M. Elaiw, N.H. AlsHamrani, Global stability of humoral immunity virus dynamics models with nonlinear infection rate and removal, Nonlinear Anal. Real World Appl. 26 (2015) 161–190.

[56] J.P. LaSalle, The Stability of Dynamical Systems, SIAM, Philadelphia, 1976.

[57] A. Bellen, Y. Taira, Stabilization in a chemotaxis model for virus infection, Discrete Continuous Dyn. Syst. Ser. S 13 (2) (2020) 105–117.

[58] A.M. Elaiw, A.D. Al Agha, M.A. Alshaihk, Global stability of a within-host SARS-CoV-2/cancer model with immunity and diffusion, Int. J. Biomath. 15(2) (2021) 2150093.
[59] N. Bellomo, D. Burini, N. Outada, Multiscale models of Covid-19 with mutations and variants, Netw. Heterogen. Media 17 (3) (2022) 293–310.

[60] N. Bellomo, D. Burini, N. Outada, Pandemics of mutating virus and society: a multi-scale active particles approach, Philos. Trans. Ser. Math. Phys. Eng. Sci. 380 (2224) (2022) 1–14.

[61] C. Dineshkumar, R. Udhayakumar, V. Vijayakumar, K.S. Nisar, A. Shukla, A note on the approximate controllability of Sobolev type fractional stochastic integro-differential delay inclusions with order $1 < r < 2$, Math. Comput. Simul. 190 (2021) 1003–1026.

[62] K.S. Nisar, K. Logeswari, V. Vijayaraj, H.M. Baskonus, C. Ravichandran, Fractional order modeling the Gemini virus in capsicum annuum with optimal control, Fract. Fract. 6 (2) (2022) 61.

[63] K. Kavitha, V. Vijayakumar, R. Udhayakumar, C. Ravichandran, Results on controllability of Hilfer fractional differential equations with infinite delay via measures of noncompactness, Asian J. Control (2021) DOI: 10.1002/asjc.2549.

[64] V. Vijayakumar, S.K. Panda, K.S. Nisar, H.M. Baskonus, Results on approximate controllability results for second-order Sobolev-type impulsive neutral differential evolution inclusions with infinite delay, Numer. Methods Partial Different. Eqs. 37 (2) (2021) 1200–1221.

[65] K.S. Nisar, V. Vijayakumar, Results concerning to approximate controllability of non-densely defined Sobolev-type Hilfer fractional neutral delay differential system, Math. Methods Appl. Sci. 44 (17) (2021) 13615-13632.