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Mathematical Model of SAR-CoV-2 and Influenza A Virus Coinfection within Host with CTL-Mediated Immunity

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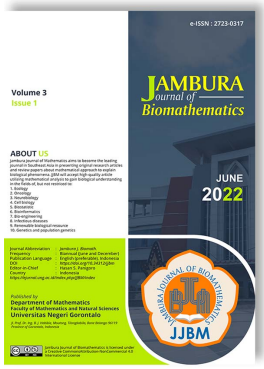

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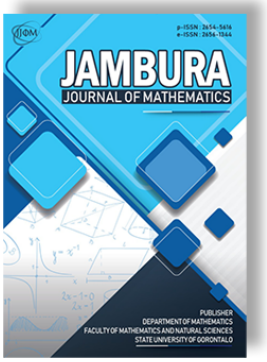

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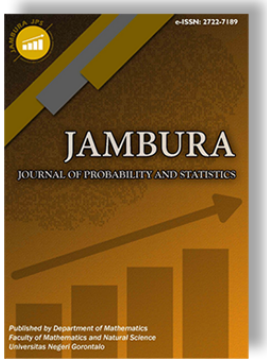

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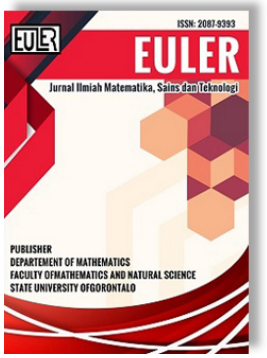

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Research Article

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Mathematical Model of SAR-CoV-2 and Influenza A Virus Coinfection within Host with CTL-Mediated Immunity

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ABSTRACT. *Coinfection of SARS-CoV-2 and Influenza A virus within a host poses a unique challenge in understanding immunological dynamics, especially the role of cytotoxic T lymphocytes (CTL) in mediating the immune response. This work present a mathematical model to examine the dynamics of coinfection within a host, highlighting CTL-mediated immunity. Generally, this model encompasses several compartments, including epithelial cells, free viruses, and CTLs specific of both SARS-CoV-2 and Influenza A. The basic properties of the model, equilibrum state analysis, stability using the Lyapunov function, and numerical simulations are examined to investigate the dynamics behavior of the model. Eight equilibrium states are identified: the virus-free equilibrium (E_0), single SARS-CoV-2 infection without CTLs (E_1), single Influenza A virus infection without CTLs (E_2), single SARS-CoV-2 infection with SARS-CoV-2-specific CTLs (E_3), single Influenza A virus infection with Influenza A virus-specific CTLs (E_4), SARS-CoV-2 and Influenza A virus coinfection with SARS-CoV-2-specific CTLs (E_5), SARS-CoV-2 and Influenza A virus coinfection with Influenza A virus-specific CTLs (E_6), and SARS-CoV-2 and Influenza A virus coinfection with both SARS-CoV-2-specific and Influenza A virus-specific CTLs (E_7). The existence and stability regions for each equilibrium state are determined and represented in the R_1-R_2 plane as threshold functions within the model. Numerical simulations confirm the results of the qualitative analysis, demonstrating that CTLs specific to SARS-CoV-2 and Influenza A virus can be activated, reducing the number of infected epithelial cells as well as inhibiting virus transmission within epithelial cells. Furthermore, analysis of parameter changes shows that increasing the proliferation rate of epithelial cells and CTLs, while lowering the virus formation rate, can shift the system's stability threshold and stabilize it at the virus-free equilibrium.*

1. Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the virus responsible for the COVID-19 pandemic, which emerged in Wuhan, China, in December 2019 and subsequently spread globally, leading to an international health emergency for several years [1, 2]. According to the World Health Organization (WHO), as of September 2024, the number of COVID-19 confirmed cases globally exceeds 776 million, with more than 7 million deaths. In Indonesia, approximately 6.8 million confirmed cases and 162 thousand deaths have been reported [3]. In addition, influenza viruses, similar to SARS-CoV-2, also cause respiratory infections in humans, resulting in seasonal outbreaks. These viruses infect up to 25% of the global human population [4]. There are four types of influenza viruses: A, B, C, and D, with Influenza A viruses being capable of causing flu pandemics [5].

Coinfections, where a host is simultaneously infected by multiple pathogens, can lead to more severe symptoms in patients due to immune system complications, decreased treatment effectiveness, and higher risk of misdiagnosis. These conditions also present a higher challenge to the healthcare process due to overlapping clinical traits [6, 7]. SARS-CoV-2 and Influenza A both infect the epithelial cells of the host's respiratory tract and have similar clinical symptoms such as shortness of breath, cough, and fever [8, 9]. A study reported that the coinfection rate of SARS-CoV-2 and Influenza A reached 49.8% among COVID-19 patients in Wuhan. A study in the UK also revealed that 19% of COVID-19 patients tested positive for both Influenza A virus and SARS-CoV-2 during the first outbreak of COVID-19 from January to April 2020 [10]. Individuals with coinfections of Influenza and SARS-CoV-2 experience a higher risk of severe symptoms and an increased mortality rate compared to those with a single SARS-CoV-2 infection [11, 12]. Cytotoxic T Lymphocytes (CTL), or killer T cells, are crucial components of the immune system that detect and kill virus-infected cells. CTLs derive from T cells, a subtype of lymphocytes, that undergo maturation in the thymus. They are generated when naive T cells, which circulate in the body, recognize specific viral antigens shown on the surface of infected cells. Once activated by these antigens, T cells differentiate into CTLs, which subsequently locate and eliminate infected cells [13, 14]. CTLs, which are specific to SARS-CoV-2 and Influenza A, are critical components of the immune response, both identifying and targeting cells infected by their respective viruses through the detection of unique viral antigens. Both types of CTLs exhibit

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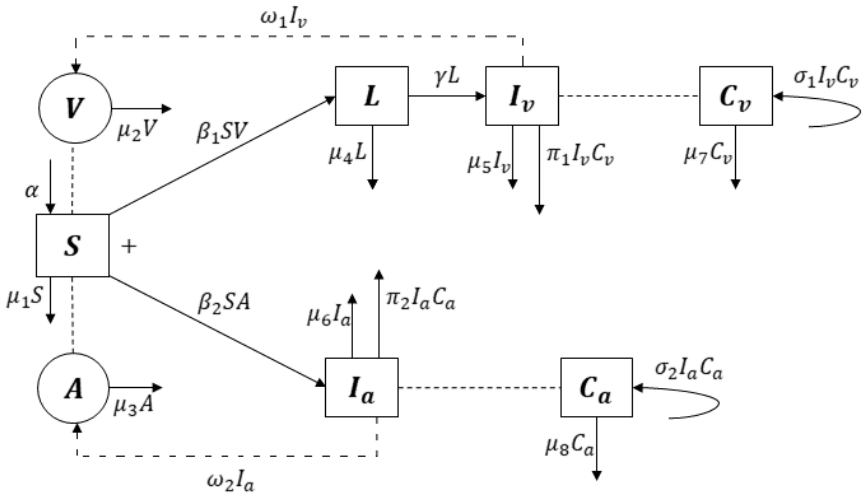


Figure 1. Compartment diagram of SARS-CoV-2 and Influenza A Virus coinfection

strong antigen-specificity, indicating that CTLs specific to SARS-CoV-2 generally do not identify or attack cells infected with Influenza A, and vice versa [15, 16].

Mathematical models provide a systematic approach to investigate and predict how coinfections of SARS-CoV-2 and Influenza A evolve within the host. Previously, single infection models of Influenza A virus or SARS-CoV-2 have been studied [17–29]. Those studies examine several mathematical approaches, including spatio-temporal analysis, deterministic and stochastic models, discrete models with delay, or using a fractal-fractional derivative order in the model. Strategies such as quarantine or treatment are used to control disease transmission.

S. Chowdhury et al. [30] constructed a mathematical model of COVID-19 that considers the interaction between the immune system and SARS-CoV-2 within a host. The model analyzes single infections caused by SARS-CoV-2 and explores the viral load dynamics within the host, considering the roles of natural killer cells and T-cells. M. Ojo et al. [31] developed a coinfection model for COVID-19 and influenza by analyzing 15 compartments, including the exposed (latent) compartment. However, their model focuses on transmission between individuals rather than within a host, with the primary analysis centered on optimal control. Additionally, a study by Ahmed M. Elaiw et al. in 2023 [32] developed a coinfection model of IAV and SARS-CoV-2 that incorporates the eclipse (latent) phase and specific antibody immunity. This model examines the interactions among nine compartments, including uninfected epithelial cells, latent and active SARS-CoV-2-infected cells, latent and active IAV-infected cells, free SARS-CoV-2 particles, free IAV particles, SARS-CoV-2-specific antibodies, and IAV-specific antibodies.

Compared to the previous study [32], which adopts a virus-antibody-specific approach to modeling IAV/SARS-CoV-2 coinfection, this paper presents a mathematical model for the coinfection of SARS-CoV-2 and Influenza A virus within a host, focusing on the role of Cytotoxic T lymphocytes (CTLs) specific to each virus. The key difference lies in target of immune response, CTLs directly target and eliminate infected or abnormal cells (e.g., virus-infected or cancer cells), whereas virus-specific antibodies bind to free virus particles, preventing them from entering cells (neutralization) but do not directly affect infected cells [33, 34]. A latency compartment is included to account for the latency period or eclipse phase during which the virus enters epithelial cells and begins replicating without producing or releasing infectious virions. Furthermore, as the eclipse phase for SARS-CoV-2 is longer than that for Influenza A, the latency phase is incorporated solely into the SARS-CoV-2 infection dynamics in this model.

Next, the process of constructing the model, along with its basic qualitative properties and equilibrium states, will be analyzed. Global stability will be assessed using the Lyapunov function, and stability regions will be thoroughly examined to complement the analytical results. Furthermore, numerical simulations will be conducted to validate the findings from the analytical analysis.

2. Mathematical Model and Analysis

2.1. *Model formulation*

In this section, we present the model for coinfection of SARS-CoV-2 and Influenza A virus in a host with CTL immunity. This model involves interactions among eight compartments, namely uninfected epithelial cells (S), latent SARS-CoV-2-infected cells (L), active SARS-CoV-2-infected cells (I_v), free SARS-CoV-2 particles (V), Influenza A virus-infected cells (I_a), free Influenza A virus particles (A), SARS-CoV-2-specific CTLs (C_v), and Influenza A virus-specific CTLs (C_a). In this model, uninfected epithelial cells are targeted by both SARS-CoV-2 and Influenza A virus. SARS-CoV-2-Infected cells undergo an intracellular latency period (eclipse phase) before releasing the viral particle to infect other uninfected epithelial cells. However, as Influenza A virus-infected cells have shorter intracellular latency period, this model assumes no latency compartment for Infected Influenza A. Free SARS-CoV-2 particles (V) and free Influenza A virus particles (A) are released from the SAR-CoV-2-infected cells and Influenza-A virus infected cells, respectively. On the other hand, CTLs-specific cells, both SAR-CoV-2 or Influenza A, are activated and proliferated when the infected cells present and release the virus. These CTLs then circulate through the body, and killing infected cells displaying the same viral antigen. The coinfection process diagram of SARS-CoV-2 and Influenza A virus within a host with CTL immunity are illustrated in Figure 1.

Table 1. Parameters in the model of coinfection of SARS-CoV-2 and Influenza A virus

Parameter	Description	Unit
α	The proliferation rate of uninfected epithelial cells	cell/time
μ_1	The natural death rate of uninfected epithelial cells	1/time
μ_2	The natural death rate of SARS-CoV-2	1/time
μ_3	The natural death rate of Influenza A virus	1/time
μ_4	The natural death rate of laten SARS-CoV-2-infected cells	1/time
μ_5	The natural death rate of SARS-CoV-2-infected cells	1/time
μ_6	The natural death rate of Influenza A virus-infected cells	1/time
μ_7	The natural death rate of SARS-CoV-2-specific CTL	1/time
μ_8	The natural death rate of Influenza A-specific CTL	1/time
β_1	The transmission rate of SARS-CoV-2 particle	1/(time.cell)
β_2	The transmission rate of Influenza A virus particle	1/(time.cell)
γ	The transition rate from latent SARS-CoV-2-infected cells to active	1/time
ω_1	The formation rate of new SARS-CoV-2 particles	1/time
ω_2	The formation rate of new Influenza A virus particles	1/time
π_1	The killing rate of active SARS-CoV-2-infected cells by SARS-CoV-2-specific CTL	1/(time.cell)
π_2	The killing rate of Influenza A virus infected cells by Influenza A virus specific CTL	1/(time.cell)
σ_1	The proliferation rate of SARS-CoV-2-specific CTL	1/(time.cell)
σ_2	The proliferation rate of Influenza A virus-specific CTL	1/(time.cell)

Based on the compartment diagram in Figure 1, the coinfection of SARS-CoV-2 and Influenza A virus in a host with CTL immunity can be modeled as a system of nonlinear ordinary differential equations as follows:

$$\begin{aligned}
\frac{dS}{dt} &= \alpha - \beta_1 SV - \beta_2 SA - \mu_1 S,\\
\frac{dL}{dt} &= \beta_1 SV - \gamma L - \mu_4 L,\\
\frac{dI_v}{dt} &= \gamma L - \pi_1 I_v C_v - \mu_5 I_v,\\
\frac{dI_a}{dt} &= \beta_2 SA - \pi_2 I_a C_a - \mu_6 I_a,\\
\frac{dV}{dt} &= \omega_1 I_v - \mu_2 V,\\
\frac{dA}{dt} &= \omega_2 I_a - \mu_3 A,\\
\frac{dC_v}{dt} &= \sigma_1 I_v C_v - \mu_7 C_v,\\
\frac{dC_a}{dt} &= \sigma_2 I_a C_a - \mu_8 C_a.
\end{aligned} \tag{1}$$

with initial values $S(0) \geq 0$, $L(0) \geq 0$, $I_v(0) \geq 0$, $I_a(0) \geq 0$, $V(0) \geq 0$, $A(0) \geq 0$, $C_v(0) \geq 0$, $C_a(0) \geq 0$. The parameter descriptions for System (1) are provided in Table 1.

2.2. The non-negativity and boundedness of solution

In this section, the solutions of System (1) will be proven non-negative and bounded for $t > 0$, ensuring consistency with its biological interpretation.

Theorem 1. *The solutions of differential equation system (1): $S(t)$, $L(t)$, $I_v(t)$, $I_a(t)$, $V(t)$, $A(t)$, $C_v(t)$, and $C_a(t)$ are non-negative with the given initial values $S(0) \geq 0$, $L(0) \geq 0$, $I_v(0) \geq 0$, $I_a(0) \geq 0$, $V(0) \geq 0$, $A(0) \geq 0$, $C_v(0) \geq 0$, and $C_a(0) \geq 0$, respectively.*

Proof. From the system (1), the change of uninfected epithelial cells is written as

$$\frac{dS}{dt} = \alpha - (\beta_1 V + \beta_2 A + \mu_1)S \;\geq\; -(\beta_1 V + \beta_2 A + \mu_1)S.$$

By using integrating factor method, we get

$$\begin{aligned}
\int_0^t \frac{dS(\tau)}{S(\tau)} &\geq \int_0^t -(\beta_1 V + \beta_2 A + \mu_1)d\tau,\\
\ln S(\tau)\,\big|_0^t &\geq -\mu_1 t - \int_0^t (\beta_1 V + \beta_2 A)d\tau,\\
\ln \frac{S(t)}{S(0)} &\geq -\mu_1 t - \int_0^t (\beta_1 V + \beta_2 A)d\tau,\\
S(t) &\geq S(0)\, exp\left[-\mu_1 t - \int_0^t (\beta_1 V + \beta_2 A)d\tau\right].
\end{aligned}$$

Thus, for every $t \geq 0$, the solution of $S(t)$ remains nonnegative, since the exponential function is always positive and $S(0) \geq 0$. By applying the same method, it can be derived that $L(t)$, $I_v(t)$, $I_a(t)$, $V(t)$, $A(t)$, $C_v(t)$, and $C_a(t)$ are all nonnegative. □

Theorem 2. *The solutions of differential equation system (1) are bounded, and the region define by*

$$D = \left\{(S, L, I_v, I_a, V, A, C_v, C_a) \in \mathbb{R}^8 : 0 \leq N \leq \frac{\alpha}{\rho}\right\}.$$

with

$$N = S + L + I_v + I_a + \frac{\mu_5}{2\omega_1}V + \frac{\mu_6}{2\omega_2}A + \frac{\pi_1}{\sigma_1}C_v + \frac{\pi_2}{\sigma_2}C_a,$$

is nonegativity invariant.

Proof. Let

$$N = S + L + I_v + I_a + \frac{\mu_5}{2\omega_1}V + \frac{\mu_6}{2\omega_2}A + \frac{\pi_1}{\sigma_1}C_v + \frac{\pi_2}{\sigma_2}C_a.$$

Its derivative can be expressed as

$$\begin{aligned}
\frac{dN}{dt} &= \frac{dS}{dt} + \frac{dL}{dt} + \frac{dI_v}{dt} + \frac{dI_a}{dt} + \frac{\mu_5}{2\omega_1}\cdot\frac{dV}{dt} + \frac{\mu_6}{2\omega_2}\cdot\frac{dA}{dt} \\
&\quad + \frac{\pi_1}{\sigma_1}\cdot\frac{dC_v}{dt} + \frac{\pi_2}{\sigma_2}\cdot\frac{dC_a}{dt}, \\
\frac{dN}{dt} &= \alpha - \beta_1 SV - \beta_2 SA - \mu_1 S + \beta_1 SV - \gamma L - \mu_4 L + \gamma L \\
&\quad - \pi_1 I_v C_v - \mu_5 I_v + \beta_2 SA - \pi_2 I_a C_a - \mu_6 I_a + \frac{\mu_5}{2\omega_1}[\omega_1 I_v \\
&\quad - \mu_2 V] + \frac{\mu_6}{2\omega_2}[\omega_2 I_a - \mu_3 A] + \frac{\pi_1}{\sigma_1}[\sigma_1 I_v C_v - \mu_7 C_v] \\
&\quad + \frac{\pi_2}{\sigma_2}[\sigma_2 I_a C_a - \mu_8 C_a], \\
\frac{dN}{dt} &= \alpha - \mu_1 S - \mu_4 L - \mu_5 I_v - \mu_6 I_a + \frac{\mu_5 I_v}{2} - \frac{\mu_5\mu_2}{2\omega_1}V + \frac{\mu_6 I_a}{2} \\
&\quad - \frac{\mu_6\mu_3}{2\omega_2}A - \frac{\pi_1\mu_7}{\sigma_1}C_v - \frac{\pi_2\mu_8}{\sigma_2}C_a, \\
\frac{dN}{dt} &= \alpha - \mu_1 S - \mu_4 L - \mu_5 I_v - \mu_6 I_a - \frac{\mu_5\mu_2}{2\omega_1}V - \frac{\mu_6\mu_3}{2\omega_2}A \\
&\quad - \frac{\pi_1\mu_7}{\sigma_1}C_v - \frac{\pi_2\mu_8}{\sigma_2}C_a, \\
\frac{dN}{dt} &\le \alpha - \rho\left[S + L + I_v + I_a + \frac{\mu_5}{2\omega_1}V + \frac{\mu_6}{2\omega_2}A + \frac{\pi_1}{\sigma_1}C_v + \frac{\pi_2}{\sigma_2}C_a\right] \\
\frac{dN}{dt} &\le \alpha - \rho N.
\end{aligned}$$

where $\rho = \min\left\{\mu_1, \mu_4, \frac{\mu_5}{2}, \frac{\mu_6}{2}, \mu_2, \mu_3, \mu_7, \mu_8\right\}$. By using integrating factor method, we get

$$\begin{aligned}
\frac{dN(t)}{dt}\cdot e^{\rho t} + \rho N(t)\cdot e^{\rho t} &\le \alpha\cdot e^{\rho t}, \\
\int_0^t d\left(N(t)\cdot e^{\rho t}\right) &\le \int_0^t \alpha\cdot e^{\rho t} d\tau, \\
N(t)\cdot e^{\rho t} - N(0) &\le \frac{\alpha}{\rho}(e^{\rho t} - 1), \\
N(t) &\le \frac{\alpha}{\rho} + \left(N(0) - \frac{\alpha}{\rho}\right)e^{-\rho t}.
\end{aligned}$$

If $N(0) \le \frac{\alpha}{\rho}$, then we have $0 \le N(t) \le \frac{\alpha}{\rho}$ for $t > 0$. Taking the supremum limit of $N(t)$ as $t \to \infty$, we obtain

$$\limsup_{t\to\infty} N(t) = \lim_{t\to\infty}\left[\frac{\alpha}{\rho} + \left(N(0) - \frac{\alpha}{\rho}\right)e^{-\rho t}\right] = \frac{\alpha}{\rho},$$

Thus $N(t)$ is upper-bounded. Next, from Theorem 1, since all solutions are nonnegative, if

$$\begin{aligned}
0 \le\ & S(0) + L(0) + I_v(0) + I_a(0) + \frac{\mu_5}{2\omega_1}V(0) \le \frac{\alpha}{\rho}, \\
& + \frac{\mu_6}{2\omega_2}A(0) + \frac{\pi_1}{\sigma_1}C_v(0) + \frac{\pi_2}{\sigma_2}C_a(0)
\end{aligned}$$

then we have

$$\begin{aligned}
0 \le\ & S(t) + L(t) + I_v(t) + I_a(t) + \frac{\mu_5}{2\omega_1}V(t) \le \frac{\alpha}{\rho} \\
& + \frac{\mu_6}{2\omega_2}A(t) + \frac{\pi_1}{\sigma_1}C_v(t) + \frac{\pi_2}{\sigma_2}C_a(t)
\end{aligned}$$

or

$$\begin{aligned}
0 \le S(t), L(t), I_v(t), I_a(t) &\le \frac{\alpha}{\rho}; \\
0 \le V(t) &\le \frac{2\alpha\omega_1}{\rho\mu_5}; \\
0 \le A(t) &\le \frac{2\alpha\omega_2}{\rho\mu_6}; \\
0 \le C_v(t) &\le \frac{\alpha\sigma_1}{\rho\pi_1}; \\
0 \le C_a(t) &\le \frac{\alpha\sigma_2}{\rho\pi_2}.
\end{aligned}$$

To conclude, it has been proven that the solutions of System (1) are bounded and nonnegativity invariant. □

2.3. Equilibrium States

The equilibrium states of the mathematical model of SARS-CoV-2 and Influenza A coinfection in a host with CTL-mediated immunity are obtained when each of the differential equations in System (1) equals zero.

$$\begin{aligned}
\alpha - \beta_1 SV - \beta_2 SA - \mu_1 S &= 0, \\
\beta_1 SV - \gamma L - \mu_4 L &= 0, \\
\gamma L - \pi_1 I_v C_v - \mu_5 I_v &= 0, \\
\beta_2 SA - \pi_2 I_a C_a - \mu_6 I_a &= 0, \\
\omega_1 I_v - \mu_2 V &= 0, \\
\omega_2 I_a - \mu_3 A &= 0, \\
\sigma_1 I_v C_v - \mu_7 C_v &= 0, \\
\sigma_2 I_a C_a - \mu_8 C_a &= 0.
\end{aligned} \tag{2}$$

By solving the equations system (2), we obtain eight equilibrium states, as follows:

1. The virus-free equilibrium state (E_0):

$$\begin{aligned}
E_0 &= (S, L, I_v, I_a, V, A, C_v, C_a), \\
&= \left(\frac{\alpha}{\mu_1}, 0, 0, 0, 0, 0, 0, 0\right).
\end{aligned}$$

2. The equilibrium state of single SARS-CoV-2 infection without CTL (E_1):

$$\begin{aligned}
E_1 &= (S, L, I_v, I_a, V, A, C_v, C_a), \\
&= (S_1, L_1, I_{v1}, 0, V_1, 0, 0, 0),
\end{aligned}$$

with

$$\begin{aligned}
S_1 &= \frac{\xi\mu_2\mu_5}{\gamma\beta_1\omega_1}, & L_1 &= \frac{\mu_1\mu_2\mu_5}{\beta_1\omega_1\gamma}(R_1 - 1), \\
I_{v1} &= \frac{\mu_1\mu_2}{\beta_1\omega_1}(R_1 - 1), & V_1 &= \frac{\mu_1}{\beta_1}(R_1 - 1), \\
\xi &= (\gamma + \mu_4), & R_1 &= \frac{\alpha\gamma\beta_1\omega_1}{\xi\mu_1\mu_2\mu_5}.
\end{aligned}$$

Note that the equilibrium state E_1 exists when $R_1 > 1$.

3. The equilibrium state of single Influenza-A virus infection without CTL (E_2):

$$\begin{aligned}
E_2 &= (S, L, I_v, I_a, V, A, C_v, C_a), \\
&= (S_2, 0, 0, I_{a2}, 0, A_2, 0, 0),
\end{aligned}$$

with

$$S_2 = \frac{\mu_3\mu_6}{\beta_2\omega_2}, \qquad I_{a2} = \frac{\mu_1\mu_3}{\beta_2\omega_2}(R_2-1),$$
$$A_2 = \frac{\mu_1}{\beta_2}(R_2-1), \quad R_2 = \frac{\alpha\beta_2\omega_2}{\mu_1\mu_3\mu_6}.$$

Note that the equilibrium state E_2 exists when $R_2 > 1$.

4. The equilibrium state of single SARS-CoV-2 infection with SARS-CoV-2 specific CTL (E_3):

$$E_3 = (S, L, I_v, I_a, V, A, C_v, C_a), = (S_3, L_3, I_{v3}, 0, V_3, 0, C_{v3}, 0),$$

with

$$S_3 = \frac{\alpha\mu_2\sigma_1}{\beta_1\mu_7\omega_1+\mu_1\mu_2\sigma_1}, \qquad I_{v3} = \frac{\mu_7}{\sigma_1},$$
$$L_3 = \frac{\alpha\beta_1\omega_1\mu_7}{\xi(\beta_1\mu_7\omega_1+\mu_1\mu_2\sigma_1)}, \quad V_3 = \frac{\mu_7\omega_1}{\sigma_1\mu_2},$$
$$C_{v3} = \frac{\mu_5}{\pi_1}\left(\frac{R_1}{h_1}-1\right), \qquad \xi = \gamma+\mu_4,$$
$$h_1 = \frac{\alpha}{\mu_1 S_3}.$$

Thus, the equilibrium state E_3 exists when $R_1 > h_1$.

5. The equilibrium state of single Influenza-A virus infection with Influenza A specific CTL (E_4):

$$E_4 = (S, L, I_v, I_a, V, A, C_v, C_a), = (S_4, 0, 0, I_{a4}, 0, A_4, 0, C_{a4}),$$

with

$$S_4 = \frac{\alpha\mu_3\sigma_2}{\beta_2\mu_8\omega_2+\mu_1\mu_3\sigma_2}, \qquad I_{a4} = \frac{\mu_8}{\sigma_2},$$
$$A_4 = \frac{\mu_8\omega_2}{\sigma_2\mu_3}, \qquad C_{a4} = \frac{\mu_6}{\pi_2}\left(\tfrac{R_2}{h_2}-1\right),$$
$$h_2 = \frac{\alpha}{\mu_1 S_4}.$$

Note that the equilibrium state E_4 exists when $R_2 > h_2$.

6. The equilibrium state of coinfection with SARS-CoV-2 and Influenza A virus, with only SARS-CoV-2 specific CTL (E_5):

$$E_5 = (S, L, I_v, I_a, V, A, C_v, C_a), = (S_5, L_5, I_{v5}, I_{a5}, V_5, A_5, C_{v5}, 0),$$

with

$$S_5 = \frac{\mu_3\mu_6}{\beta_2\omega_2}, \qquad L_5 = \frac{\mu_7\mu_3\mu_6\beta_1\omega_1}{\sigma_1\beta_2\omega_2\xi\mu_2},$$
$$I_{v5} = \frac{\mu_7}{\sigma_1}, \qquad V_5 = \frac{\mu_7\omega_1}{\sigma_1\mu_2},$$
$$I_{a5} = \frac{\alpha h_1}{\mu_6 R_2}\left(\frac{R_2}{h_1}-1\right), \; A_5 = \frac{\alpha\omega_2 h_1}{\mu_3\mu_6 R_2}\left(\frac{R_2}{h_1}-1\right),$$
$$C_{v5} = \frac{\mu_5}{\pi_1}\left[\frac{\gamma\beta_1\mu_3\mu_6\omega_1}{\xi\beta_2\mu_2\mu_5\omega_2}-1\right] = \frac{\mu_5}{\pi_1}\left[\frac{R_1}{R_2}-1\right],$$
$$\xi = \gamma+\mu_4, \qquad h_1 = \frac{\alpha}{\mu_1 S_3}.$$

Thus, the equilibrium state E_5 exists when $R_2 > h_1$ and $R_1 > R_2$.

7. The equilibrium state of coinfection with SARS-CoV-2 and Influenza A virus, with only Influenza A specific CTL stimulated (E_6):

$$E_6 = (S, L, I_v, I_a, V, A, C_v, C_a), = (S_6, L_6, I_{v6}, I_{a6}, V_6, A_6, 0, C_{a6}),$$

with

$$S_6 = \frac{\xi\mu_2\mu_5}{\gamma\beta_1\omega_1}, \qquad L_6 = \frac{\alpha h_2}{\xi R_1}\left(\frac{R_1}{h_2}-1\right),$$
$$I_{v6} = \frac{\alpha\gamma h_2}{\xi\mu_5 R_1}\left(\frac{R_1}{h_2}-1\right), \quad I_{a6} = \frac{\mu_8}{\sigma_2},$$
$$V_6 = \frac{\alpha\gamma\omega_1 h_2}{\xi\mu_2\mu_5 R_1}\left(\frac{R_1}{h_2}-1\right), \; A_6 = \frac{\mu_8\omega_2}{\sigma_2\mu_3},$$
$$C_{a6} = \frac{\mu_6}{\pi_2}\left[\frac{\xi\beta_2\mu_2\mu_5\omega_2}{\gamma\beta_1\mu_3\mu_6\omega_1}-1\right] = \frac{\mu_6}{\pi_2}\left[\frac{R_2}{R_1}-1\right],$$
$$\xi = \gamma+\mu_4, \qquad h_2 = \frac{\alpha}{\mu_1 S_4}.$$

Thus, the equilibrium state E_6 exists when $R_1 > h_2$ and $R_2 > R_1$.

8. The equilibrium state of coinfection with SARS-CoV-2 and Influenza A virus, with stimulation of both SARS-CoV-2 and Influenza A specific CTL (E_7):

$$E_7 = (S, L, I_v, I_a, V, A, C_v, C_a), = (S_7, L_7, I_{v7}, I_{a7}, V_7, A_7, C_{v7}, C_{a7}),$$

with

$$S_7 = \frac{\mu_3\beta_2\omega_2}{\mu_6 R_b}, \qquad L_7 = \frac{\mu_8\gamma\sigma_1}{\mu_5 R_a},$$
$$I_{v7} = \frac{\mu_7}{\sigma_1}, \qquad I_{a7} = \frac{\mu_8}{\sigma_2},$$
$$V_7 = \frac{\mu_7\omega_1}{\sigma_1\mu_2}, \qquad A_7 = \frac{\mu_8\omega_2}{\sigma_2\mu_3},$$
$$C_{v7} = \frac{\mu_5}{\pi_1}(R_a-1), \qquad \xi = \gamma+\mu_4,$$
$$C_{a7} = \frac{\mu_6}{\pi_2}(R_b-1),$$
$$R_a = \frac{\alpha\gamma\beta_1\mu_3\omega_1\sigma_1\sigma_2}{\xi\mu_5(\beta_1\mu_3\mu_7\omega_1\sigma_2+\beta_2\mu_2\mu_8\omega_2\sigma_1+\mu_1\mu_2\mu_3\sigma_1\sigma_2)},$$
$$R_b = \frac{\alpha\beta_2\mu_2\omega_2\sigma_1\sigma_2}{\mu_6(\beta_1\mu_3\mu_7\omega_1\sigma_2+\beta_2\mu_2\mu_8\omega_2\sigma_1+\mu_1\mu_2\mu_3\sigma_1\sigma_2)}.$$

Note that,

$$\frac{R_1}{h_1+h_2} = \frac{\alpha\gamma\beta_1\mu_3\omega_1\sigma_1\sigma_2}{\xi\mu_5(\beta_1\mu_3\mu_7\omega_1\sigma_2+\beta_2\mu_2\mu_8\omega_2\sigma_1+2\mu_1\mu_2\mu_3\sigma_1\sigma_2)} > R_a,$$
$$\frac{R_2}{h_1+h_2} = \frac{\alpha\beta_2\mu_2\omega_2\sigma_1\sigma_2}{\mu_6(\beta_1\mu_3\mu_7\omega_1\sigma_2+\beta_2\mu_2\mu_8\omega_2\sigma_1+2\mu_1\mu_2\mu_3\sigma_1\sigma_2)} > R_b.$$

As shown, C_{v7} and C_{a7} will be positive when $\frac{R_1}{h_1+h_2} > R_a > 1$ and $\frac{R_2}{h_1+h_2} > R_b > 1$. Thus, the equilibrium state E_7 exists when $R_1 > h_1+h_2$ and $R_2 > h_1+h_2$.

2.4. Stability Analysis

In this section, we analyze the global stability of equilibrium states using a Lyapunov function. The definition of the Lyapunov function is presented as follows:

Definition 1. [35] Let x_e be an equilibrium state of the differential equation $\dot{x} = f(x)$. A function $\psi : R^n \to R^n$ is called a Lyapunov function for x_e if there exists a neighborhood $D \subseteq R^n$ around x_e that satisfies the following conditions:

1. Function $\psi(x) > 0$ for $x \in D$ with $x \neq x_e$ and $\psi(x_e) = 0$ for $x = x_e$.
2. If $\dot{\psi}(x) \leq 0$ for every $x \in D$, then the equilibrium state x_e stable.
3. If $\dot{\psi}(x) < 0$ for $x \in D$, with $x \neq x_e$, then the equilibrium state x_e globally asymptotically stable.

Definition 2. Define a function

$$f(x) = x - 1 - \ln x. \tag{3}$$

This function has a positive domain and a nonnegative range, with a minimum value of 0 at $x = 1$.

Moreover, we will also apply the Arithmetic Mean-Geometric Mean (AM-GM) inequality [36] in analyzing the stability of System (1). Let $a_1, a_2, a_3, \ldots, a_n \in \mathbf{R}^+$ with $n \geq 2$, then the following inequalities hold.

$$\frac{a_1 + a_2 + \cdots + a_n}{n} \geq \sqrt[n]{a_1 a_2 \cdots a_n}, a_i \geq 0,\ i = 1, 2, \cdots, n. \tag{4}$$

Now let $E = (S, L, I_v, I_a, V, A, C_v, C_a)$, the stabilities of the different equilibrium states of System (1) are described by the following theorems.

Theorem 3. *If $R_1 \leq 1$ and $R_2 \leq 1$, then the equilibrium state E_0 is globally asymptotically stable in D.*

Proof. Define the Lyapunov function as follows:

$$\psi_0(E) = S_0\left(\frac{S}{S_0} - 1 - \ln\left(\frac{S}{S_0}\right)\right) + L + \frac{\xi}{\gamma} I_v + I_a + \frac{\xi\mu_5}{\gamma\omega_1} V + \frac{\mu_6}{\omega_2} A + \frac{\xi\pi_1}{\gamma\sigma_1} C_v + \frac{\pi_2}{\sigma_2} C_a.$$

Based on Definition 1 and 2, we have:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_0$, the inequality $\psi_0(E) > 0$ holds. Furthermore, if $E = E_0$, then $\psi_0(E) = 0$.
2. The derivative of the function ψ_0 with respect to t is:

$$\begin{aligned}
\dot{\psi}_0(E) &= \frac{d\psi_0}{dS}\cdot\frac{dS}{dt} + \frac{d\psi_0}{dL}\cdot\frac{dL}{dt} + \frac{d\psi_0}{dI_v}\cdot\frac{dI_v}{dt} + \frac{d\psi_0}{dI_a}\cdot\frac{dI_a}{dt} \\
&\quad + \frac{d\psi_0}{dV}\cdot\frac{dV}{dt} + \frac{d\psi_0}{dA}\cdot\frac{dA}{dt} + \frac{d\psi_0}{dC_v}\cdot\frac{dC_v}{dt} \\
&\quad + \frac{d\psi_0}{dC_a}\cdot\frac{dC_a}{dt}, \\
\dot{\psi}_0(E) &= \left(1 - \frac{S_0}{S}\right)[\alpha - \beta_1 SV - \beta_2 SA - \mu_1 S] + \beta_1 SV \\
&\quad - \xi L + \frac{\xi}{\gamma}[\gamma L - \pi_1 I_v C_v - \mu_5 I_v] + \beta_2 SA \\
&\quad - \pi_2 I_a C_a - \mu_6 I_a + \frac{\xi\mu_5}{\gamma\omega_1}[\omega_1 I_v - \mu_2 V] \\
&\quad + \frac{\mu_6}{\omega_2}[\omega_2 I_a - \mu_3 A] + \frac{\xi\pi_1}{\gamma\sigma_1}[\sigma_1 I_v C_v - \mu_7 C_v] \\
&\quad + \frac{\pi_2}{\sigma_2}[\sigma_2 I_a C_a - \mu_8 C_a,], \\
\dot{\psi}_0(E) &= \left(1 - \frac{S_0}{S}\right)(\alpha - \mu_1 S) + \beta_1 S_0 V + \beta_2 S_0 A \\
&\quad - \frac{\xi\mu_5\mu_2}{\gamma\omega_1} V - \frac{\mu_6\mu_3}{\omega_2} A - \frac{\xi\pi_1\mu_7}{\gamma\sigma_1} C_v - \frac{\pi_2\mu_8}{\sigma_2} C_a.
\end{aligned}$$

Substituting $S_0 = \frac{\alpha}{\mu_1}$ or $\alpha = \mu_1 S_0$, we obtain:

$$\begin{aligned}
\dot{\psi}_0(E) &= \frac{\mu_6\mu_3}{\omega_2}\left(\frac{\alpha\beta_2\omega_2}{\mu_1\mu_3\mu_6} - 1\right) A - \frac{\pi_2\mu_8}{\sigma_2} C_a \\
&\quad + \frac{\xi\mu_5\mu_2}{\gamma\omega_1}\left(\frac{\alpha\gamma\beta_1\omega_1}{\xi\mu_1\mu_2\mu_5} - 1\right) V - \frac{\xi\pi_1\mu_7}{\gamma\sigma_1} C_v \\
&\quad + \left(1 - \frac{S_0}{S}\right)(\mu_1 S_0 - \mu_1 S), \\
\dot{\psi}_0(E) &= \frac{\xi\mu_5\mu_2}{\gamma\omega_1}(R_1 - 1) V - \frac{\mu_1 (S - S_0)^2}{S} - \frac{\pi_2\mu_8}{\sigma_2} C_a \\
&\quad + \frac{\mu_6\mu_3}{\omega_2}(R_2 - 1) A - \frac{\xi\pi_1\mu_7}{\gamma\sigma_1} C_v.
\end{aligned}$$

It follows that $\dot{\psi}_0(E) < 0$ when $R_1 \leq 1$ and $R_2 \leq 1$. This implies that $\psi_0(E)$ is a Lyapunov function, and the equilibrium state E_0 is globally asymptotically stable if $R_1 \leq 1$ and $R_2 \leq 1$. □

Theorem 4. *If $R_2 \leq R_1$ and $1 < R_1 \leq h_1$ with $h_1 = \frac{\alpha}{\mu_1 S_3}$, then the equilibrium state E_1 is globally asymptotically stable in D.*

Proof. Define the Lyapunov function as follows:

$$\begin{aligned}
\psi_1(E) &= S_1\left(\frac{S}{S_1} - 1 - \ln\left(\frac{S}{S_1}\right)\right) + L_1\left(\frac{L}{L_1} - 1 - \ln\left(\frac{L}{L_1}\right)\right) \\
&\quad + \frac{\xi}{\gamma} I_{v1}\left(\frac{I_v}{I_{v1}} - 1 - \ln\left(\frac{I_v}{I_{v1}}\right)\right) + I_a + \frac{\mu_6}{\omega_2} A + \frac{\xi\pi_1}{\gamma\sigma_1} C_v \\
&\quad + \frac{\xi\mu_5}{\gamma\omega_1} V_1\left(\frac{V}{V_1} - 1 - \ln\left(\frac{V}{V_1}\right)\right) + \frac{\pi_2}{\sigma_2} C_a.
\end{aligned}$$

Based on Definition 1 and 2, we have:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_1$, we get $\psi_1(E) > 0$. Furthermore, if $E = E_1$, then $\psi_1(E) = 0$.
2. The derivative of the function ψ_1 with respect to t is expressed by:

$$\begin{aligned}
\dot{\psi}_1(E) &= \left(1 - \frac{S_1}{S}\right)(\mu_1 S_1 - \mu_1 S) + \frac{\mu_6\mu_3}{\omega_2}\left(\frac{\beta_2\omega_2}{\mu_3\mu_6} S_1 - 1\right) A \\
&\quad + 2\beta_1 S_1 V_1 - \beta_1 S_1 V_1 \frac{S_1}{S} - \beta_1 S_1 V_1 \frac{L_1 SV}{LS_1 V_1} \\
&\quad - \beta_1 S_1 V_1 \frac{I_{v1} L}{I_v L_1} - \beta_1 S_1 V_1 \frac{I_v V_1}{I_{v1} V} - \frac{\pi_2\mu_8}{\sigma_2} C_a \\
&\quad + \frac{\xi\pi_1\mu_7}{\gamma\sigma_1}\left(\frac{\sigma_1}{\mu_7} I_{v1} - 1\right) C_v,
\end{aligned}$$

$$\dot{\psi}_1(E) = -\frac{\mu_1 (S-S_1)^2}{S} + \beta_1 S_1 V_1 \left(2 - \frac{S_1}{S} - \frac{L_1 S V}{L S_1 V_1} - \frac{I_{v1} L}{I_v L_1} - \frac{I_v V_1}{I_{v1} V}\right) + \frac{\mu_6 \mu_3}{\omega_2}\left(\frac{R_2}{R_1} - 1\right) A + \frac{\xi \pi_1 \mu_7}{\gamma \sigma_1}\left(\frac{R_1}{h_1} - 1\right) C_v - \frac{\pi_2 \mu_8}{\sigma_2} C_a.$$

Using the inequality (4), we obtain:

$$2 - \frac{S_1}{S} - \frac{L_1 S V}{L S_1 V_1} - \frac{I_{v1} L}{I_v L_1} - \frac{I_v V_1}{I_{v1} V} \leq 0.$$

It follows that if $R_2 \leq R_1$ and $R_1 \leq h_1$ with $R_1 > 1$ as the existence condition for E_1, then $\dot{\psi}_1(E) < 0$. Therefore, it can be concluded that $\psi_1(E)$ is a Lyapunov function, and the equilibrium state E_1 is globally asymptotically stable under the conditions $R_2 \leq R_1$ and $1 < R_1 \leq h_1$. □

Theorem 5. *If $R_1 \leq R_2$ and $1 < R_2 \leq h_2$ with $h_2 = \frac{\alpha}{\mu_1 S_4}$, then the equilibrium state E_2 is globally asymptotically stable in D.*

Proof. Define the Lyapunov function as follows:

$$\psi_2(E) = S_2\left(\frac{S}{S_2} - 1 - \ln\left(\frac{S}{S_2}\right)\right) + L + \frac{\xi}{\gamma} I_v + \frac{\xi \mu_5}{\gamma \omega_1} V + I_{a2}\left(\frac{I_a}{I_{a2}} - 1 - \ln\left(\frac{I_a}{I_{a2}}\right)\right) + \frac{\xi \pi_1}{\gamma \sigma_1} C_v + \frac{\pi_2}{\sigma_2} C_a + \frac{\mu_6}{\omega_2} A_2 \left(\frac{A}{A_2} - 1 - \ln\left(\frac{A}{A_2}\right)\right).$$

Based on Definition 1 and 2, we have:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_2$ we have $\psi_2(E) > 0$. Furthermore, if $E = E_2$ then $\psi_2(E) = 0$.
2. The derivative of the function ψ_2 with respect to t is given by:

$$\dot{\psi}_2(E) = \left(1 - \frac{S_2}{S}\right)(\mu_1 S_2 - \mu_1 S) + \beta_2 S_2 A_2 - \beta_2 S_2 A_2 \frac{S_2}{S} - \beta_2 S_2 A_2 \frac{I_{a2} S A}{I_a S_2 A_2} + \frac{\xi \mu_5 \mu_2}{\gamma \omega_1}\left(\frac{\beta_1 \gamma \omega_1}{\xi \mu_5 \mu_2} S_2 - 1\right) V - \beta_2 S_2 A_2 \frac{I_a A_2}{I_{a2} A} + \frac{\pi_2 \mu_8}{\sigma_2}\left(\frac{\sigma_2}{\mu_8} I_{a2} - 1\right) C_a \frac{\xi \pi_1 \mu_7}{\gamma \sigma_1} C_v,$$

$$\dot{\psi}_2(E) = -\frac{\mu_1 (S-S_2)^2}{S} + \beta_2 S_2 A_2 \left(1 - \frac{S_2}{S} - \frac{I_{a2} S A}{I_a S_2 A_2} - \frac{I_a A_2}{I_{a2} A}\right) + \frac{\xi \mu_5 \mu_2}{\gamma \omega_1}\left(\frac{R_1}{R_2} - 1\right) V - \frac{\xi \pi_1 \mu_7}{\gamma \sigma_1} C_v + \frac{\pi_2 \mu_8}{\sigma_2}\left(\frac{R_2}{h_2} - 1\right) C_a.$$

Hence, when $R_1 \leq R_2$, $R_2 \leq h_2$, and applying the inequality (4), we obtain $\dot{\psi}_2(E) < 0$. Note that the existence condition of E_2 is $R_2 > 1$. Thus, $\psi_2(E)$ qualifies as a Lyapunov function and the equilibrium state E_2 is globally asymptotically stable under the conditions $R_1 \leq R_2$ and $1 < R_2 \leq h_2$. □

Theorem 6. *The equilibrium state E_3 is globally asymptotically stable within domain D If $R_2 \leq h_1$ with $h_1 = \frac{\alpha}{\mu_1 S_3}$.*

Proof. Define the Lyapunov function as follows:

$$\psi_3(E) = S_3\left(\frac{S}{S_3} - 1 - \ln\left(\frac{S}{S_3}\right)\right) + L_3\left(\frac{L}{L_3} - 1 - \ln\left(\frac{L}{L_3}\right)\right) + \frac{\xi}{\gamma} I_{v3}\left(\frac{I_v}{I_{v3}} - 1 - \ln\left(\frac{I_v}{I_{v3}}\right)\right) + I_a + \frac{\pi_2}{\sigma_2} C_a + \frac{\xi \mu_5}{\gamma \omega_1} V_3\left(\frac{V}{V_3} - 1 - \ln\left(\frac{V}{V_3}\right)\right) + \frac{\mu_6}{\omega_2} A + \frac{\xi \pi_1}{\gamma \sigma_1} C_{v3}\left(\frac{C_v}{C_{v3}} - 1 - \ln\left(\frac{C_v}{C_{v3}}\right)\right).$$

Based on Definition 1 and 2, we have:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_3$ we have $\psi_3(E) > 0$. Furthermore, if $E = E_3$, then $\psi_3(E) = 0$.
2. The derivative of the function ψ_3 with respect to t is given by:

$$\dot{\psi}_3(E) = \left(1 - \frac{S_3}{S}\right)(\mu_1 S_3 - \mu_1 S) + 3\beta_1 S_3 V_3 - \beta_1 S_3 V_3 \frac{S_3}{S} - \beta_1 S_3 V_3 \frac{L_3 S V}{L S_3 V_3} - \beta_1 S_3 V_3 \frac{I_{v3} L}{I_v L_3} - \beta_1 S_3 V_3 \frac{I_v V_3}{I_{v3} V} - \beta_1 S_3 V_3 \frac{I_v}{I_{v3}} + \frac{\mu_6 \mu_3}{\omega_2}\left(\frac{\beta_2 \omega_2}{\mu_3 \mu_6} S_3 - 1\right) A - \frac{\pi_2 \mu_8}{\sigma_2} C_a,$$

$$\dot{\psi}_3(E) = -\frac{\mu_1 (S-S_3)^2}{S} + \beta_1 S_3 V_3 \left(3 - \frac{S_3}{S} - \frac{L_3 S V}{L S_3 V_3} - \frac{I_{v3} L}{I_v L_3} - \frac{I_v V_3}{I_{v3} V} - \frac{I_v}{I_{v3}}\right) + \frac{\mu_6 \mu_3}{\omega_2}(R_2 - h_1) A - \frac{\pi_2 \mu_8}{\sigma_2} C_a.$$

Therefore, if $R_2 \leq h_1$ and applying the inequality (4), we find $\dot{\psi}_3(E) < 0$. Thus, it can be concluded that $\psi_3(E)$ is a Lyapunov function, and the equilibrium state E_3 is globally asymptotically stable if $R_2 \leq h_1$. □

Theorem 7. *The equilibrium state E_4 is globally asymptotically stable within domain D if $R_1 \leq h_2$ with $h_2 = \frac{\alpha}{\mu_1 S_4}$.*

Proof. Define the Lyapunov function as follows:

$$\psi_4(E) = S_4\left(\frac{S}{S_4} - 1 - \ln\left(\frac{S}{S_4}\right)\right) + L + \frac{\xi}{\gamma} I_v + I_{a4}\left(\frac{I_a}{I_{a4}} - 1 - \ln\left(\frac{I_a}{I_{a4}}\right)\right) + \frac{\mu_6}{\omega_2} A_4\left(\frac{A}{A_4} - 1 - \ln\left(\frac{A}{A_4}\right)\right) + \frac{\xi \mu_5}{\gamma \omega_1} V + \frac{\pi_2}{\sigma_2} C_{a4}\left(\frac{C_a}{C_{a4}} - 1 - \ln\left(\frac{C_a}{C_{a4}}.\right)\right) + \frac{\xi \pi_1}{\gamma \sigma_1} C_v.$$

Based on Definition 1 and 2, we have:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_4$ we have $\psi_4(E) > 0$. Furthermore, if $E = E_4$, then $\psi_4(E) = 0$.
2. The derivative of the function ψ_4 with respect to t is express as:

$$\begin{aligned}\dot{\psi}_4(E) = &\left(1 - \frac{S_4}{S}\right)(\mu_1 S_4 - \mu_1 S) + 2\beta_2 S_4 A_4 - \beta_2 S_4 A_4 \frac{S_4}{S} \\ &- \beta_2 S_4 A_4 \frac{I_{a4} SA}{I_a S_4 A_4} - \beta_2 S_4 A_4 \frac{I_a A_4}{I_{a4} A} - \beta_2 S_4 A_4 \frac{I_a}{I_{a4}} \\ &+ \frac{\xi \mu_5 \mu_2}{\gamma \omega_1}\left(\frac{\beta_1 \gamma \omega_1}{\xi \mu_5 \mu_2} S_4 - 1\right) V - \frac{\xi \pi_1 \mu_7}{\gamma \sigma_1} C_v, \\ \dot{\psi}_4(E) = &-\frac{\mu_1 (S - S_4)^2}{S} + \beta_2 S_4 A_4 \left(2 - \frac{S_4}{S} - \frac{I_{a4} SA}{I_a S_4 A_4}\right. \\ &\left. - \frac{I_a A_4}{I_{a4} A} - \frac{I_a}{I_{a4}}\right) + \frac{\xi \mu_5 \mu_2}{\gamma \omega_1}\left(\frac{R_1}{h_2} - 1\right) V - \frac{\xi \pi_1 \mu_7}{\gamma \sigma_1} C_v.\end{aligned}$$

Therefore, if $R_1 \leq h_2$, and applying the inequality (4), it follows that $\dot{\psi}_4(E) < 0$. Thus, $\psi_4(E)$ can be concluded as a Lyapunov function and the equilibrium state E_4 is globally asymptotically stable when $R_1 \leq h_2$. □

Theorem 8. *If $R_2 \leq h_1 + h_2$ with $h_1 = \frac{\alpha}{\mu_1 S_3}$ and $h_2 = \frac{\alpha}{\mu_1 S_4}$, then the equilibrium state E_5 is globally asymptotically stable within domain D.*

Proof. Define the Lyapunov function as follows:

$$\begin{aligned}\psi_5(E) = &S_5\left(\frac{S}{S_5} - 1 - \ln\left(\frac{S}{S_5}\right)\right) + L_5\left(\frac{L}{L_5} - 1 - \ln\left(\frac{L}{L_5}\right)\right) \\ &+ \frac{\xi}{\gamma} I_{v5}\left(\frac{I_v}{I_{v5}} - 1 - \ln\left(\frac{I_v}{I_{v5}}\right)\right) + I_{a5}\left(\frac{I_a}{I_{a5}} - 1\right. \\ &\left. - \ln\left(\frac{I_a}{I_{a5}}\right)\right) + \frac{\xi \mu_5}{\gamma \omega_1} V_5\left(\frac{V}{V_5} - 1 - \ln\left(\frac{V}{V_5}\right)\right) + \frac{\pi_2}{\sigma_2} C_a \\ &+ \frac{\mu_6}{\omega_2} A_5\left(\frac{A}{A_5} - 1 - \ln\left(\frac{A}{A_5}\right)\right) + \frac{\xi \pi_1}{\gamma \sigma_1} C_{v5}\left(\frac{C_v}{C_{v5}} 1\right. \\ &\left. - \ln\left(\frac{C_v}{C_{v5}}\right)\right).\end{aligned}$$

Based on Definition 1 and 2, we obtain:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_5$ we have $\psi_5(E) > 0$. Furthermore, if $E = E_5$, then $\psi_5(E) = 0$.
2. The derivative of the function ψ_5 with respect to t is given by:

$$\begin{aligned}\dot{\psi}_5(E) = &\left(1 - \frac{S_5}{S}\right)(\mu_1 S_5 - \mu_1 S) + 3\beta_1 S_5 V_5 + \beta_2 S_5 A_5 \\ &- \beta_1 S_5 V_5 \frac{S_5}{S} - \beta_5 S_5 A_5 \frac{S_5}{S} - \beta_1 S_5 V_5 \frac{L_5 SV}{L S_5 V_5} \\ &- \beta_1 S_5 V_5 \frac{I_{v5} L}{I_v L_5} - \beta_1 S_5 V_5 \frac{I_v V_5}{I_{v5} V} - \beta_1 S_5 V_5 \frac{I_v}{I_{v5}} \\ &- \beta_2 S_5 A_5 \frac{I_{a5} SA}{I_a S_5 A_5} + \frac{\pi_2 \mu_8}{\sigma_2}\left(\frac{\sigma_2}{\mu_8} I_{a5} - 1\right) C_a \\ &- \beta_2 S_5 A_5 \frac{I_a A_5}{I_{a5} A},\end{aligned}$$

$$\begin{aligned}\dot{\psi}_5(E) = &-\frac{\mu_1 (S - S_5)^2}{S} + \beta_1 S_5 V_5 \left(3 - \frac{S_5}{S} - \frac{L_5 SV}{L S_5 V_5}\right. \\ &\left. - \frac{I_{v5} L}{I_v L_5} - \frac{I_v V_5}{I_{v5} V} - \frac{I_v}{I_{v5}}\right) + \beta_2 S_5 A_5 \left(1 - \frac{S_5}{S}\right. \\ &\left. - \frac{I_{a5} SA}{I_a S_5 A_5} - \frac{I_a A_5}{I_{a5} A}\right) + \frac{\pi_2 \mu_8}{\sigma_2}(R_b - 1) C_a.\end{aligned}$$

Consider that $\frac{R_2}{h1 + h2} < R_b$ implies:

$$\begin{aligned}\dot{\psi}_5(E) < &-\frac{\mu_1 (S - S_5)^2}{S} + \beta_1 S_5 V_5 \left(3 - \frac{S_5}{S} - \frac{L_5 SV}{L S_5 V_5}\right. \\ &\left. - \frac{I_{v5} L}{I_v L_5} - \frac{I_v V_5}{I_{v5} V} - \frac{I_v}{I_{v5}}\right) + \beta_2 S_5 A_5 \left(1 - \frac{S_5}{S}\right. \\ &\left. - \frac{I_{a5} SA}{I_a S_5 A_5} - \frac{I_a A_5}{I_{a5} A}\right) + \frac{\pi_2 \mu_8}{\sigma_2}\left(\frac{R_2}{h_2 + h_3} - 1\right) C_a,\end{aligned}$$

Therefore, if $R_2 \leq h_1 + h_2$ and by applying the inequality (4), we have $\dot{\psi}_5(E) < 0$. Thus, it can be concluded that $\psi_5(E)$ is a Lyapunov function, and the equilibrium state E_5 is globally asymptotically stable when $R_2 \leq h_1 + h_2$. □

Theorem 9. *If $R_1 \leq h_1 + h_2$ with $h_1 = \frac{\alpha}{\mu_1 S_3}$ and $h_2 = \frac{\alpha}{\mu_1 S_4}$, then the equilibrium state E_6 is globally asymptotically stable in domain D.*

Proof. Define the Lyapunov function as follows:

$$\begin{aligned}\psi_6(E) = &S_6\left(\frac{S}{S_6} - 1 - \ln\left(\frac{S}{S_6}\right)\right) + L_6\left(\frac{L}{L_6} - 1 - \ln\left(\frac{L}{L_6}\right)\right) \\ &+ \frac{\xi}{\gamma} I_{v6}\left(\frac{I_v}{I_{v6}} - 1 - \ln\left(\frac{I_v}{I_{v6}}\right)\right) + I_{a6}\left(\frac{I_a}{I_{a6}} - 1\right. \\ &\left. - \ln\left(\frac{I_a}{I_{a6}}\right)\right) + \frac{\xi \mu_5}{\gamma \omega_1}\left(V - V_6 - V_6 \ln\left(\frac{V}{V_6}\right)\right) \\ &+ \frac{\mu_6}{\omega_2} A_6\left(\frac{A}{A_6} - 1 - \ln\left(\frac{A}{A_6}\right)\right) + \frac{\xi \pi_1}{\gamma \sigma_1} C_v \\ &+ \frac{\pi_2}{\sigma_2} C_{a6}\left(\frac{C_a}{C_{a6}} - 1 - \ln\left(\frac{C_a}{C_{a6}}\right)\right)\end{aligned}$$

Based on Definition 1 and 2, we have:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_6$ we have $\psi_6(E) > 0$. Furthermore, if $E = E_6$, then $\psi_6(E) = 0$.
2. The derivative of the function ψ_6 with respect to t can be written as:

$$\begin{aligned}\dot{\psi}_6(E) = &\left(1 - \frac{S_6}{S}\right)(\mu_1 S_6 - \mu_1 S) + 2\beta_1 S_6 V_6 + 2\beta_2 S_6 A_6 \\ &- \beta_1 S_6 V_6 \frac{S_6}{S} - \beta_1 S_6 V_6 \frac{L_6 SV}{L S_6 V_6} - \beta_1 S_6 V_6 \frac{I_{v6} L}{I_v L_6} \\ &- \beta_1 S_6 V_6 \frac{I_v V_6}{I_{v6} V} - \beta_2 S_6 A_6 \frac{I_{a6} SA}{I_a S_6 A_6} + \frac{\xi \pi_1 \mu_7}{\gamma \sigma_1}\left(\frac{\sigma_1}{\mu_7} I_{v6}\right. \\ &\left. - 1\right) C_v - \beta_2 S_6 A_6 \frac{I_a A_6}{I_{a6} A} - \beta_2 S_6 A_6 \frac{I_a}{I_{a6}}, \\ \dot{\psi}_6(E) = &-\frac{\mu_1 (S - S_6)^2}{S} + \beta_1 S_6 V_6 \left(2 - \frac{S_6}{S} - \frac{L_6 SV}{L S_6 V_6}\right.\end{aligned}$$

Table 2. Existance and stability conditions for System (1)

Equilibrium	Existance conditions	Global stability conditions
E_0	-	$R_1 \leq 1$ and $R_2 \leq 1$
E_1	$R_1 > 1$	$R_2 \leq R_1$ and $1 < R_1 \leq h_1$
E_2	$R_2 > 1$	$R_1 \leq R_2$ and $1 < R_2 \leq h_2$
E_3	$R_1 > h_1$	$R_2 \leq h_1$
E_4	$R_2 > h_2$	$R_1 \leq h_2$
E_5	$R_2 > h_1$ and $R_1 > R_2$	$R_2 \leq h_1 + h_2$
E_6	$R_1 > h_2$ and $R_2 > R_1$	$R_1 \leq h_1 + h_2$
E_7	$R_1 > h_1 + h_2$ and $R_2 > h_1 + h_2$	-

$$-\frac{I_{v6}L}{I_vL_6}-\frac{I_vV_6}{I_{v6}V}\Bigg)+\beta_2S_6A_6\left(2-\frac{S_6}{S}-\frac{I_{a6}SA}{I_aS_6A_6}\right.$$
$$\left.-\frac{I_aA_6}{I_{a6}A}-\frac{I_a}{I_{a6}}\right)+\frac{\xi\pi_1\mu_7}{\gamma\sigma_1}\left(R_a-1\right)C_v.$$

Consider that $\dfrac{R_1}{h_1+h_2} < R_a$ implies:

$$\dot{\psi}_6(E) = -\frac{\mu_1\left(S-S_6\right)^2}{S}+\beta_1S_6V_6\left(2-\frac{S_6}{S}-\frac{L_6SV}{LS_6V_6}\right.$$
$$\left.-\frac{I_{v6}L}{I_vL_6}-\frac{I_vV_6}{I_{v6}V}\right)+\beta_2S_6A_6\left(2-\frac{S_6}{S}-\frac{I_{a6}SA}{I_aS_6A_6}\right.$$
$$\left.-\frac{I_aA_6}{I_{a6}A}-\frac{I_a}{I_{a6}}\right)+\frac{\xi\pi_1\mu_7}{\gamma\sigma_1}\left(\frac{R_1}{h_1+h_2}-1\right)C_v.$$

Therefore, when $R_1 \leq h_1 + h_2$ and by applying the inequality (4), then $\dot{\psi}_6(E) < 0$. Thus, $\psi_6(E)$ is a Lyapunov function, and the equilibrium state E_6 is globally asymptotically stable when $R_1 \leq h_1 + h_2$. □

Theorem 10. *If $R_1 > h_1 + h_2$ and $R_2 > h_1 + h_2$, then the equilibrium state E_7 exists and is globally asymptotically stable in domain D.*

Proof. Define the Lyapunov function as follows:

$$\psi_7(E) = S_7\left(\frac{S}{S_7}-1-\ln\left(\frac{S}{S_7}\right)\right)+L_7\left(\frac{L}{L_7}-1-\ln\left(\frac{L}{L_7}\right)\right)$$
$$+\frac{\xi}{\gamma}I_{v7}\left(\frac{I_v}{I_{v7}}-1-\ln\left(\frac{I_v}{I_{v7}}\right)\right)+I_{a7}\left(\frac{I_a}{I_{a7}}-1\right.$$
$$\left.-\ln\left(\frac{I_a}{I_{a7}}\right)\right)+\frac{\xi\mu_5}{\gamma\omega_1}\left(V-V_7-V_7\ln\left(\frac{V}{V_7}\right)\right)$$
$$+\frac{\mu_6}{\omega_2}A_7\left(\frac{A}{A_7}-1-\ln\left(\frac{A}{A_7}\right)\right)+\frac{\xi\pi_1}{\gamma\sigma_1}C_{v7}\left(\frac{C_v}{C_{v7}}-1\right.$$
$$\left.-\ln\left(\frac{C_v}{C_{v7}}\right)\right)+\frac{\pi_2}{\sigma_2}C_{a7}\left(\frac{C_a}{C_{a7}}-1-\ln\left(\frac{C_a}{C_{a7}}\right)\right).$$

Based on Definition 1 and 2, we have:

1. For any $E = (S, L, I_v, I_a, V, A, C_v, C_a) \in D$ with $E \neq E_7$ we have $\psi_7(E) > 0$. Furthermore, if $E = E_7$, then $\psi_7(E) = 0$.
2. The derivative of the function ψ_7 with respect to t is written as:

$$\dot{\psi}_7(E) = \left(1-\frac{S_7}{S}\right)\left(\mu_1S_7-\mu_1S\right)+3\beta_1S_7V_7+2\beta_2S_7A_7$$
$$-\beta_1S_7V_7\frac{S_7}{S}-\beta_2S_7A_7\frac{S_7}{S}-\beta_1S_7V_7\frac{L_7SV}{LS_7V_7}$$
$$-\beta_1S_7V_7\frac{I_{v7}L}{I_vL_7}-\beta_1S_7V_7\frac{I_vV_7}{I_{v7}V}-\beta_1S_7V_7\frac{I_v}{I_{v7}}$$
$$-\beta_2S_7A_7\frac{I_{a7}SA}{I_aS_7A_7}-\beta_2S_7A_7\frac{I_aA_7}{I_{a7}A}-\beta_2S_7A_7\frac{I_a}{I_{a7}},$$
$$\dot{\psi}_7(E) = -\frac{\mu_1\left(S-S_7\right)^2}{S}+\beta_1S_7V_7\left(3-\frac{S_7}{S}-\frac{L_7SV}{LS_7V_7}\right.$$
$$\left.-\frac{I_{v7}L}{I_vL_7}-\frac{I_vV_7}{I_{v7}V}-\frac{I_v}{I_{v7}}\right)+\beta_2S_7A_7\left(2-\frac{S_7}{S}\right.$$
$$\left.-\frac{I_{a7}SA}{I_aS_7A_7}-\frac{I_aA_7}{I_{a7}A}-\frac{I_a}{I_{a7}}\right).$$

Thus, by using inequality (4), we have $\dot{\psi}_7(E) < 0$. Therefore, using the LaSalle invariance principle [37], it can be concluded that $\psi_7(E)$ is a Lyapunov function and the equilibrium state E_7 is globally asymptotically stable in domain D. □

Table 2 provides a summary of the existence and stability conditions for all equilibrium states. The graph illustrating the stability region is presented in Figure 2. It can be observed that $R_1 = 1$ and $R_2 = 1$ serve as thresholds for E_0, E_1, and E_2, while the values of h_1 h_2, serve as thresholds for all equilibrium states except E_0.

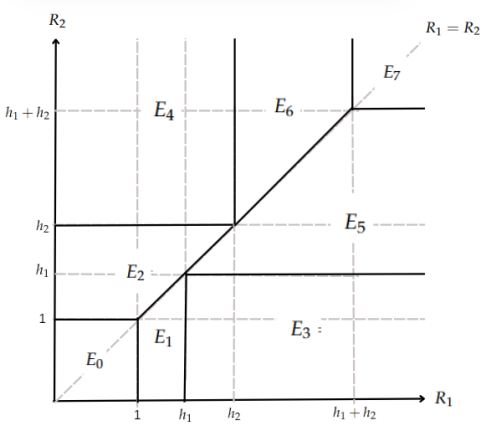
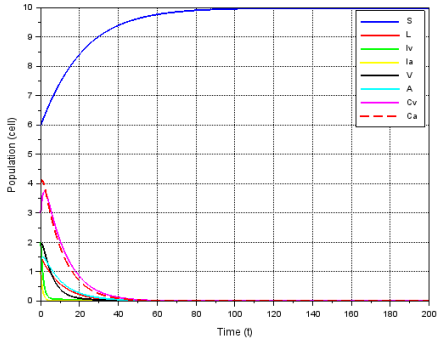


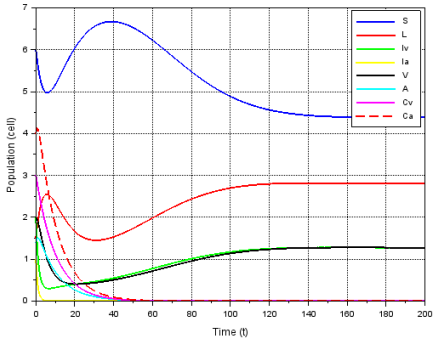
Figure 2. Stability regions for the equilibrium state in the R_1-R_2 plane with $h_1 < h_2$.

3. Numerical Simulation

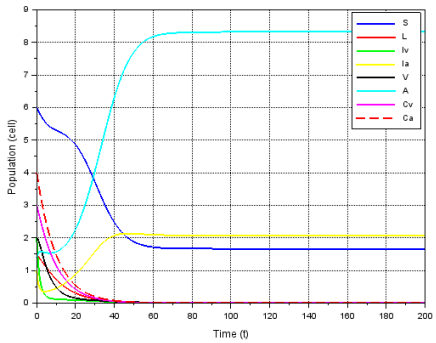
This section present a numerical simulation to examine how the coexistence of SARS-CoV-2 and Influenza A virus influences the transmission dynamics of epithelial cells, along with the role of CTLs in modulating the interaction between these viruses. Eight simulations are conducted to represent the stability conditions of each equilibrium state. The parameter values used for the simulation are provided in Table 3, with the given initial conditions $(S(0), L(0), I_v(0), I_a(0), V(0), A(0), C_v(0), C_a(0)) = (6, 1.5, 2, 1, 2, 1.4, 3, 4)$.



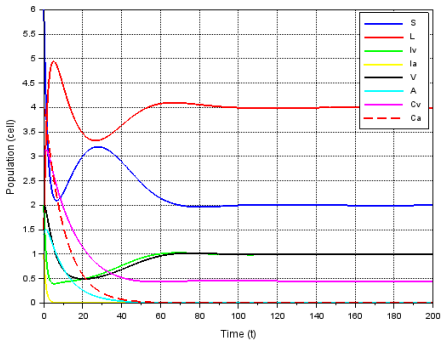
(a) Stability of E_0



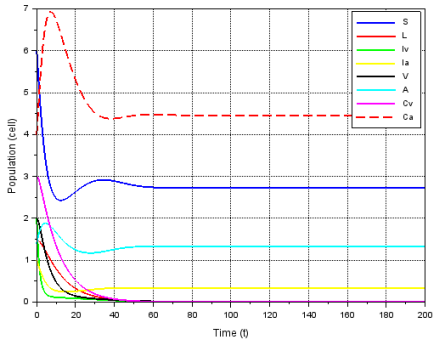
(b) Stability of E_1



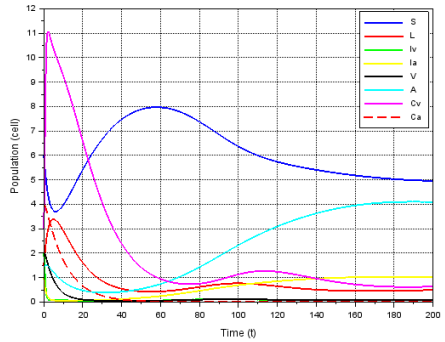
(c) Stability of E_3



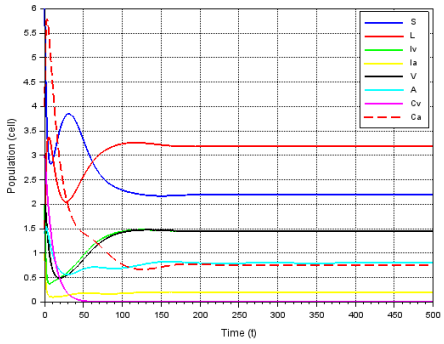
(d) Stability of E_4



(e) Stability of E_5



(f) Stability of E_6



(g) Stability of E_7

Figure 3. Graph depicting the numerical solution of System (1) under the stability conditions of each equilibrium state.

Table 3. Parameter values for numerical simulation.

Parameter	α	γ	μ_1	μ_2	μ_3	μ_4	μ_5	μ_6	ω_1	ω_2	Reference
Value	0.5	0.05	0.05	0.2	0.1	0.05	0.11	0.2	0.2	0.4	[32]
Parameter	μ_7	μ_8	π_1	π_2	σ_1	σ_2	β_1	β_2			Reference
Value	0.1	0.1	0.2	0.2	varied	varied	varied	varied			assumption

The descriptions of each dynamic behavior in Figure 3 are as follows.

(a) **Simulation 1**: $R_1 \leq 1$ and $R_2 \leq 1$. Set the parameter values $\beta_1 = 0.001$, $\beta_2 = 0.001$, $\sigma_1 = 0.2$, $\sigma_2 = 0.2$, and the solution converges towards E_0. Under this conditions, infections of both SARS-CoV-2 and Influenza A virus will be eradicated, resulting in no further infection within the host cells.

(b) **Simulation 2**: $R_1 > 1$, $R_2 \leq R_1$, and $1 \leq R_1 \leq h_1$. Set the parameter values $\beta_1 = 0.05$, $\beta_2 = 0.001$, $\sigma_1 = 0.003$, and $\sigma_2 = 0.2$, and the solution converges towards E_1. In this scenario, a single infection caused by SARS-CoV-2 occurs, accompanied by a lack of response from CTL, suggesting the potential for persistent SARS-CoV-2 infection.

(c) **Simulation 3**: $R_2 > 1$, $R_1 \leq R_2$, and $1 \leq R_2 \leq h_2$. Set the parameter values $\beta_1 = 0.005$, $\beta_2 = 0.03$, $\sigma_1 = 0.01$, $\sigma_2 = 0.001$, and the solution converges towards E_2. In this case, there is a single infection caused by the Influenza A virus without a response from CTL, indicating the potential for a persistent Influenza infection.

(d) **Simulation 4**: $R_1 > h_1$ and $R_2 \leq h_1$. Set the parameter values $\beta_1 = 0.2$, $\beta_2 = 0.001$, $\sigma_1 = 0.1$, and $\sigma_2 = 0.05$, and the solution converges towards E_3. In this case, there is a single infection by SARS-CoV-2 where the immune response is activated by CTL specific to SARS-CoV-2.

(e) **Simulation 5**: $R_2 > h_1$ and $R_1 \leq h_2$. Set the parameter values $\beta_1 = 0.01$, $\beta_2 = 0.1$, $\sigma_1 = 0.05$, $\sigma_2 = 0.3$, and the solution converges towards E_4. In this case, a single infection by Influenza A virus occurs, where the immune response is triggered by CTL specific to Influenza A virus.

(f) **Simulation 6**: $R_2 > h_1$, $R_1 > R_2$, and $R_2 \leq h_1 + h_2$. The selected parameter values are $\beta_1 = 0.1$, $\beta_2 = 0.01$, $\sigma_1 = 1$, and $\sigma_2 = 0.09$, resulting in the solution converging towards E_5. In this scenario, a coinfection occurs involving SARS-CoV-2 and Influenza A virus. The immune response mediated by CTLs specific to SARS-CoV-2 is active, while the immune response mediated by CTLs specific to Influenza A virus remains inactive.

(g) **Simulation 7**: $R_1 > h_2$, $R_2 > R_1$, and $R_1 \leq h_1 + h_2$. The selected parameter values are $\beta_1 = 0.1$, $\beta_2 = 0.04$, $\sigma_1 = 0.01$, $\sigma_2 = 0.5$, resulting in the solution converging towards E_6. In this case, a coinfection occurs involving SARS-CoV-2 and Influenza A virus and the immune response mediated by CTLs specific to the Influenza A virus is active, while the immune response mediated by CTLs specific to SARS-CoV-2 remains inactive.

(h) **Simulation 8**: $R_1 > h_2 + h2$, $R_2 > h_1 + h_2$. The selected parameter values are $\beta_1 = 0.3$, $\beta_2 = 0.3$, $\sigma_1 = 0.4$, $\sigma_2 = 0.4$, resulting in the solution converging towards E_7. In this case, a coinfection occurs involving SARS-CoV-2 and Influenza A virus, with the immune responses mediated by CTLs specific to both viruses being active.

Next, the effect of parameter variations on the thresholds of each equilibrium point will be analyzed, based on the following considerations:

- ω_1 and ω_2, representing the formation rates of SARS-CoV-2 and Influenza A virus, respectively, indicate the efficiency of viral replication within infected cells. The control mechanism involves the use of replication inhibitors and combination therapies to limit viral load [38].
- α, representing the proliferation rate of uninfected epithelial cells, determines the regeneration capacity of epithelial cells. The control mechanism involves the administration of growth factors or cytokines, such as IL-22, to promote epithelial cell proliferation [39, 40].
- σ_1 and σ_2, representing the proliferation rates of SARS-CoV-2-specific CTLs and Influenza A virus-specific CTLs, respectively, can be regulated through immunotherapies designed to enhance CTL effectiveness against their target viruses [41].
- π_1 and π_2, representing the killing rates of infected cells by virus-specific CTLs, describe the effectiveness of cytotoxic T lymphocytes (CTLs) in eliminating infected cells. The control mechanism involves vaccination to enhance CTL responses. However, these parameters do not directly influence the treshold R_1 and R_2 as defined in the model [42]
- γ, representing the transition rate from latent to active infection in SARS-CoV-2-infected cells, describe the latent period, which can be extended to delay active infection and giving the immune system more time to respond [43].

Furthermore, the effects of changes in the parameters ω_1, ω_2, α, σ_1, and σ_2 on the stability thresholds R_1, R_2, h_1, h_2, and $h_1 + h_2$ are examined. Using data from **Simulation 1**, the relationships between these parameters are presented in Figure 4.

Figures 4a and 4b illustrates the relationship between R_1 and R_2 as functions of α–ω_1 and α–ω_2, respectively. As the proliferation rate of epithelial cells (α), the formation rates of SARS-CoV-2 (ω_1), and Influenza A virus (ω_2) increase, R_1 and R_2 also increase. However, for fixed values of R_1 and R_2, α is inversely proportional to ω_1 or ω_2. Therefore, a combined control strategy to stabilize the system into the virus-free state, achieved by reducing R_1 and R_2, can be implemented by decreasing ω_1 and ω_2 while simultaneously increasing α.

In addition, Figures 4c and 4d illustrates the relationship between h_1 and h_2 as functions of σ_1–ω_1 and σ_2–ω_2, respectively. Increasing σ_1 and σ_2, which represent the proliferation rates of CTLs, while decreasing ω_1 and ω_2, will lower the values of h_1 and h_2 and the system stabilizes to a single infection state. Lastly, from Figure 4e, increasing σ_1 and σ_2 also lowers the threshold $(h_1 + h_2)$, thereby avoiding the coinfection condition. For fixed

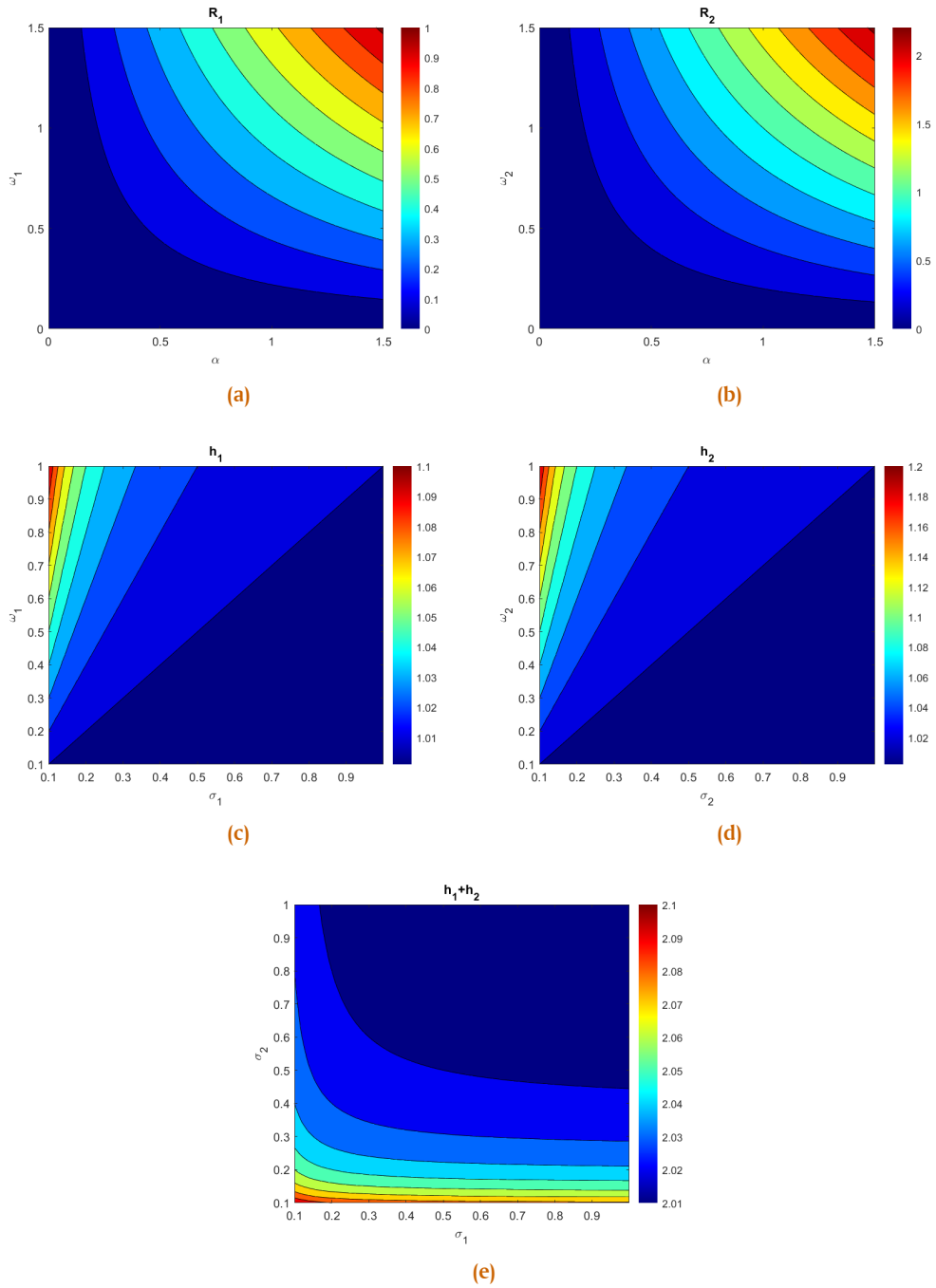


Figure 4. Contour plot of the thresholds (a) R_1 as a function of α and ω_1, (b) R_2 as a function of α and ω_2, (c) h_1 as a function of σ_1 and ω_1, (d) h_2 as a function of σ_2 and ω_2, (e) $(h_1 + h_2)$ as a function of σ_2 and σ_2

values of $h_1 + h_2$, parameter σ_1 is inversely proportional to σ_2, and it is shown that the effect of changes in σ_1 is not as significant as those in σ_2 to the change of $h_1 + h_2$.

4. Conclusion

In this study, a mathematical model of coinfection involving SARS-CoV-2 and Influenza A virus with CTL-mediated immunity is developed and analyzed to understand the dynamics and the behavior of this biological process within the host. The model identifies eight equilibrium points, describing various conditions i.e. virus-free state, single infections (either SARS-CoV-2 or Influenza A virus, with and without CTLs), and coinfection state (with and without CTLs). The existence and stability of each equilibrium point is associated with the threshold represented in R_1, R_2, h_1, and h_2. Moreover, using Lyapunov analysis, these equilibrium points are proven to be globally asymptotically stable under the specified conditions.

Furthermore, numerical simulations using both referenced and assumed parameter values demonstrate consistency with the analytical findings. The simulations reveal that CTLs specific to

SARS-CoV-2 and Influenza A viruses are activated, targeting and eliminating infected epithelial cells from both viruses. The role of CTLs enhances the analytical results of the virus transmission model by providing more precise estimates for the solutions of the model. The simulations also illustrate how changes in several parameters, such as the proliferation rate (α), the formation rate of SARS-CoV-2 (ω_1), the formation rate of Influenza A virus (ω_2), the proliferation rate of SARS-CoV-2-specific CTLs (σ_1), and the proliferation rate of Influenza A virus-specific CTLs (σ_2), affect the thresholds for stability criteria. Increasing the proliferation rate of epithelial cells and CTLs, while lowering the formation rate of viruses can shift the system's threshold and stabilize it at the virus-free equilibrium.

For the next research, preventive strategies such as vaccination and medical treatments against SARS-CoV-2 and Influenza A can be incorporated into the model to provide valuable insights into the virus transmission dynamics. Additionally, optimal control analysis can be applied to minimize the number of infected cells through effective strategies.

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