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RESEARCH PAPER

Local and global stability of a fractional viral infection model with two routes of propagation, cure rate and non-lytic humoral immunity

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Abstract

A fractional viral model is proposed in this work, as fractional-order calculus is considered more suitable than integer-order calculus for modeling virological systems with inherent memory and long-range interactions. The model incorporates virus-to-cell infection, cell-to-cell transmission, cure rate, and humoral immunity. Additionally, the non-lytic immunological mechanism, which prevents viral reproduction and reduces cell infection, is included. Caputo fractional derivatives are utilized in each compartment to capture long-term memory effects and non-local behavior. It is demonstrated that the model has nonnegative and bounded solutions. Three equilibrium states are identified in the improved viral model: the virus-clear steady state $\mathcal{G}^{\circ}$, the immunity-free steady state $\mathcal{G}_1^{\star}$ and the infection steady state with humoral immunity $\mathcal{G}_2^{\star}$. The local stability of the equilibria is investigated using the Routh-Hurwitz criteria and the Matignon condition, while the global stability is shown through the Lyapunov approach and the fractional LaSalle invariance principle. Finally, the theoretical conclusions are validated by numerous numerical simulations.

Keywords: Infection model; fractional-order model; non-lytic humoral immunity; stability

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1 Introduction

Modeling and simulation serve as the primary decision-making tools for managing viral infections. Mathematical virology, namely compartmental models, is a key tool for understanding viral prevalence dynamics [1–3] and immunological responses to infection. These immune responses are crucial to preventing or combating infection. Specific immunity is represented by cellular and humoral immunity, linked respectively to T cells (responsible for eliminating infected cells) and B cells (responsible for neutralizing viruses). Several researchers have examined various models of viral dynamics including humoral immunity and neglecting cellular immunity, or vice versa, for example, [4–7]. Numerous viral models integrating cellular and humoral immune responses have been proposed, see, e.g., [8–10].

The host immune response to a viral infection typically consists of two parts: a lytic component that kills infected cells and a non-lytic component that inhibits viral replication via soluble mediators released by immune cells [11]. In the current context, there are several viral systems that use both lytic and non-lytic mechanisms [12–14]. In [15], the authors investigated the overall stability of a viral system with both lytic and non-lytic cellular immunity. They also investigated the impact of viral replication inhibition through the non-lytic effector pathway on viral infection. The following system was suggested by Dhar et al. [16] to build up an infection model with a non-lytic humoral immune response, they presented a thorough examination of local and global stability.

$$\begin{cases} \frac{d\mathcal{M}(t)}{dt} = \Lambda - \mu_1 \mathcal{M}(t) - \frac{\beta \mathcal{M}(t)\mathcal{P}(t)}{1+\alpha \mathcal{Q}(t)} + \sigma \mathcal{N}(t), \quad t \geq 0, \\ \frac{d\mathcal{N}(t)}{dt} = \frac{\beta \mathcal{M}(t)\mathcal{P}(t)}{1+\alpha \mathcal{Q}(t)} - (\mu_2 + \sigma)\mathcal{N}(t), \\ \frac{d\mathcal{P}(t)}{dt} = \theta \mathcal{N}(t) - \mu_3 \mathcal{P}(t) - \rho \mathcal{P}(t)\mathcal{Q}(t), \\ \frac{d\mathcal{Q}(t)}{dt} = v \mathcal{P}(t)\mathcal{Q}(t) - \mu_4 \mathcal{Q}(t), \end{cases} \tag{1}$$

here, $\mathcal{M}, \mathcal{N}, \mathcal{P}$ and $\mathcal{Q}$ present in this order, susceptible cells, infected cells, free virus and immune response (B cells). Λ indicates the birth rate of $\mathcal{M}$ cells, θ designates the production rate of $\mathcal{P}$, v is the immune growth rate. μ_1, μ_2, μ_3 and μ_4 are the rates of natural mortality of $\mathcal{M}, \mathcal{N}, \mathcal{P}$ and $\mathcal{Q}$, respectively, ρ is the rate of viral neutralization by immunity, σ is the rate of cured infected cells, and $\frac{\beta \mathcal{M}\mathcal{P}}{1+\alpha \mathcal{Q}}$ is the infection function with non-lytic process, where α is the non-lytic force. The findings in [16] are intriguing and aid in our understanding of the long-term impacts of infection in the case of local characteristics of the integer derivative. This kind of mathematical approach has certain limitations, and system (1) may be updated and improved by taking into account the fractional derivative, which reflects non-local effects.

Fractional calculus is a fascinating field of practical mathematics that examines arbitrary order integrals and derivatives [17, 18]. The idea of non-integer derivatives began in 1695 with Leibniz's inquiry into the meaning of half derivative, which can more precisely represent intricate epidemiological processes. As a result, modelling accuracy is increased, particularly when it comes to simulating the long-term behaviors and scaling characteristics of epidemiological systems [19, 20]. As well as, the fractional derivative improves our model by taking into account the memory effect. Because it is a nonlocal operator, while the classical ordinary derivative is a local operator that is unable to model the hereditary properties and memory effect [21–25]. In [26], Naim et al. investigated the local and global stability of a fractional SEIR epidemic model with latent infection and nonlinear incidence. In [27], the authors investigated how two delays affect the dynamics of a

fractional viral system with non-lytic immune response. The model's equilibria are calculated to provide stability analysis and examine associated dynamical bifurcations.
The viral model (1) has another limitation, which is that it only considers the virus-cell mode of infection. However, in a realistic setting, most viruses can be spread in two ways: by virus-cell infection and by direct cell-cell contact. In fact, cell-to-cell transmission has a great impact on virus infection [28], which can not be ignored. To account for the effects of both virus-to-cell and cell-to-cell transmissions, many mathematical studies of virus models have been performed, see, e.g., [29–31]. Hattaf et al. [32] proposed and studied a COVID-19 model that properly integrates the two types of viral transmission, two classes of infected cells, antiviral treatment, and non-lytic immune responses. Chen and Zhou [33] investigated the effects of general virus-to-cell and cell-to-cell infection rates on the dynamics of HIV infection. The main contribution of this article is to extend the model (1) to a new fractional-order system, dealing with the said limitation. Specifically, we propose a fractional viral dynamic model that considers both virus-to-cell and cell-to-cell transmission modes with non-lytic humoral immunity. The following new form serves to illustrate the proposed model:

$$\begin{cases} {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{M}(t) = & \Lambda - \mu_1\mathcal{M}(t) - \frac{\beta_1\mathcal{M}(t)\mathcal{P}(t)}{1+\alpha_1\mathcal{Q}(t)} - \frac{\beta_2\mathcal{M}(t)\mathcal{N}(t)}{1+\alpha_2\mathcal{Q}(t)} + \sigma\mathcal{N}(t), \quad t \geq 0, \\ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{N}(t) = & \frac{\beta_1\mathcal{M}(t)\mathcal{P}(t)}{1+\alpha_1\mathcal{Q}(t)} + \frac{\beta_2\mathcal{M}(t)\mathcal{N}(t)}{1+\alpha_2\mathcal{Q}(t)} - (\mu_2+\sigma)\,\mathcal{N}(t), \\ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{P}(t) = & \theta\mathcal{N}(t) - \mu_3\mathcal{P}(t) - \rho\mathcal{P}(t)\mathcal{Q}(t), \\ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{Q}(t) = & v\mathcal{P}(t)\mathcal{Q}(t) - \mu_4\mathcal{Q}(t), \end{cases} \tag{2}$$

where ${}_0^C\mathfrak{D}^{\mathbf{m}}$ is the Caputo derivative with fractional order $\mathbf{m} \in (0,1]$ [34]. β_1 and β_2 are the infection rates of both types of infection which are inhibited by non-lytic immune responses at rates $1+\alpha_1\mathcal{Q}$ and $1+\alpha_2\mathcal{Q}$, respectively. Other parameters and variables of system (2) have the same meaning as those of model (1).

Remark 1 *Notably, the fractional-order formulation* (2) *transforms into a system of ordinary differential equations when* $\mathbf{m} = 1$. *As a result, when* $\mathbf{m} = 1$ *and* $\beta_2 = 0$, *the system* (1) *is a particular case of the model* (2). *Also, if* $\mathbf{m} = 1$ *and* $\alpha_1 = \alpha_2 = 0$, *we get the model investigated in [29].*

This essay aims to investigate the stability of the fractional differential system (2). Our approach provides a reliable prediction of viral behavior based on the model. To achieve our purpose, we structure the rest of the manuscript as follows: Section 2 presents some preliminary findings about fractional calculus. In Section 3, we establish the nonnegativity and boundedness of our model's solutions. We next define two key values to investigate the criteria for the existence of the equilibria. Section 4 provides theoretical explanations for the stability of equilibria. In Section 5, we use numerical simulations to examine how fractional order affects the system's stability and validate our findings. Section 6 focuses on the conclusion.

2 Preliminaries

Definition 1 *[34] For* $\mathcal{H} \in \mathcal{C}^1(\mathbb{R}_+, \mathbb{R})$, *the Caputo derivative of order* $\mathbf{m} \in (0,1]$ *is given by*

$${}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{H}(t) = \begin{cases} \frac{1}{\Gamma(1-\mathbf{m})}\int_0^t \frac{\mathcal{H}'(s)}{(t-s)^{\mathbf{m}}}ds, \text{ if } 0 < \mathbf{m} < 1, \\ \mathcal{H}'(t), \text{ if } \mathbf{m} = 1, \end{cases}$$

where Γ *represents the Gamma function.*

Lemma 1 *[35] If* $\mathcal{H} \in \mathcal{C}([\mathbf{a},\mathbf{b}],\mathbb{R})$ *and* ${}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{H}(t) \in \mathcal{C}((\mathbf{a},\mathbf{b}],\mathbb{R})$, *where* $\mathbf{m} \in (0,1]$, *then we have*

(*i*) $\mathcal{H}$ *is non-decreasing on* $[\mathbf{a},\mathbf{b}]$ *if* ${}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{H}(t) \geq 0\ \forall t \in (\mathbf{a},\mathbf{b}]$,
(*ii*) $\mathcal{H}$ *is non-increasing on* $[\mathbf{a},\mathbf{b}]$ *if* ${}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{H}(t) \leq 0\ \forall t \in (\mathbf{a},\mathbf{b}]$.

The following lemmas will be used to examine our model's asymptotic stability globally.

Lemma 2 *[36] Let* $x(t) \in \mathcal{C}^1(\mathbb{R}_+,\mathbb{R}_+)$. *Then, for all* $t \geq 0$, $\mathbf{m} \in (0,1]$, *and* $x^* > 0$, *we get*

$$ {}_0^C\mathfrak{D}^{\mathbf{m}}\left(x^*\mathcal{H}\left(\frac{x(t)}{x^*}\right)\right) \leq \left(1-\frac{x^*}{x(t)}\right){}_0^C\mathfrak{D}^{\mathbf{m}}x(t),$$

where $\mathcal{H}$ *is a nonnegative function with the formula* $\mathcal{H}(x) = x - 1 - \ln x,\ x > 0$. *The above inequality becomes equality when* $\mathbf{m} = \mathbf{1}$.

Lemma 3 *[37] Let* $x(t) \in \mathcal{C}^1(\mathbb{R}_+,\mathbb{R}_+)$. *Then, for every* $t \geq 0$, $\mathbf{m} \in (0,1]$, *we get*

$$\frac{1}{2}{}_0^C\mathfrak{D}^{\mathbf{m}}x^2(t) \leq x(t)\,{}_0^C\mathfrak{D}^{\mathbf{m}}x(t).$$

3 Boundedness and equilibrium

Nonnegativity and boundedness

When evaluating a biological model, the first step is to see if there is a unique and nonnegative bounded solution. We present the following result to show these features.

Theorem 1 *With any non-negative initial condition, the fractional model* (2) *is well-posed in the sens that there is a unique nonnegative bounded solution.*

Proof Using Theorem 3.1 and Remark 3.2 in [38], we may show that the solution to system (2) exists and is unique. We now demonstrate that this solution is nonnegative. System (2) allows us to observe that

$$ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{M}\big|_{\mathcal{M}=0} = \Lambda + \sigma\mathcal{N} > 0,$$

$$ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{N}\big|_{\mathcal{N}=0} = \frac{\beta_1\mathcal{M}\mathcal{P}}{1+\alpha_1\mathcal{Q}} \geq 0,$$

$$ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{P}\big|_{\mathcal{P}=0} = \theta\mathcal{N} \geq 0,$$

$$ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{Q}\big|_{\mathcal{Q}=0} = 0 \geq 0.$$

Using the fact in Lemma 1, it is concluded that the solutions of system (2) are nonnegative. We now look at the solutions' boundedness. Define

$$\mathcal{B}(t) = \mathcal{M}(t) + \mathcal{N}(t) + \frac{\mu_2}{2\theta}\mathcal{P}(t) + \frac{\rho\mu_2}{2\theta v}\mathcal{Q}(t).$$

Thus,

$$\begin{aligned} {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{B}(t) &= \Lambda - \mu_1\mathcal{M}(t) - \frac{\mu_2}{2}\mathcal{N}(t) - \frac{\mu_2\mu_3}{2\theta}\mathcal{P}(t) - \frac{\rho\mu_2\mu_4}{2\theta v}\mathcal{Q}(t) \\ &\leq \Lambda - \mu\mathcal{B}(t), \end{aligned}$$

where $\mu = \min\left\{\mu_1, \frac{\mu_2}{2}, \mu_3, \mu_4\right\}$. Then, according to Lemma 3 in [39], we obtain

$$\begin{aligned} \mathcal{B}(t) &\leq \left(\mathcal{B}(0) - \frac{\Lambda}{\mu}\right)\mathcal{O}_{\mathbf{m}}(-\mu t^{\mathbf{m}}) + \frac{\Lambda}{\mu} \\ &= \frac{\Lambda}{\mu}\left(1 - \mathcal{O}_{\mathbf{m}}(-\mu t^{\mathbf{m}})\right) + \mathcal{B}(0)\,\mathcal{O}_{\mathbf{m}}(-\mu t^{\mathbf{m}}), \end{aligned}$$

where

$$\mathcal{O}_{\mathbf{m}}(z) = \sum_{j=0}^{\infty} \frac{z^j}{\Gamma(\mathbf{m}j+1)}, \quad z \in \mathbb{C},$$

is the Mittag-Leffler function for parameter $\mathbf{m} > 0$ [40]. Since $0 < \mathcal{O}_{\mathbf{m}}(-\mu t^{\mathbf{m}}) \leq 1$ (see Lemma 2 in [41]), so one achieves

$$\mathcal{B}(t) \leq \frac{\Lambda}{\mu} + \mathcal{B}(0).$$

Therefore, we get the boundedness of $\mathcal{M}, \mathcal{N}, \mathcal{P}$ and $\mathcal{Q}$.

Equilibrium points

This part provides the equilibrium points. To find the equilibrium, set the right-hand side of each equation in the proposed model (2) to zero [31].

In system (2), there is always a virus-clear equilibrium determined by $\mathcal{G}^\circ = (\mathcal{M}^\circ, 0, 0, 0)$, where $\mathcal{M}^\circ = \frac{\Lambda}{\mu_1}$. Model (2) has the following basic reproduction number [29]:

$$\mathcal{C}_0 = \frac{(\beta_1\theta + \beta_2\mu_3)\,\mathcal{M}^\circ}{\mu_3(\mu_2 + \sigma)}.$$

If $\mathcal{C}_0 > 1$, there is an immunity-free equilibrium for system (2) as follows:

$$\mathcal{G}_1^\star = (\mathcal{M}_1^\star, \mathcal{N}_1^\star, \mathcal{P}_1^\star, 0) = \left(\frac{\mathcal{M}^\circ}{\mathcal{C}_0}, \frac{\mu_1}{\mu_2}(\mathcal{C}_0 - 1)\,\mathcal{M}_1^\star, \frac{\theta}{\mu_3}\mathcal{N}_1^\star, 0\right).$$

The formula in the below equation, which stands for the threshold parameter of the humoral immune response, can be denoted by $\mathcal{C}_1$ as follows:

$$\mathcal{C}_1 = \frac{\Lambda\theta v(\beta_1\theta + \beta_2\mu_3)}{\mu_2\mu_3\mu_4(\beta_1\theta + \beta_2\mu_3) + \mu_1\mu_3\theta v(\mu_2 + \sigma)}.$$

Theorem 2 *If $\mathcal{C}_1 > 1$, system (2) has a unique immunity-activated equilibrium $\mathcal{G}_2^* = (\mathcal{M}_2^*, \mathcal{N}_2^*, \mathcal{P}_2^*, \mathcal{Q}_2^*)$.*

Proof Assume that $\mathcal{C}_1 > 1$. Suppose that $(\mathcal{M}, \mathcal{N}, \mathcal{P}, \mathcal{Q})$ is any positive equilibrium of (2), so

$$\begin{aligned}
\mathcal{P} &= \frac{\mu_4}{v}, \\
\mathcal{N} &= \frac{\Lambda - \mu_1 \mathcal{M}}{\mu_2}, \\
\mathcal{Q} &= \frac{v\theta\mathcal{N} - \mu_3\mu_4}{\rho\mu_4} = \frac{v\theta\left(\Lambda - \mu_1\mathcal{M}\right) - \mu_2\mu_3\mu_4}{\rho\mu_2\mu_4},
\end{aligned}$$

and

$$\frac{\mu_2\mu_4\beta_1\mathcal{M}}{v\left(\Lambda - \mu_1\mathcal{M}\right)\left(1 + \alpha_1\mathcal{Q}\right)} + \frac{\beta_2\mathcal{M}}{1 + \alpha_2\mathcal{Q}} - \left(\mu_2 + \sigma\right) = 0.$$

We have $\mathcal{N} > 0$ and $\mathcal{Q} > 0$ implies that $\mathcal{M} < \frac{\Lambda v\theta - \mu_2\mu_3\mu_4}{\mu_1 v\theta}$. Hence, no biological equilibrium if $\mathcal{M} \geq \frac{\Lambda v\theta - \mu_2\mu_3\mu_4}{\mu_1 v\theta}$ or $\frac{\Lambda v\theta - \mu_2\mu_3\mu_4}{\mu_1 v\theta} \leq 0$. It is easily proved that $\mathcal{C}_1 > 1$ implies $\frac{\Lambda v\theta - \mu_2\mu_3\mu_4}{\mu_1 v\theta} > 0$. Then, we take the function $\mathcal{U}$ defined on $\mathcal{I} = \left[0, \frac{\Lambda v\theta - \mu_2\mu_3\mu_4}{\mu_1 v\theta}\right]$ by

$$\mathcal{U}(\mathcal{M}) = \frac{\mu_2\mu_4\beta_1\mathcal{M}}{v\left(\Lambda - \mu_1\mathcal{M}\right)\left(1 + \alpha_1 f\left(\mathcal{M}\right)\right)} + \frac{\beta_2\mathcal{M}}{1 + \alpha_2 f\left(\mathcal{M}\right)} - \left(\mu_2 + \sigma\right),$$

where $f\left(\mathcal{M}\right) = \frac{v\theta\left(\Lambda - \mu_1\mathcal{M}\right) - \mu_2\mu_3\mu_4}{\rho\mu_2\mu_4} \geq 0$ in $\mathcal{I}$. Since

$$f'\left(\mathcal{M}\right) = -\frac{\mu_1 v\theta}{\rho\mu_2\mu_4} < 0,$$

and

$$\begin{aligned}
\mathcal{U}'(\mathcal{M}) &= \frac{\mu_2\mu_4\beta_1}{v}\frac{\left(\Lambda - \mu_1\mathcal{M}\right)\left(1 + \alpha_1 f\left(\mathcal{M}\right) - \alpha_1\mathcal{M}f'\left(\mathcal{M}\right)\right) + \mu_1\mathcal{M}\left(1 + \alpha_1 f\left(\mathcal{M}\right)\right)}{\left(\Lambda - \mu_1\mathcal{M}\right)^2\left(1 + \alpha_1 f\left(\mathcal{M}\right)\right)^2} \\
&\quad + \beta_2\frac{1 + \alpha_2 f\left(\mathcal{M}\right) - \alpha_2\mathcal{M}f'\left(\mathcal{M}\right)}{\left(1 + \alpha_2 f\left(\mathcal{M}\right)\right)^2},
\end{aligned}$$

then $\mathcal{U}'(\mathcal{M}) > 0$. Additionally, we have

$$\begin{aligned}
\mathcal{U}(0) &= -\left(\mu_2 + \sigma\right) < 0, \\
\mathcal{U}\left(\frac{\Lambda v\theta - \mu_2\mu_3\mu_4}{\mu_1 v\theta}\right) &= \left(\frac{\mu_2\mu_4\left(\beta_1\theta + \beta_2\mu_3\right)}{\mu_1 v\theta} + \mu_2 + \sigma\right)\left(\mathcal{C}_1 - 1\right) > 0.
\end{aligned}$$

Thus, the equation $\mathcal{U}(\mathcal{M}) = 0$ admits a unique solution $\mathcal{M}_2^* \in \left(0, \frac{\Lambda v\theta - \mu_2\mu_3\mu_4}{\mu_1 v\theta}\right)$. This demonstrates that model (2) has a unique equilibrium $\mathcal{G}_2^* = \left(\mathcal{M}_2^*, \frac{\Lambda - \mu_1\mathcal{M}_2^*}{\mu_2}, \frac{\mu_4}{v}, \frac{v\theta\left(\Lambda - \mu_1\mathcal{M}_2^*\right) - \mu_2\mu_3\mu_4}{\rho\mu_2\mu_4}\right)$ when $\mathcal{C}_1 > 1$.

4 Stability analysis

Stability analysis is among the main areas of research in mathematical biology. Here, we examine stability analysis of the three equilibrium points $\mathcal{G}^\circ$, $\mathcal{G}_1^\star$ and $\mathcal{G}_2^\star$ of system (2).

Local stability

This subsection presents results regarding the local stability of the suggested model's steady points.
The provided matrix

$$\mathcal{J} = \begin{pmatrix} -\mu_1 - \frac{\beta_1 \mathcal{P}}{1+\alpha_1 \mathcal{Q}} - \frac{\beta_2 \mathcal{N}}{1+\alpha_2 \mathcal{Q}} & -\frac{\beta_2 \mathcal{M}}{1+\alpha_2 \mathcal{Q}} + \sigma & -\frac{\beta_1 \mathcal{M}}{1+\alpha_1 \mathcal{Q}} & \frac{\alpha_1 \beta_1 \mathcal{M}\mathcal{P}}{(1+\alpha_1 \mathcal{Q})^2} + \frac{\alpha_2 \beta_2 \mathcal{M}\mathcal{N}}{(1+\alpha_2 \mathcal{Q})^2} \\ \frac{\beta_1 \mathcal{P}}{1+\alpha_1 \mathcal{Q}} + \frac{\beta_2 \mathcal{N}}{1+\alpha_2 \mathcal{Q}} & \frac{\beta_2 \mathcal{M}}{1+\alpha_2 \mathcal{Q}} - (\mu_2 + \sigma) & \frac{\beta_1 \mathcal{M}}{1+\alpha_1 \mathcal{Q}} & -\frac{\alpha_1 \beta_1 \mathcal{M}\mathcal{P}}{(1+\alpha_1 \mathcal{Q})^2} - \frac{\alpha_2 \beta_2 \mathcal{M}\mathcal{N}}{(1+\alpha_2 \mathcal{Q})^2} \\ 0 & \theta & -\mu_3 - \rho \mathcal{Q} & -\rho \mathcal{P} \\ 0 & 0 & \upsilon \mathcal{Q} & -\mu_4 + \upsilon \mathcal{P} \end{pmatrix}, \quad (3)$$

is defined the Jacobian matrix at any equilibrium $\mathcal{G} = (\mathcal{M}, \mathcal{N}, \mathcal{P}, \mathcal{Q})$.

Theorem 3 *For every* $\mathbf{m} \in (0,1]$, $\mathcal{G}^\circ$ *is locally asymptotically stable if* $\mathcal{C}_0 < 1$. $\mathcal{G}^\circ$ *is unstable if* $\mathcal{C}_0 > 1$.

Proof For Jacobian matrix (3) at $\mathcal{G}^\circ$, the characteristic polynomial is

$$(\lambda + \mu_1)(\lambda + \mu_4)\left[\lambda^2 + (\mu_2 + \sigma - \beta_2 \mathcal{M}^\circ + \mu_3)\lambda + \mu_3(\mu_2 + \sigma) - (\beta_1 \theta + \beta_2 \mu_3)\mathcal{M}^\circ\right] = 0. \quad (4)$$

It is obvious that Eq. (4) has two real roots that are negative, $\lambda_1 = -\mu_1$ and $\lambda_2 = -\mu_4$, then $|\arg(\lambda_{1,2})| = \pi > \frac{\mathbf{m}\pi}{2}$ for any $\mathbf{m} \in (0,1]$. The following equation governs the other two roots of (4)

$$\lambda^2 + \mathbf{c}_1 \lambda + \mathbf{c}_0 = 0, \quad (5)$$

where

$$\begin{aligned} \mathbf{c}_1 &= \mu_3 + (\mu_2 + \sigma)\left(1 - \mathcal{C}_0 + \frac{\beta_1 \theta \mathcal{M}^\circ}{\mu_3(\mu_2 + \sigma)}\right), \\ \mathbf{c}_0 &= \mu_3(\mu_2 + \sigma)(1 - \mathcal{C}_0). \end{aligned}$$

Based to the Routh-Hurwitz criterion [42], if $\mathcal{C}_0 < 1$ is true, Eq. (5) has two roots λ_i $(i = 3, 4)$ with negative real parts. Thus, $|\arg(\lambda_{3,4})| > \frac{\pi}{2} \geq \frac{\mathbf{m}\pi}{2}$ for any $\mathbf{m} \in (0,1]$ when $\mathcal{C}_0 < 1$. If $\mathcal{C}_0 > 1$, then Eq. (4) has a positive real root λ^*, then $|\arg(\lambda^*)| = 0 < \frac{\mathbf{m}\pi}{2}$ for all $\mathbf{m} \in (0,1]$. As a result, Lemma 1 in [26] states that $\mathcal{G}^\circ$ is unstable if $\mathcal{C}_0 > 1$ and locally asymptotically stable if $\mathcal{C}_0 < 1$.

Theorem 4 $\mathcal{G}_1^\star$ *is locally asymptotically stable for all* $\mathbf{m} \in (0,1]$ *if* $\mathcal{C}_1 < 1 < \mathcal{C}_0$. *If* $\mathcal{C}_1 > 1$, $\mathcal{G}_1^\star$ *is unstable.*

Proof At $\mathcal{G}_1^\star$, the characteristic polynomial of the Jacobian matrix (3) is

$$(\lambda + \mu_4 - \upsilon \mathcal{P}_1^\star)\left(\lambda^3 + \mathbf{e}_2 \lambda^2 + \mathbf{e}_1 \lambda + \mathbf{e}_0\right) = 0, \quad (6)$$

where

$$\begin{aligned} \mathbf{e}_2 &= \mu_1 + \mu_3 + \beta_1 \mathcal{P}_1^\star + \frac{\beta_1 \mathcal{M}_1^\star \mathcal{P}_1^\star}{\mathcal{N}_1^\star} + \beta_2 \mathcal{N}_1^\star, \\ \mathbf{e}_1 &= \mu_1\left(\mu_3 + \frac{\beta_1 \mathcal{N}_1^\star \mathcal{P}_1^\star}{\mathcal{N}_1^\star}\right) + (\beta_1 \mathcal{P}_1^\star + \beta_2 \mathcal{N}_1^\star)(\mu_2 + \mu_3), \\ \mathbf{e}_0 &= \mu_2 \mu_3 (\beta_1 \mathcal{P}_1^\star + \beta_2 \mathcal{N}_1^\star). \end{aligned}$$

One of the roots of Eq. (6) is

$$\lambda_1 = v\mathcal{P}_1^\star - \mu_4 = \left(\mu_4 + \frac{\mu_1 v\theta}{\mu_2\mu_3}\mathcal{M}_1^\star\right)(\mathcal{C}_1 - 1).$$

Thus, $|\arg(\lambda_1)| = \pi > \frac{\mathbf{m}\pi}{2}$ for every $\mathbf{m} \in (0,1]$ if $\mathcal{C}_1 < 1$ and $|\arg(\lambda_1)| = 0 < \frac{\mathbf{m}\pi}{2}$ for all $\mathbf{m} \in (0,1]$ if $\mathcal{C}_1 > 1$. The following equation governs the other roots of (6)

$$\lambda^3 + \mathbf{e}_2\lambda^2 + \mathbf{e}_1\lambda + \mathbf{e}_0 = 0. \tag{7}$$

It is simple to say that $\mathbf{e}_2 > 0$, $\mathbf{e}_1 > 0$ and $\mathbf{e}_0 > 0$. Therefore,

$$\mathbf{e}_2\mathbf{e}_1 - \mathbf{e}_0 = \left(\mu_1 + \beta_1\mathcal{P}_1^\star + \frac{\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{\mathcal{N}_1^\star} + \beta_2\mathcal{N}_1^\star\right)\mathbf{e}_1 + \mu_1\mu_3\left(\mu_3 + \frac{\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{\mathcal{N}_1^\star}\right) + \mu_3^2\left(\beta_1\mathcal{P}_1^\star + \beta_2\mathcal{N}_1^\star\right) > 0.$$

Therefore, according to the Routh-Hurwitz criteria, all roots λ_i $(i = 2,3,4)$ of (7) have negative real part, and for all $\mathbf{m} \in (0,1]$, $\left|\arg(\lambda_{2,3,4})\right| > \frac{\pi}{2} \geq \frac{\mathbf{m}\pi}{2}$ if $\mathcal{C}_0 > 1$. Thus, $\mathcal{G}_1^\star$ is unstable if $\mathcal{C}_1 > 1$ and locally asymptotically stable if $\mathcal{C}_1 < 1 < \mathcal{C}_0$.

Theorem 5 *Assume that* $\mathcal{C}_1 > 1$.

(i) *$\mathcal{G}_2^\star$ is locally asymptotically stable for all* $\mathbf{m} \in (0,1]$ *if* $\mathfrak{C}_1\left(\mathfrak{C}_3\mathfrak{C}_2 - \mathfrak{C}_1\right) - \mathfrak{C}_3^2\mathfrak{C}_0 > 0$, *where* $\mathfrak{C}_i$ $(i = 0,1,2,3)$ *are defined by Eq. (9).*

(ii) *$\mathcal{G}_2^\star$ is locally asymptotically stable for all* $\mathbf{m} \in (0, \frac{1}{3})$ *if* $\mathcal{D}_4(\mathcal{G}_2^\star) < 0$, *where* $\mathcal{D}_4(\mathcal{G}_2^\star)$ *is given by Eq. (10). Additionally, if we combine the preceding condition with the hypotheses* $\mathfrak{C}_2 = \frac{\mathfrak{C}_3\mathfrak{C}_0}{\mathfrak{C}_1} + \frac{\mathfrak{C}_1}{\mathfrak{C}_3}$, *then* $\mathcal{G}_2^\star$ *is locally asymptotically stable for all* $\mathbf{m} \in (0,1)$.

Proof The characteristic polynomial of the Jacobian matrix (3) at $\mathcal{G}_2^*$ is

$$\lambda^4 + \mathfrak{C}_3\lambda^3 + \mathfrak{C}_2\lambda^2 + \mathfrak{C}_1\lambda + \mathfrak{C}_0 = 0, \tag{8}$$

where

$$\begin{aligned}
\mathfrak{C}_3 &= \mu_1 + \mu_3 + \sigma + \rho\mathcal{Q}_2^\star + \frac{\beta_1\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star} + \frac{\beta_2\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star} + \frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)},\\
\mathfrak{C}_2 &= \mu_4\rho\mathcal{Q}_2^\star + \mu_1\left(\mu_3 + \rho\mathcal{Q}_2^\star + \frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\right) + \left(\mu_2 + \mu_3 + \rho\mathcal{Q}_2^\star\right)\left(\frac{\beta_1\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star} + \frac{\beta_2\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star}\right),\\
\mathfrak{C}_1 &= \mu_4\rho\mathcal{Q}_2^\star\left(\mu_1 + \frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\right) + \left(\frac{\beta_1\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star} + \frac{\beta_2\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star}\right)\left(\mu_4\rho\mathcal{Q}_2^\star + \mu_2\left(\mu_3 + \rho\mathcal{Q}_2^\star\right)\right)\\
&\quad + \theta v\mathcal{Q}_2^\star\left(\frac{\alpha_1\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\left(1+\alpha_1\mathcal{Q}_2^\star\right)^2} + \frac{\alpha_2\beta_2\mathcal{M}_2^\star\mathcal{N}_2^\star}{\left(1+\alpha_2\mathcal{Q}_2^\star\right)^2}\right),\\
\mathfrak{C}_0 &= \mu_1\mu_4\rho\mathcal{Q}_2^\star\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)} + \mu_2\mu_4\rho\mathcal{Q}_2^\star\left(\frac{\beta_1\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star} + \frac{\beta_2\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star}\right)\\
&\quad + \mu_1\theta v\mathcal{Q}_2^\star\left(\frac{\alpha_1\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\left(1+\alpha_1\mathcal{Q}_2^\star\right)^2} + \frac{\alpha_2\beta_2\mathcal{M}_2^\star\mathcal{N}_2^\star}{\left(1+\alpha_2\mathcal{Q}_2^\star\right)^2}\right).
\end{aligned} \tag{9}$$

(i) It is clear that $\mathfrak{C}_0 > 0$, $\mathfrak{C}_1 > 0$, $\mathfrak{C}_2 > 0$ and $\mathfrak{C}_3 > 0$. For $\mathfrak{C}_1\left(\mathfrak{C}_3\mathfrak{C}_2 - \mathfrak{C}_1\right) - \mathfrak{C}_3^2\mathfrak{C}_0 > 0$, it follows by

the Routh-Hurwitz criterion, that all roots λ_j $(j = 1, 2, 3, 4)$ of (8) have negative real part, which means that $\left|\arg(\lambda_j)\right| > \frac{\pi}{2} \geq \frac{\mathbf{m}\pi}{2}$. The equilibrium $\mathcal{G}_2^*$ is therefore locally asymptotically stable as stated by Lemma 1 in [26].

(ii) Let $\mathcal{D}_4(\mathcal{G}_2^\star)$ represent the discriminant of the polynomial (8), then

$$\begin{aligned}
\mathcal{D}_4(\mathcal{G}_2^\star) &= \begin{vmatrix}
1 & \mathfrak{C}_3 & \mathfrak{C}_2 & \mathfrak{C}_1 & \mathfrak{C}_0 & 0 & 0 \\
0 & 1 & \mathfrak{C}_3 & \mathfrak{C}_2 & \mathfrak{C}_1 & \mathfrak{C}_0 & 0 \\
0 & 0 & 1 & \mathfrak{C}_3 & \mathfrak{C}_2 & \mathfrak{C}_1 & \mathfrak{C}_0 \\
4 & 3\mathfrak{C}_3 & 2\mathfrak{C}_2 & \mathfrak{C}_1 & 0 & 0 & 0 \\
0 & 4 & 3\mathfrak{C}_3 & 2\mathfrak{C}_2 & \mathfrak{C}_1 & 0 & 0 \\
0 & 0 & 4 & 3\mathfrak{C}_3 & 2\mathfrak{C}_2 & \mathfrak{C}_1 & 0 \\
0 & 0 & 0 & 4 & 3\mathfrak{C}_3 & 2\mathfrak{C}_2 & \mathfrak{C}_1
\end{vmatrix} \\
&= 18\mathfrak{C}_3^2\mathfrak{C}_2\mathfrak{C}_1\mathfrak{C}_0 - 27\mathfrak{C}_3^4\mathfrak{C}_0^2 - 4\mathfrak{C}_3^3\mathfrak{C}_1^3 - 4\mathfrak{C}_3^2\mathfrak{C}_0^3\mathfrak{C}_4 + \mathfrak{C}_3^2\mathfrak{C}_2^3\mathfrak{C}_1^3 + 144\mathfrak{C}_3^2\mathfrak{C}_2\mathfrak{C}_1^2 \\
&\quad -6\mathfrak{C}_3^2\mathfrak{C}_1^2\mathfrak{C}_0 - 80\mathfrak{C}_3\mathfrak{C}_2^2\mathfrak{C}_1\mathfrak{C}_0 + 18\mathfrak{C}_3\mathfrak{C}_2\mathfrak{C}_1^3 - 192\mathfrak{C}_3\mathfrak{C}_2\mathfrak{C}_0^2 + 16\mathfrak{C}_2^4\mathfrak{C}_0 - 4\mathfrak{C}_2^3\mathfrak{C}_1^2 \\
&\quad -128\mathfrak{C}_2^2\mathfrak{C}_0^2 + 144\mathfrak{C}_3\mathfrak{C}_2^2\mathfrak{C}_0 - 27\mathfrak{C}_1^4 + 256\mathfrak{C}_0^3.
\end{aligned} \tag{10}$$

For $\mathcal{D}_4(\mathcal{G}_2^\star) < 0$, and since $\mathfrak{C}_i > 0$, the only condition that can be met by applying the fractional Routh-Hurwitz conditions in Theorem 6 in [43] is (iii), $\mathcal{G}_2^*$ is therefore locally asymptotically stable for $\mathbf{m} \in (0, \frac{1}{3})$. Furthermore, the condition (iv) in Theorem 6 in [43] is met if $\mathfrak{C}_2 = \frac{\mathfrak{C}_3\mathfrak{C}_0}{\mathfrak{C}_1} + \frac{\mathfrak{C}_1}{\mathfrak{C}_3}$. Therefore, for all $\mathbf{m} \in (0, 1)$, $\mathcal{G}_2^\star$ is locally asymptotically stable.

Global stability

This subsection focuses on the global stability of the three equilibrium states. We shall employ some appropriate Lyapunov functions and the fractional LaSalle's invariant principle to this goal.

Theorem 6 *If $\mathcal{C}_0 \leq 1$, then $\mathcal{G}^\circ$ is globally asymptotically stable for all $\mathbf{m} \in (0, 1]$.*

Proof Let the following Lyapunov function

$$\begin{aligned}
\mathcal{K}_\circ(t) &= \mathcal{M}^\circ \mathcal{H}\left(\frac{\mathcal{M}(t)}{\mathcal{M}^\circ}\right) + \mathcal{N}(t) + \frac{\beta_1 \mathcal{M}^\circ}{\mu_3}\mathcal{P}(t) + \frac{\rho\beta_1\mathcal{M}^\circ}{v\mu_3}\mathcal{Q}(t) \\
&\quad + \frac{\sigma}{2(\mu_1+\mu_2)\mathcal{M}^\circ}\left(\mathcal{M}(t) - \mathcal{M}^\circ + \mathcal{N}(t)\right)^2,
\end{aligned}$$

where $\mathcal{H}(v) = v - 1 - \ln v$, $v > 0$. Applying Lemma 2 and Lemma 3, we get

$$\begin{aligned}
{}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_\circ &\leq \left(1 - \frac{\mathcal{M}^\circ}{\mathcal{M}}\right) {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{M} + {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{N} + \frac{\beta_1\mathcal{M}^\circ}{\mu_3}\,{}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{P} + \frac{\rho\beta_1\mathcal{M}^\circ}{v\mu_3}\,{}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{Q} \\
&\quad + \frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}^\circ}\left(\mathcal{M} - \mathcal{M}^\circ + \mathcal{N}\right)\left({}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{M} + {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{N}\right) \\
&= \left(1 - \frac{\mathcal{M}^\circ}{\mathcal{M}}\right)\left(\Lambda - \mu_1\mathcal{M} - \frac{\beta_1\mathcal{M}\mathcal{P}}{1+\alpha_1\mathcal{Q}} - \frac{\beta_2\mathcal{M}\mathcal{N}}{1+\alpha_2\mathcal{Q}} + \sigma\mathcal{N}\right) + \frac{\beta_1\mathcal{M}\mathcal{P}}{1+\alpha_1\mathcal{Q}} \\
&\quad + \frac{\beta_2\mathcal{M}\mathcal{N}}{1+\alpha_2\mathcal{Q}} - (\mu_2+\sigma)\mathcal{N} + \frac{\beta_1\mathcal{M}^\circ}{\mu_3}\left(\theta\mathcal{N} - \mu_3\mathcal{P} - \rho\mathcal{P}\mathcal{Q}\right) \\
&\quad + \frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}^\circ}\left(\mathcal{M} - \mathcal{M}^\circ + \mathcal{N}\right)\left(\Lambda - \mu_1\mathcal{M} - \mu_2\mathcal{N}\right)
\end{aligned}$$

$$
\begin{aligned}
&= -\mu_1\frac{(\mathcal{M}-\mathcal{M}^\circ)^2}{\mathcal{M}} + \sigma\mathcal{N}\left(1-\frac{\mathcal{M}^\circ}{\mathcal{M}}\right) + \frac{\beta_1\mathcal{M}^\circ\mathcal{P}}{1+\alpha_1\mathcal{Q}} + \frac{\beta_2\mathcal{M}^\circ\mathcal{N}}{1+\alpha_2\mathcal{Q}} - (\mu_2+\sigma)\,\mathcal{N}\\
&- \frac{\beta_1\theta\mathcal{M}^\circ}{\mu_3}\mathcal{N} - \beta_1\mathcal{M}^\circ\mathcal{P} - \frac{\mu_4\rho\beta_1\mathcal{M}^\circ\mathcal{Q}}{v\mu_3}\\
&- \frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}^\circ}(\mathcal{M}-\mathcal{M}^\circ+\mathcal{M})\,(\mu_1\,(\mathcal{M}-\mathcal{M}^\circ)+\mu_2\mathcal{N})\\
&= -\left(\mu_1\mathcal{M}^\circ+\sigma\mathcal{N}+\frac{\sigma\mu_1\mathcal{M}}{\mu_1+\mu_2}\right)\frac{(\mathcal{M}-\mathcal{M}^\circ)^2}{\mathcal{M}\mathcal{M}^\circ} - \frac{\mu_2\sigma\mathcal{N}^2}{(\mu_1+\mu_2)\mathcal{M}^\circ} - \frac{\alpha_1\beta_1\mathcal{M}^\circ\mathcal{P}\mathcal{Q}}{1+\alpha_1\mathcal{Q}}\\
&- \frac{\mu_4\rho\beta_1\mathcal{M}^\circ\mathcal{Q}}{v\mu_3} + (\mu_2+\sigma)\,\mathcal{N}\left(\frac{\beta_1\theta\mathcal{M}^\circ}{\mu_3\,(\mu_2+\sigma)} + \frac{\beta_2\mathcal{M}^\circ}{(1+\alpha_2\mathcal{Q})\,(\mu_2+\sigma)} - 1\right)\\
&\leq -\left(\mu_1\mathcal{M}^\circ+\sigma\mathcal{N}+\frac{\sigma\mu_1\mathcal{M}}{\mu_1+\mu_2}\right)\frac{(\mathcal{M}-\mathcal{M}^\circ)^2}{\mathcal{M}\mathcal{M}^\circ} - \frac{\mu_2\sigma\mathcal{N}^2}{(\mu_1+\mu_2)\mathcal{M}^\circ} - \frac{\alpha_1\beta_1\mathcal{M}^\circ\mathcal{P}\mathcal{Q}}{1+\alpha_1\mathcal{Q}}\\
&- \frac{\mu_4\rho\beta_1\mathcal{M}^\circ\mathcal{Q}}{v\mu_3} + (\mu_2+\sigma)\,(\mathcal{C}_0-1)\,\mathcal{N}.
\end{aligned}
$$

Therefore, $\mathcal{C}_0 \leq 1$ makes sure that ${}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_\circ \leq 0$. Furthermore, it is straightforward to confirm that $\{\mathcal{G}^\circ\}$ is the largest compact invariant set in $\left\{(\mathcal{M},\mathcal{N},\mathcal{P},\mathcal{Q}) \in \mathbb{R}_+^4 : {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_\circ = 0\right\}$. By Lemma 4.6 in [44], which is the fractional version of LaSalle's invariance principle, we may conclude that $\mathcal{G}^\circ$ is globally asymptotically stable if $\mathcal{C}_0 \leq 1$. For the global stability of $\mathcal{G}_1^\star$, we presume that

$$
\frac{\mathcal{P}_1^\star}{\mathcal{P}} - \frac{1}{1+\alpha_1\mathcal{Q}} \leq 0, \quad \frac{\mathcal{N}_1^\star}{\mathcal{N}} - \frac{1}{1+\alpha_2\mathcal{Q}} \leq 0. \tag{H_1}
$$

Theorem 7 *If $\mathcal{C}_1 \leq 1 < \mathcal{C}_0 \leq 1+\frac{\mu_2}{\sigma}$ and (H_1) holds, then $\mathcal{G}_1^\star$ is globally asymptotically stable for any $\mathbf{m} \in (0,1]$.*

Proof Define a Lyapunov functional

$$
\begin{aligned}
\mathcal{K}_1(t) \;=\; & \mathcal{M}_1^\star\mathcal{H}\left(\frac{\mathcal{M}(t)}{\mathcal{M}_1^\star}\right) + \mathcal{N}_1^\star\mathcal{H}\left(\frac{\mathcal{N}(t)}{\mathcal{N}_1^\star}\right) + \frac{\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{\theta\mathcal{N}_1^\star}\mathcal{P}_1^\star\mathcal{H}\left(\frac{\mathcal{P}(t)}{\mathcal{P}_1^\star}\right) + \frac{\rho\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{v\theta\mathcal{N}_1^\star}\mathcal{Q}(t)\\
& + \frac{\sigma}{2(\mu_1+\mu_2)\mathcal{M}_1^\star}\left(\mathcal{M}(t)-\mathcal{M}_1^\star+\mathcal{N}(t)-\mathcal{N}_1^\star\right)^2.
\end{aligned}
$$

Then, the Caputo fractional derivative of $\mathcal{K}_1$ along system (2) satisfies

$$
\begin{aligned}
{}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_1 &\leq \left(1-\frac{\mathcal{M}_1^\star}{\mathcal{M}}\right){}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{M} + \left(1-\frac{\mathcal{N}_1^\star}{\mathcal{N}}\right){}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{N} + \frac{\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{\theta\mathcal{N}_1^\star}\left(1-\frac{\mathcal{P}_1^\star}{\mathcal{P}}\right){}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{P}\\
&+ \frac{\rho\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{v\theta\mathcal{N}_1^\star}{}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{Q} + \frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}_1^\star}\left(\mathcal{M}-\mathcal{M}_1^\star+\mathcal{N}-\mathcal{N}_1^\star\right)\left({}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{M} + {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{N}\right)\\
&= \left(1-\frac{\mathcal{M}_1^\star}{\mathcal{M}}\right)\left(\Lambda-\mu_1\mathcal{M}-\frac{\beta_1\mathcal{M}\mathcal{P}}{1+\alpha_1\mathcal{Q}}-\frac{\beta_2\mathcal{M}\mathcal{N}}{1+\alpha_2\mathcal{Q}}+\sigma\mathcal{N}\right)\\
&+ \left(1-\frac{\mathcal{N}_1^\star}{\mathcal{N}}\right)\left(\frac{\beta_1\mathcal{M}\mathcal{P}}{1+\alpha_1\mathcal{Q}}+\frac{\beta_2\mathcal{M}\mathcal{N}}{1+\alpha_2\mathcal{Q}}-(\mu_2+\sigma)\,\mathcal{N}\right)
\end{aligned}
$$

$$+\frac{\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{\theta\mathcal{N}_1^\star}\left(1-\frac{\mathcal{P}_1^\star}{\mathcal{P}}\right)(\theta\mathcal{N}-\mu_3\mathcal{P}-\rho\mathcal{P}\mathcal{Q})+\frac{\rho\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{v\theta\mathcal{N}_1^\star}(v\mathcal{P}\mathcal{Q}-\mu_4\mathcal{Q})$$
$$+\frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}_1^\star}(\mathcal{M}-\mathcal{M}_1^\star+\mathcal{N}-\mathcal{N}_1^\star)(\Lambda-\mu_1\mathcal{M}-\mu_2\mathcal{M}).$$

Note that $\Lambda=\mu_1\mathcal{M}_1^\star+\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star+\beta_2\mathcal{M}_1^\star\mathcal{N}_1^\star-\sigma\mathcal{N}_1^\star$, $\mu_2+\sigma=\frac{\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{\mathcal{N}_1^\star}+\beta_2\mathcal{M}_1^\star$ and $\mu_3=\frac{\theta\mathcal{N}_1^\star}{\mathcal{P}_1^\star}$. Therefore,

$$\begin{aligned}
{}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_1 &\le \mu_1\left(1-\frac{\mathcal{M}_1^\star}{\mathcal{M}}\right)(\mathcal{M}_1^\star-\mathcal{M})+\sigma(\mathcal{N}-\mathcal{N}_1^\star)\left(1-\frac{\mathcal{M}_1^\star}{\mathcal{M}}\right)\\
&+\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star\left(3-\frac{\mathcal{M}_1^\star}{\mathcal{M}}-\frac{\mathcal{P}}{\mathcal{P}_1^\star}+\frac{\mathcal{P}}{\mathcal{P}_1^\star}\frac{1}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{M}\mathcal{N}_1^\star\mathcal{P}}{\mathcal{M}_1^\star\mathcal{N}\mathcal{P}_1^\star}\frac{1}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{N}\mathcal{P}_1^\star}{\mathcal{N}_1^\star\mathcal{P}}\right)\\
&+\beta_2\mathcal{M}_1^\star\mathcal{N}_1^\star\left(2-\frac{\mathcal{M}_1^\star}{\mathcal{M}}-\frac{\mathcal{M}}{\mathcal{M}_1^\star}\frac{1}{1+\alpha_2\mathcal{Q}}+\frac{\mathcal{N}}{\mathcal{N}_1^\star}\frac{1}{1+\alpha_2\mathcal{Q}}-\frac{\mathcal{N}}{\mathcal{N}_1^\star}\right)+\frac{\rho\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{v\theta\mathcal{N}_1^\star}(v\mathcal{P}_1^\star-\mu_4)\mathcal{Q}\\
&-\frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}_1^\star}(\mathcal{M}-\mathcal{M}_1^\star+\mathcal{N}-\mathcal{N}_1^\star)(\mu_1(\mathcal{M}-\mathcal{M}_1^\star)+\mu_2(\mathcal{N}-\mathcal{N}_1^\star))\\
&=-\left(\mu_1\mathcal{M}_1^\star+\sigma\mathcal{N}-\sigma\mathcal{N}_1^\star+\frac{\sigma\mu_1\mathcal{M}}{\mu_1+\mu_2}\right)\frac{(\mathcal{M}-\mathcal{M}_1^\star)^2}{\mathcal{M}\mathcal{M}_1^\star}-\frac{\sigma\mu_2}{(\mu_1+\mu_2)\mathcal{M}_1^\star}(\mathcal{N}-\mathcal{N}_1^\star)^2\\
&+\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star\left(4-\frac{\mathcal{M}_1^\star}{\mathcal{M}}-(1+\alpha_1\mathcal{Q})-\frac{\mathcal{M}\mathcal{N}_1^\star\mathcal{P}}{\mathcal{M}_1^\star\mathcal{N}\mathcal{P}_1^\star}\frac{1}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{N}\mathcal{P}_1^\star}{\mathcal{N}_1^\star\mathcal{P}}\right)\\
&+\alpha_1\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star\left(1-\frac{\mathcal{P}}{\mathcal{P}_1^\star}\frac{1}{1+\alpha_1\mathcal{Q}}\right)\mathcal{Q}+\alpha_2\beta_2\mathcal{M}_1^\star\mathcal{N}_1^\star\left(1-\frac{\mathcal{N}}{\mathcal{N}_1^\star}\frac{1}{1+\alpha_2\mathcal{Q}}\right)\mathcal{Q}\\
&+\beta_2\mathcal{M}_1^\star\mathcal{N}_1^\star\left(3-\frac{\mathcal{M}_1^\star}{\mathcal{M}}-(1+\alpha_2\mathcal{Q})-\frac{\mathcal{M}}{\mathcal{M}_1^\star}\frac{1}{1+\alpha_2\mathcal{Q}}\right)\\
&+\frac{\rho\beta_1\mathcal{M}_1^\star\mathcal{P}_1^\star}{v\theta\mathcal{N}_1^\star}\left(\mu_4+\frac{\mu_1 v\theta}{\mu_2\mu_3}\mathcal{M}_1^\star\right)(\mathcal{C}_1-1)\mathcal{Q}.
\end{aligned}$$

The arithmetic-geometric mean inequality enables us to deduce

$$\begin{aligned}
4-\frac{\mathcal{M}_1^\star}{\mathcal{M}}-(1+\alpha_1\mathcal{Q})-\frac{\mathcal{M}\mathcal{N}_1^\star\mathcal{P}}{\mathcal{M}_1^\star\mathcal{N}\mathcal{P}_1^\star}\frac{1}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{N}\mathcal{P}_1^\star}{\mathcal{N}_1^\star\mathcal{P}} &\le 0,\\
3-\frac{\mathcal{M}_1^\star}{\mathcal{M}}-(1+\alpha_2\mathcal{Q})-\frac{\mathcal{M}}{\mathcal{M}_1^\star}\frac{1}{1+\alpha_2\mathcal{Q}} &\le 0.
\end{aligned}$$

From (H_1), we have

$$\begin{aligned}
1-\frac{\mathcal{P}}{\mathcal{P}_1^\star}\frac{1}{1+\alpha_1\mathcal{Q}} &= \frac{\mathcal{P}}{\mathcal{P}_1^\star}\left(\frac{\mathcal{P}_1^\star}{\mathcal{P}}-\frac{1}{1+\alpha_1\mathcal{Q}}\right)\le 0,\\
1-\frac{\mathcal{N}}{\mathcal{N}_1^\star}\frac{1}{1+\alpha_2\mathcal{Q}} &= \frac{\mathcal{N}}{\mathcal{N}_1^\star}\left(\frac{\mathcal{N}_1^\star}{\mathcal{N}}-\frac{1}{1+\alpha_2\mathcal{Q}}\right)\le 0.
\end{aligned}$$

Further, we have

$$\mu_1\mathcal{M}_1^\star-\sigma\mathcal{N}_1^\star=\frac{\Lambda}{\mathcal{C}_0}\left(1-\frac{\sigma}{\mu_2}(\mathcal{C}_\circ-1)\right).$$

Thus, ${}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_1\le 0$ if $\mathcal{C}_1\le 1<\mathcal{C}_0\le 1+\frac{\mu_2}{\sigma}$. Furthermore, the largest compact invariant

set in $\{(\mathcal{M},\mathcal{N},\mathcal{P},\mathcal{Q}) \in \mathbb{R}^4_+ : {}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{K}_1 = 0\}$ is $\{\mathcal{G}_1^\star\}$, then $\mathcal{G}_1^\star$ is globally asymptotically stable if $\mathcal{C}_1 \leq 1 < \mathcal{C}_0 \leq 1 + \frac{\mu_2}{\sigma}$.
For the global stability of $\mathcal{G}_2^\star$, we make an additional hypothesis as follows:

$$(\mathcal{Q}-\mathcal{Q}_2^\star)\left(\frac{1+\alpha_1\mathcal{Q}}{1+\alpha_1\mathcal{Q}_2^\star}-\frac{\mathcal{P}}{\mathcal{P}_2^\star}\right)\leq 0,\quad (\mathcal{Q}-\mathcal{Q}_2^\star)\left(\frac{1+\alpha_2\mathcal{Q}}{1+\alpha_2\mathcal{Q}_2^\star}-\frac{\mathcal{N}}{\mathcal{N}_2^\star}\right)\leq 0. \tag{H_2}$$

Theorem 8 *If $\mathcal{C}_1 > 1$, $\mathcal{M}_2^\star \geq \frac{\sigma}{\mu_1}\mathcal{N}_2^\star$ and (H_2) holds, then $\mathcal{G}_2^\star$ is globally asymptotically stable for any $\mathbf{m} \in (0,1]$.*

Proof Let $\mathcal{K}_2$ be the Lyapunov functional defined as

$$\begin{aligned}\mathcal{K}_2(t) &= \mathcal{M}_2^\star\mathcal{H}\left(\frac{\mathcal{M}(t)}{\mathcal{M}_2^\star}\right)+\mathcal{N}_2^\star\mathcal{H}\left(\frac{\mathcal{N}(t)}{\mathcal{N}_2^\star}\right)+\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\theta\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\mathcal{P}_2^\star\mathcal{H}\left(\frac{\mathcal{P}(t)}{\mathcal{P}_2^\star}\right)\\&+\frac{\rho\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{v\theta\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\mathcal{Q}_2^\star\mathcal{H}\left(\frac{\mathcal{Q}(t)}{\mathcal{Q}_2^\star}\right)\\&+\frac{\sigma}{2(\mu_1+\mu_2)\mathcal{M}_2^\star}\left(\mathcal{M}(t)-\mathcal{M}_2^\star+\mathcal{N}(t)-\mathcal{N}_2^\star\right)^2.\end{aligned}$$

Then, the Caputo fractional derivative of $\mathcal{K}_2$ along system (2) satisfies

$$\begin{aligned}{}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{K}_2 &\leq \left(1-\frac{\mathcal{M}_2^\star}{\mathcal{M}}\right){}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{M}+\left(1-\frac{\mathcal{N}_2^\star}{\mathcal{N}}\right){}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{N}+\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\theta\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\left(1-\frac{\mathcal{P}_2^\star}{\mathcal{P}}\right){}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{P}\\&+\frac{\rho\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{v\theta\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\left(1-\frac{\mathcal{Q}_2^\star}{\mathcal{Q}}\right){}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{Q}\\&+\frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}_2^\star}\left(\mathcal{M}-\mathcal{M}_2^\star+\mathcal{N}-\mathcal{N}_2^\star\right)\left({}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{M}+{}^{C}_{0}\mathfrak{D}^{\mathbf{m}}\mathcal{N}\right)\\&=\left(1-\frac{\mathcal{M}_2^\star}{\mathcal{M}}\right)\left(\Lambda-\mu_1\mathcal{M}-\frac{\beta_1\mathcal{M}\mathcal{P}}{1+\alpha_1\mathcal{Q}}-\frac{\beta_2\mathcal{M}\mathcal{N}}{1+\alpha_2\mathcal{Q}}+\sigma\mathcal{N}\right)\\&+\left(1-\frac{\mathcal{N}_2^\star}{\mathcal{N}}\right)\left(\frac{\beta_1\mathcal{M}\mathcal{P}}{1+\alpha_1\mathcal{Q}}+\frac{\beta_2\mathcal{M}\mathcal{N}}{1+\alpha_2\mathcal{Q}}-(\mu_2+\sigma)\mathcal{N}\right)\\&+\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\theta\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\left(1-\frac{\mathcal{P}_2^\star}{\mathcal{P}}\right)(\theta\mathcal{N}-\mu_3\mathcal{P}-\rho\mathcal{P}\mathcal{Q})\\&+\frac{\rho\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{v\theta\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}\left(1-\frac{\mathcal{Q}_2^\star}{\mathcal{Q}}\right)(v\mathcal{P}\mathcal{Q}-\mu_4\mathcal{Q})\\&+\frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}_2^\star}(\mathcal{M}-\mathcal{M}_2^\star+\mathcal{N}-\mathcal{N}_2^\star)\left(\Lambda-\mu_1\mathcal{M}-\mu_2\mathcal{M}\right).\end{aligned}$$

Note that

$$\begin{aligned}\Lambda &= \mu_1\mathcal{M}_2^\star+\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star}+\frac{\beta_2\mathcal{M}_2^\star\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star}-\sigma\mathcal{N}_2^\star,\\ \mu_2+\sigma &= \frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{\mathcal{N}_2^\star\left(1+\alpha_1\mathcal{Q}_2^\star\right)}+\frac{\beta_2\mathcal{M}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star},\\ \mu_3 &= \frac{\theta\mathcal{N}_2^\star}{\mathcal{P}_2^\star}-\rho\mathcal{Q}_2^\star,\quad \mu_4=v\mathcal{P}_2^\star.\end{aligned}$$

Therefore,

$$
\begin{aligned}
{}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_2 \leq\ & \mu_1\left(1-\frac{\mathcal{M}_2^\star}{\mathcal{M}}\right)(\mathcal{M}_2^\star-\mathcal{M})+\sigma(\mathcal{N}-\mathcal{N}_2^\star)\left(1-\frac{\mathcal{N}_2^\star}{\mathcal{N}}\right)\\
&+\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star}\left(3-\frac{\mathcal{M}_2^\star}{\mathcal{M}}-\frac{\mathcal{P}}{\mathcal{P}_2^\star}+\frac{\mathcal{P}}{\mathcal{P}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{M}\mathcal{N}_2^\star\mathcal{P}}{\mathcal{M}_2^\star\mathcal{N}\mathcal{P}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{N}\mathcal{P}_2^\star}{\mathcal{N}_2^\star\mathcal{P}}\right)\\
&+\frac{\beta_2\mathcal{M}_2^\star\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star}\left(2-\frac{\mathcal{M}_2^\star}{\mathcal{M}}-\frac{\mathcal{M}}{\mathcal{M}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_2\mathcal{Q}}+\frac{\mathcal{N}}{\mathcal{N}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_2\mathcal{Q}}-\frac{\mathcal{N}}{\mathcal{N}_2^\star}\right)\\
&-\frac{\sigma}{(\mu_1+\mu_2)\mathcal{M}_2^\star}(\mathcal{M}-\mathcal{M}_2^\star+\mathcal{N}-\mathcal{N}_2^\star)\left(\mu_1(\mathcal{M}-\mathcal{M}_2^\star)+\mu_2(\mathcal{N}-\mathcal{N}_2^\star)\right)\\
=\ & -\left(\mu_1\mathcal{M}_2^\star-\sigma\mathcal{N}_2^\star+\sigma\mathcal{N}+\frac{\sigma\mu_1\mathcal{M}}{\mu_1+\mu_2}\right)\frac{(\mathcal{M}-\mathcal{M}_2^\star)^2}{\mathcal{M}\mathcal{M}_2^\star}-\frac{\sigma\mu_2}{(\mu_1+\mu_2)\mathcal{M}_2^\star}(\mathcal{N}-\mathcal{N}_2^\star)^2\\
&+\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star}\left(4-\frac{\mathcal{M}_2^\star}{\mathcal{M}}-\frac{1+\alpha_1\mathcal{Q}}{1+\alpha_1\mathcal{Q}_2^\star}-\frac{\mathcal{M}\mathcal{N}_2^\star\mathcal{P}}{\mathcal{M}_2^\star\mathcal{N}\mathcal{P}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{N}\mathcal{P}_2^\star}{\mathcal{N}_2^\star\mathcal{P}}\right)\\
&+\frac{\beta_1\mathcal{M}_2^\star\mathcal{P}_2^\star}{1+\alpha_1\mathcal{Q}_2^\star}\left(-1-\frac{\mathcal{P}}{\mathcal{P}_2^\star}+\frac{\mathcal{P}}{\mathcal{P}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_1\mathcal{Q}}+\frac{1+\alpha_1\mathcal{Q}}{1+\alpha_1\mathcal{Q}_2^\star}\right)\\
&+\frac{\beta_2\mathcal{M}_2^\star\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star}\left(3-\frac{\mathcal{M}_2^\star}{\mathcal{M}}-\frac{1+\alpha_2\mathcal{Q}}{1+\alpha_2\mathcal{Q}_2^\star}-\frac{\mathcal{M}}{\mathcal{M}_2^\star}\frac{1+\alpha_2\mathcal{Q}_2^\star}{1+\alpha_2\mathcal{Q}}\right)\\
&+\frac{\beta_2\mathcal{M}_2^\star\mathcal{N}_2^\star}{1+\alpha_2\mathcal{Q}_2^\star}\left(-1-\frac{\mathcal{N}}{\mathcal{N}_2^\star}+\frac{\mathcal{N}}{\mathcal{N}_2^\star}\frac{1+\alpha_2\mathcal{Q}}{1+\alpha_2\mathcal{Q}_2^\star}+\frac{1+\alpha_2\mathcal{Q}_2^\star}{1+\alpha_2\mathcal{Q}}\right).
\end{aligned}
$$

The arithmetic-geometric mean inequality enables us to deduce

$$
\begin{aligned}
4-\frac{\mathcal{M}_2^\star}{\mathcal{M}}-\frac{1+\alpha_1\mathcal{Q}}{1+\alpha_1\mathcal{Q}_2^\star}-\frac{\mathcal{M}\mathcal{N}_2^\star\mathcal{P}}{\mathcal{M}_2^\star\mathcal{N}\mathcal{P}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_1\mathcal{Q}}-\frac{\mathcal{N}\mathcal{P}_2^\star}{\mathcal{N}_2^\star\mathcal{P}} &\leq 0,\\
3-\frac{\mathcal{M}_2^\star}{\mathcal{M}}-\frac{1+\alpha_2\mathcal{Q}}{1+\alpha_2\mathcal{Q}_2^\star}-\frac{\mathcal{M}}{\mathcal{M}_2^\star}\frac{1+\alpha_2\mathcal{Q}_2^\star}{1+\alpha_2\mathcal{Q}} &\leq 0.
\end{aligned}
$$

From (H_2), we have

$$
\begin{aligned}
-1-\frac{\mathcal{P}}{\mathcal{P}_2^\star}+\frac{\mathcal{P}}{\mathcal{P}_2^\star}\frac{1+\alpha_1\mathcal{Q}_2^\star}{1+\alpha_1\mathcal{Q}}+\frac{1+\alpha_1\mathcal{Q}}{1+\alpha_1\mathcal{Q}_2^\star} &= \frac{\alpha_1(\mathcal{Q}-\mathcal{Q}_2^\star)}{1+\alpha_1\mathcal{Q}}\left(\frac{1+\alpha_1\mathcal{Q}}{1+\alpha_1\mathcal{Q}_2^\star}-\frac{\mathcal{P}}{\mathcal{P}_2^\star}\right)\leq 0,\\
-1-\frac{\mathcal{N}}{\mathcal{N}_2^\star}+\frac{\mathcal{N}}{\mathcal{N}_2^\star}\frac{1+\alpha_2\mathcal{Q}}{1+\alpha_2\mathcal{Q}_2^\star}+\frac{1+\alpha_2\mathcal{Q}_2^\star}{1+\alpha_2\mathcal{Q}} &= \frac{\alpha_2(\mathcal{Q}-\mathcal{Q}_2^\star)}{1+\alpha_2\mathcal{Q}}\left(\frac{1+\alpha_2\mathcal{Q}}{1+\alpha_2\mathcal{Q}_2^\star}-\frac{\mathcal{N}}{\mathcal{N}_2^\star}\right)\leq 0.
\end{aligned}
$$

Thus, ${}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_2\leq 0$ if $\mathcal{C}_1>1$ and $\mathcal{M}_2^\star\geq\frac{\sigma}{\mu_1}\mathcal{N}_2^\star$. Additionally, $\{\mathcal{G}_2^\star\}$ is the largest compact invariant set in $\{(\mathcal{M},\mathcal{N},\mathcal{P},\mathcal{Q})\in\mathbb{R}_+^4:\ {}_0^C\mathfrak{D}^{\mathbf{m}}\mathcal{K}_2=0\}$, then $\mathcal{G}_2^\star$ is globally asymptotically stable.

5 Numerical simulations and discussion

Here in this section, we will present different numerical simulations to show numerically the stability of each equilibrium point under the biological parameters of model (2) which given in Table 1.

The virus-clear equilibrium stability

If we put the value parameters in Table 1, we get that in this case, the dynamical behavior of model (2) converges to virus-clear equilibrium $\mathcal{G}^\circ=(10,0,0,0)$ for different values of $\mathbf{m}$ and

Table 1. The parameter definitions of model (2) with their values

Parameter	Definition	Value	Sources
Λ	The indicates rate	1	Assumed
μ_1	Death rate of $\mathcal{M}$	0.1	Assumed
β_1	The infection rate	0.01	[16]
β_2	The infection rate	0.001	Assumed
α_1	The non-lytic immune rate	0.1	[16]
α_2	The non-lytic immune rate	0.01	Assumed
σ	The healing rate	0.01	[16]
μ_2	Death rate of $\mathcal{N}$	1	[16]
θ	The designates the produce ratio	2.9	[16]
μ_3	Death rate of $\mathcal{P}$	1	[16]
ρ	The neutralizing rate	0.006	[16]
ν	The growth rate of $\mathcal{Q}$	0.1	[16]
μ_4	Death rate of $\mathcal{Q}$	0.3	[16]

$\mathcal{C}_0 = 0.283 < 1$. The condition of Theorem 3 concerning the stability of $\mathcal{G}^\circ$ is satisfied. This result is drawn by Figure 1. This numerical result demonstrates that the number of uninfected cells is steadily increasing while the other variables are diminishing toward zero.

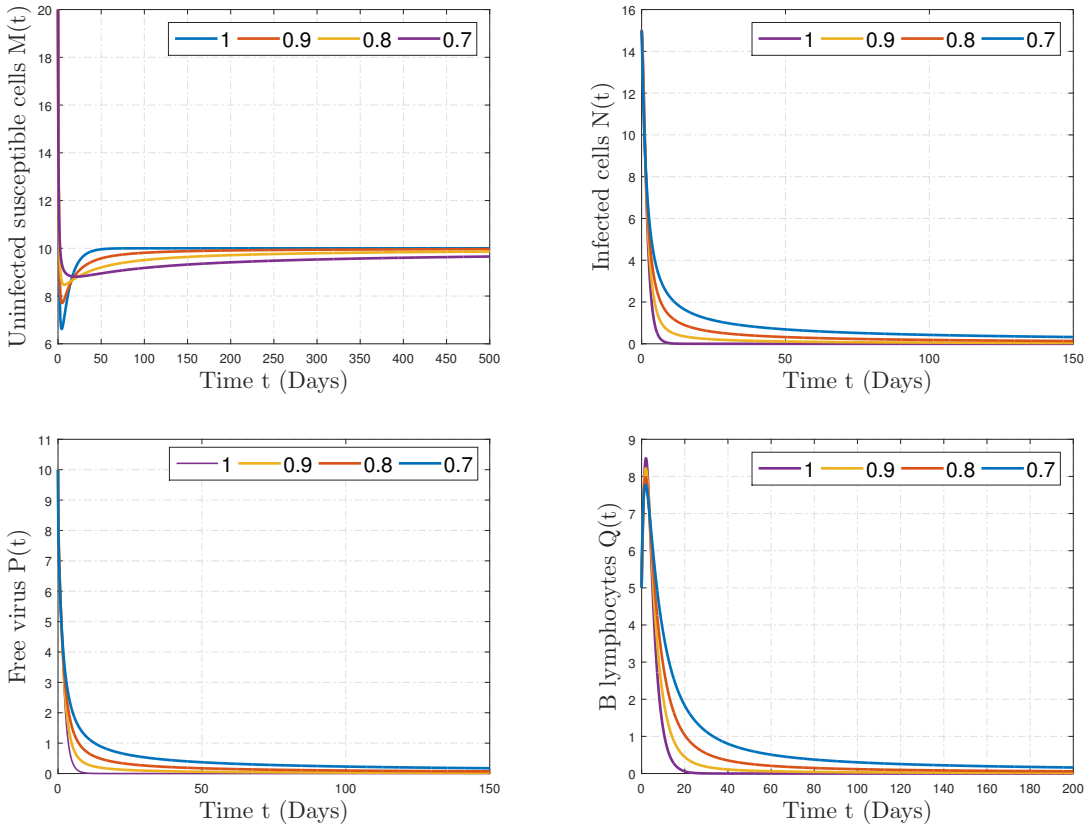

Figure 1. The simulations of model (2) of equilibrium point $\mathcal{G}^\circ$ for different **m** values and $\mathcal{C}_0 = 0.283$

The immunity-free equilibrium stability

We put $\beta_2 = 0.15$ and keeping other parameters values in Table 1, we have $\mathcal{C}_0 = 1.6887$, $\mathcal{C}_1 = 0.6255$ and we remark that all the trajectories of model (2) converge to immunity-free equilibrium

$\mathcal{G}_1^\star$ for different value of **m**. This supports the stability result of $\mathcal{G}_1^\star$ from Theorem 4. Figure 3 display this result. As may be seen from this figure, the antibodies are decreasing toward zero. In contrast, the virus load, infected cells, and uninfected cells all converge toward a strictly positive level.

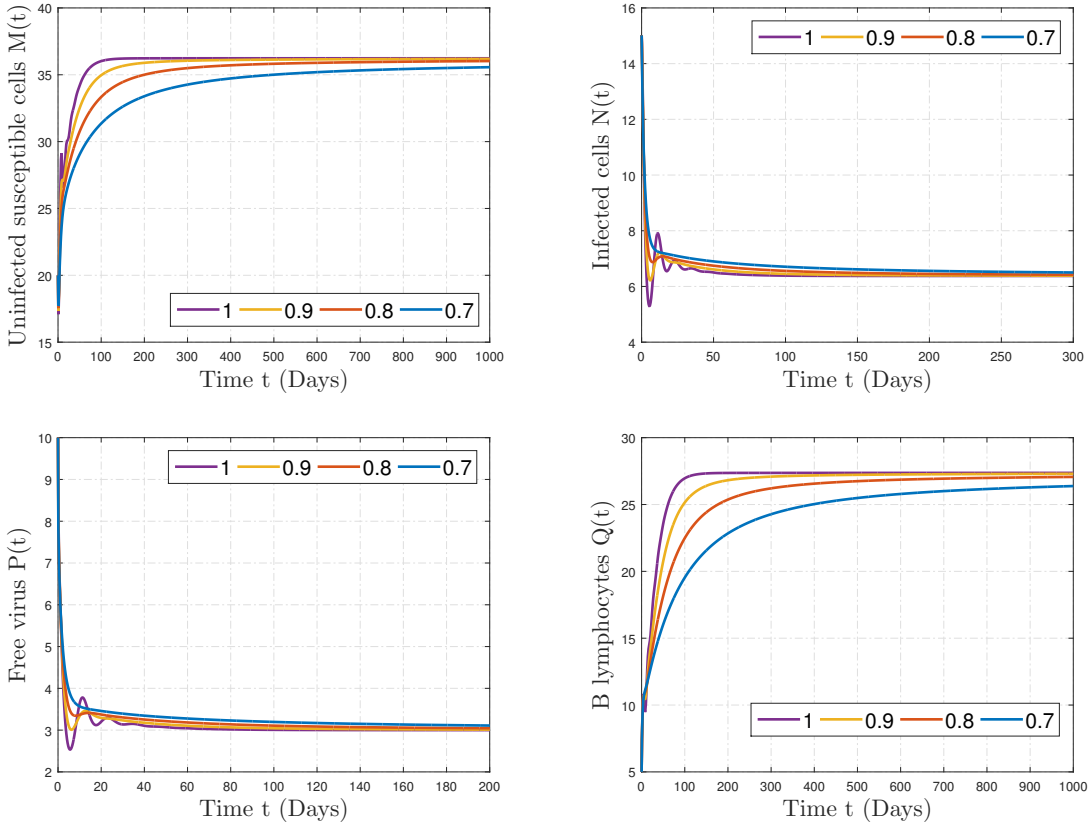

Figure 2. The simulations of model (2) of equilibrium point $\mathcal{G}_2^*$ for different **m** values and $\mathcal{C}_1 = 3.4082$

The immunity-activated equilibrium stability

If $\Lambda = 15$ and keeping other parameters values in Table 1, we have $\mathcal{C}_1 = 3.4082$ and the dynamical behavior of model (2) approaches to immunity-activated equilibrium $\mathcal{G}_2^*$ for different value of **m**. This validates the stability finding given by (i) in Theorem 5. This result is plotted by Figure 2 and Figure 4.

Impact of fractional derivative

We now investigate the impact of fractional derivatives on the infection dynamics. The thing that catches our attention, in all of this numerical research, is that as the value of the fractional-order **m** decreases, which defines long-term memory behavior, the solutions quickly reach steady states. That is, the rate of convergence decreases as the fractional order is closer to one. Thus, the convergence speed increases proportionally with the order. But, in all cases, solutions with different values of **m** reaches steady states. Consequently, the fractional order **m** impacts the time it takes to attain steady states but has no effect on the stability of the equilibria.

The sensitivity analysis

Now, we discuss the impact of some parameters on the dynamics of model (2). According to the formula of the basic reproduction number $\mathcal{C}_0$, we notice that $\mathcal{C}_0$ is increasing greater than one with if one of the values of the parameters $(\beta_1, \beta_2, \theta, \Lambda)$ is increase. Otherwise, $\mathcal{C}_0$ is decreasing less than one when one of the values of the parameters $(\sigma, \mu_2, \mu_1, \mu_3)$ is increasing (see Figure 5).

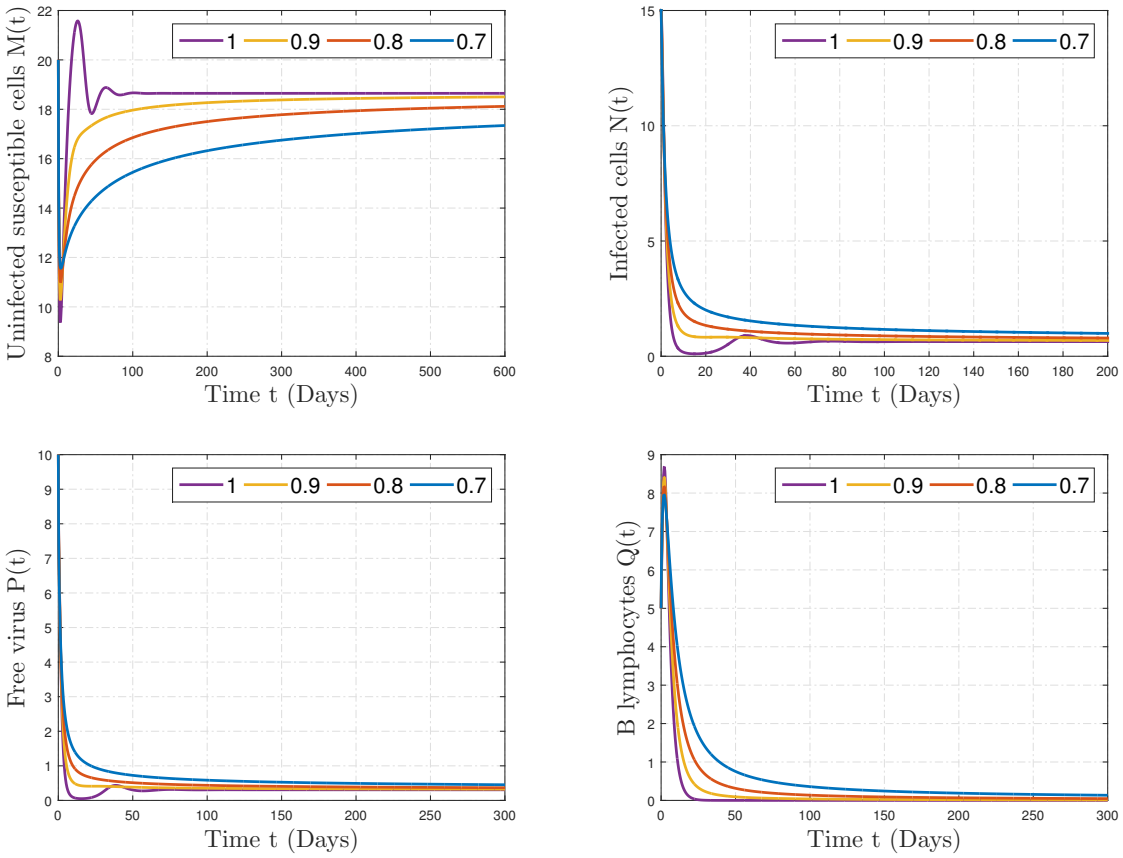

Figure 3. The simulations of $\mathcal{G}_1^\star$ in model (2) for different **m** values and $\mathcal{C}_0 = 1.6887$, $\mathcal{C}_1 = 0.6255$

6 Conclusion

We have introduced and examined a fractional-order viral model including cell-to-cell transmission in this work. In this model, both lytic and non-lytic immune responses have been taken into account. We have established the suggested viral model's existence, uniqueness, nonnegativity and boundedness. Also, we have arrived at two threshold parameters: the basic reproduction number $\mathcal{C}_0$ and the reproduction number of the humoral immunological response $\mathcal{C}_1$. The obtained results indicate that the infection level gets reduced to zero for $\mathcal{C}_0 < 1$, whereas the infection persists in the host body for $\mathcal{C}_0 > 1$. Based on Routh-Hurwitz's judgment, we have derived the requirements for the local asymptotic stability of the equilibria. LaSalle's invariance principle and Lyapunov functionals are used to generate adequate conditions that can guarantee the system's global asymptotic stability. Finally, a numerical simulation has been used to evaluate the outcomes of our theoretical work and we have performed a sensitivity analysis of threshold parameter $\mathcal{C}_0$, see Figure 5. It can be observed that with lower values of **m**, the components of our system converge to equilibria more quickly. However, large values of **m** result in much slower convergence and longer memory, see Figure 1, Figure 3 and Figure 2. In our next work, we would like to add

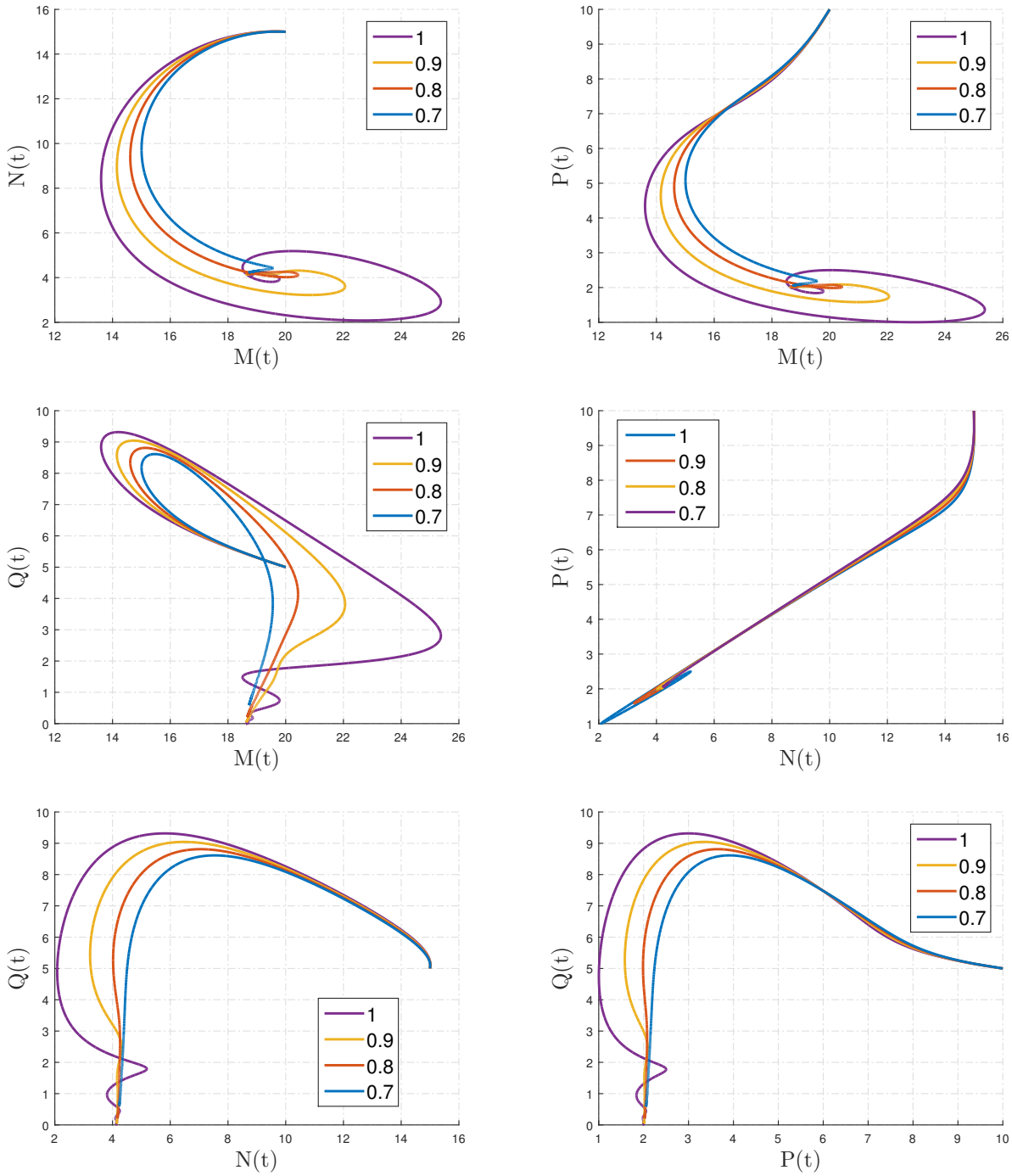

Figure 4. The phase portrait of model (2) for different **m** values with $\mathcal{C}_1 = 3.4082$

the effect of time delays [45, 46], vaccination [47] and stochastic [48, 49] on the dynamics of the suggested model.

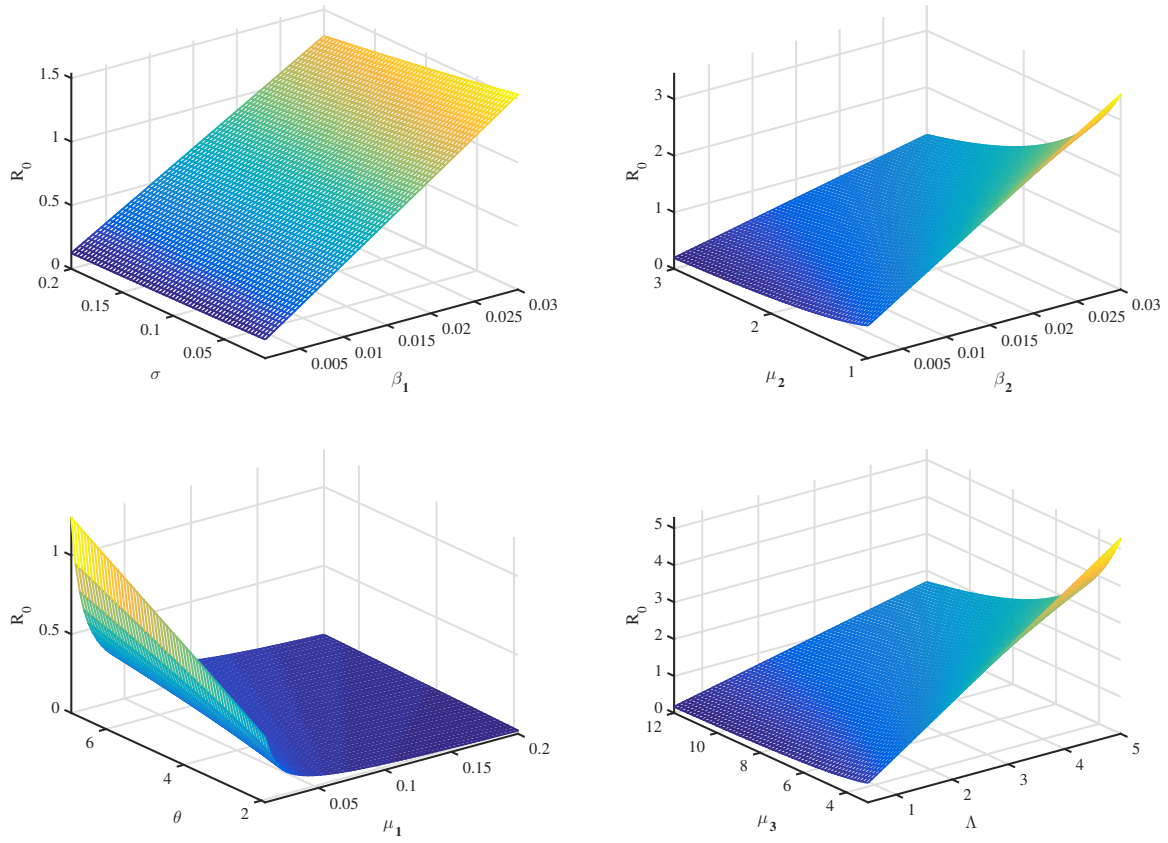

Figure 5. The relationship between $\mathcal{C}_0$ and several parameters

Declarations

Use of AI tools

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

Data availability statement

No Data associated with the manuscript.

Consent for publication

Not applicable

Conflicts of interest

The authors declare that they have no conflict of interest.

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Author's contributions

M.N.: Conceptualization, Formal Analysis, Methodology, Writing-Original draft. A.Z.: Data Curation, Writing-Original draft, Software, Validation. A.M.: Data Curation, Writing-Original draft, Software, Validation. Y.S.: Visualization, Investigation, Writing - Review & Editing. M.Y.: Supervision, Validation, Writing - Review & Editing. The authors have read and agreed to the published version of the manuscript.

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