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Stochastic probical strategies in a delay virus infection model to combat COVID-19

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Abstract

In disease model systems, random noises and time delay factors play key role in interpreting disease dynamics to comprehend deeper insights into the course of dynamics. An endeavor to forecast intercellular behavioral dynamics of SARS-CoV-2 virus via Infection model with responsive host immune mechanisms forms the crux of this research study. Incorporation of time delay factor into infection transmission rates in noisy system epitomizes spectacular view on internal viral dynamics and stability properties are rigorously analyzed around equilibrium steady states to probe feasible strategies in mitigating rapid spread. Efforts to perceive inocular view on infection dynamics are not limited to theoretical frontiers but are substantiated with empirically simulated outcomes and visualized as graphical upshots. Discussions on numerical investigations emphasized shorter incubation periods and vaccination at pertinent time intervals to restrain massive spread and exhibit total immunity against SARS-CoV-2 infections.

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1. Introduction

Mathematical modeling techniques are reliable mechanisms widely adopted by researchers [1–4] to develop frameworks in tackling environmental crises efficiently. Mathematical model structures and their analytical techniques have capitulated research interests of numerous biological scientists as they bestow them liberty to experiment without any direct species interaction yet furnishing exquisite results in compliance with experimental outcomes. Researchers rely on model methodologies as they evolved as indispensable tools to augment perspicacity into dynamics of crises and serve as vital exemplary artificial platform to analyze the dynamics in longer run at both ecological [5–7] and epidemic frontiers [8–11].

In epidemiological discipline, research studies on viruses have captured interests of many researchers transcending centuries. Virus species are significant inhabitants in epidemic clusters with competency to convulse the universe as a consequence to minuscule inopportune impetuous action in exercising control (as witnessed in contemporaneous COVID-19 pandemic) and thereby, engraving the evolution of distinct discipline coined as “Virology”, emphasizing their imperative role in effectuating biological disasters that may culminate in ecological imbalances.

Even though literature is stocked with abundant works on viral dynamics [12–19], revamping research explorations coping up with contemporary situation becomes inexorable as new viruses emerge with increased intricate behaviors (like highly contagious SARS-CoV-2 virus) or mutant variants of surviving members in viral cluster behave with augmented virulence and drag in precarious lethal complications.

Research executions in this article focuses on analytical explorations to presume the internal viral dynamics of contemporary SARS-CoV-2 virus causing COVID-19 infections to expound deeper dynamical perspectives as an attempt to avert severe life threats therein. An amalgamation with mathematical perspectives on model structure of SARS-CoV-2 virus in this study, intended to analyze internal viral dynamics is conceivable with a profound concise account on its biological aspects and thus follows imminently.

SARS-CoV-2 is a dreadfully contagious positive sense single stranded RNA virus making its host entries prominently via nasal cavities whilst imprinting cell entry by binding with alveoli ACE2 receptors with spike proteins. Proteolytically activated by proteases, they adapt structural changes to fuse with host cell to complete their reproductive cycle and merge with cell oil membrane to replicate their genomie RNA by deploying cell machinery to cause secondary infections by releasing newly produced free virus.

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particles. Misconstrued by host immune mechanisms as RNA synthesized by host cell DNA, they exit cell through lysosomes and de-acidify them to inhibit their immune actions afterward. Thus, the confounding sneaky nature of SARS-CoV-2 viruses make them un-traceable by immune systems and expedite rapid infection spread within shorter time span as witnessed via their incubation period estimations, approximated to be around 3 – 14 days.

Clinical studies on COVID -19 infections efforts to spotlight the behavioral pattern of SARS-CoV-2 viruses and consequential lethal ramifications in human beings. Based on those reminiscences, it has been perceived that COVID -19 disease may trigger respiratory tract infection affecting upper respiratory tract (sinuses, nose and throat) or lower respiratory tract (windpipe or trachea and lungs), progressing towards dementia, encephalitis, vascular disorders, pneumonia, septic shock at advanced infected stages and death at ultimate end due to cytokine release syndrome or cytokine storm (Appendix) that may damage organs apparently by killing tissues in massive accorde. Inspite of lethal complications exerted by SARS-CoV-2 infections, many infected individuals are cured despite lacking specific medicines or treatment methodologies kindling curiosity in researchers and scientists. As an addendum, certain cases reportedly tend to transmit infection actively in the community devoid of symptoms but continue to exhibit healthy behavior despite infection persistence, leaving an interesting note in viral dynamics of SARS-CoV-2 virus.

Many researchers and immunologists have pooled literature with works ever since its inception in pandemic cluster [20-26] emphasizing various dynamical perspectives of COVID-19 infections with statistical data to foresee progressions of infection dynamics over course of time and effort to enunciate behavioral characteristics like pattern of infection spread [27], feasible strategies to restrain epidemic outbreaks [28,29] etc at host indi
dividual level. Even then, the investigatory results excerpted from those studies are ambiguous pertaining to noise factors viz., variations in seasons, geographical locations, behavioral attitude and genetic variations among host population etc that may stimulate, aggravate or sublimate the spread in wider scale and are enigmatic on global accord to curb massive spread as every natural phenomenon is an element of uncertainty and random fluctuations play inevitable role in dynamics of environmental systems [15,30,31]. However, such encumbrances can be vanquished by executing stochastic probes on internal viral dynamics of SARS-CoV-2 virus to presume dynamical progressions exclusively with precision and expedite feasible control strategies with futuristic perspectives.

In literature, very few studies [32,33] have thrown light on intercellular behavioral aspects of SARS-CoV-2 virus, wherein Kai
hao Liang [33] attempted to repress infection spread with definitive comparative account on SARS and MERS infections whilst Rihan et al. in [32] effortted to apprehend qualitative studies with immunological perspectives using fractional order delay model. Thus, a qualitative analytical account to probe internal viral dy
namics of SARS-CoV-2 virus with noise perturbations is yet un
der developmental stage and our research executions attempt to explore infection progression dynamics of SARS-CoV-2 virus with noise effects. Dynamical probes in model system inevitably evolv
ing around their past states is widely acknowledged and concerning epidemiological studies, exquisite realistic dynamical expounds are achieved by executing analytical explorations inclusive of past states as time delay incorporation τ in model systems, render interesting exemplifications as seen in the works of [34-36].

Thus, in forthcoming sections, we make a novel endeavor to ex
empify qualitative analysis on infection dynamics of SARS-CoV-2 virus at intercellular level to mitigate rapid spread and infer defini
tive feasible control strategies to repress epidemic outbreaks, with modeling technique that amalgamates both noise and time delay impacts in unison from an existing viral model structure.

Since, disease dynamics in infected individuals are repercussions of their intercellular behavior, dynamical perspectives on host cells can interpreted from infection dynamics of infected indi
viduals. As propensity of infection progression on infection trans
mission rates is evident in any disease dynamics, peculiar behav
ior observed in SARS-CoV-2 infections expounds disparity and in
vestigatory research studies on COVID-19 infection propounded ineluctable role of incubation periods in SARS-CoV-2 infections. Mo
tivated by above factual interpretations, a novel endeavor is con
trived in this article to interpret minuate dynamical perspectives of SARS-CoV-2 infection in light of incubation periods via infec
tion model with responsive host immune system and probe feasibl
est strategies to mince infection spread irrespective of any preced
ing encumbrances.

1.1. Model description

In this section, we elaborate biological viability of model structure to explicate its compliance with SARS-CoV-2 infection prospects followed by mathematical perspectives.

Even though, behavioral patterns of SARS-CoV-2 infections are confounding, immune actions deployed by host immune system attempts to effectuate instantaneous evasion of further infec
tions. Henceforth, we consider virus infection model developed by Wodarz et al. in [37] to demonstrate roles of Lytic and Non-Lytic components of immune system as presented below.

\[
\begin{align*}
\frac{d\alpha(t)}{dt} &= \left( \gamma - \mu\alpha(t) - \frac{\beta\alpha(t)\lambda(t)}{1 + q\kappa(t)} \right) dt, \\
\frac{d\lambda(t)}{dt} &= \left( \frac{\beta\alpha(t)\lambda(t)}{1 + q\kappa(t)} - \alpha(t) - p\lambda(t) \right) dt, \\
\frac{d\kappa(t)}{dt} &= (\alpha(t) - b\kappa(t)) dt \\
\end{align*}
\]

Here, \(\alpha(t)\) represents cell population that are at risk of contracting infection viz., susceptible cells in respiratory tracts, alveoli, artery walls etc at time \(t\), whereas \(\lambda(t)\) attempts to delineate salient characteristics of infected cells at time \(t\). Abridging facts on life span of host cells, susceptible cells suffer natural death at the rate of \(\mu\alpha(t)\) and infected cell population decays naturally at the rate of \(\alpha\lambda(t)\) herein.

Comprehensive research studies on immunology evidences that entry of pathogens in host cell will be attenuated and discarded with pervasive forthwith immunity actions by host immune sys
tem either by adaptive or innate immune mechanisms and thus, \(\kappa(t)\) characterizes total immunity evoked in response to infection at time \(t\). Immune systems in host tend to exhibit responsive ac
tions against antigens by inhibiting replication of pathogenic gen
etic material and killing infected cells with simultaneous perforce. Wodarz et al. modeled this Non-Lytic activity as \(1 + q\kappa(t)\) with strength \(q\) to inhibit active replication of virus and Lytic actions at rates \(p\lambda(t)\) with efficacy \(p\) to evade infected cells. As im
mune responses tend to exhibit strengthened behavior with infec
tions mounting over time, we suppose that total immunity \(\kappa(t)\) gets stronger at rates proportional to the strength of infected cells \(\alpha\lambda(t)\) and decay at rates proportional to its current strength \(b\kappa(t)\).

As the incubation period in SARS-CoV-2 infections are approxi
mated to be around 3 – 14 days, viral reproductive cycle begins lesser than 2 days of infection, thereby accelerating productivity of new free virus particles to cause secondary infections in host cells at much faster pace than causing primary infection and thus, the free virus dynamics has not been included explicitly in system (1), allowing to make a quasi steady state assumption to proportionate free virus quantity to infected cell population, wherein latter can be concurred as viral load measure.

In disease dynamics, infection transmission rates play conspicuous role in admitting different contexts to course of infection dy-
namics [38] and susceptible cells contract infection either by direct contact with infected cell or by free virus particles born out of secondary infection through cell metabolic activities, thus facilitating active infection transmission.

Considering SARS-CoV-2 infections, virus particles establish symbiotic relationship with host cells exhibiting stronger immunity by exploiting cell resources to promulgate production of free virus particles, transforming them into viral reservoirs yet leaving the cell metabolic activities undisturbed. On contrary, SARS-CoV-2 virus exhibits behavioral differences with cells possessing weaker immunity and such cells are victimized by depleting cell resources completely that ultimately lead to cell death even prior to immune activity whilst SARS-CoV-2 virus attempting to conceal them as natural cell death. Even though, cells with strong immunity are unaffected by virus, they betoken rapid infection spread as active virus reservoirs transmitting infections and since, untraceable con founding nature of SARS-CoV-2 virus complicates immune activities of host, efforts attenuated to inhibit viral replications eversonce infection will be a judicious move.

Thus, compendious interpretations on infection transmission pattern of SARS-CoV-2 virus necessitates a specific type of nonlinear infection transmission rate emphasizing inhibition of free virus productivity to curb further infection spread within host cells and takes the form \( \frac{dN(t)}{dt} = \lambda(t)N(t) - a(t)N(t) - b(t)N(t) \) in model structure to probe feasible strategies to detain massive spread in shorter time period wherein infected cells are assumed to actively transmit infection at the rate of \( \beta \). As clinical studies executed to understand intricate behavior of SARS-CoV-2 infections asserts cure of infection in host individuals despite lack of specific chemotherapy, model system (1) tend to comply with internal viral dynamical standards of SARS-CoV-2 virus. Even then, a vacuum space in model structure is deliberate inspite of its efforts to evince dynamical perspectives of SARS-CoV-2 infections as noise factors like variations in susceptibility and discrepancies in immune levels of host cells, the risk to life aggravated by other infections like chronic kidney disease, coronary artery disease, diabetes etc play crucial role in infection dynamics whilst analytical interpretations inferred from model (1) proving futile in this perspective.

1.2. Virus infection model with noise and time delay

Adhering to research studies attempting to contemplate infection dynamics of SARS-CoV-2 by conforming its behavioral adjudicatory with other viruses in corona virus clusters viz., SARS, MERS etc, necessity to designate model structure that may explicate infection dynamics depicted by SARS-CoV-2 is asseverated to bridge such gaps and thus, we encase a model structure from dynamical system (1) as follows.

\[
dx(t) = \left( \gamma - \mu \alpha(t) - \frac{\beta \alpha(t)}{1 + q \kappa(t)} \int_0^h f(\lambda(t-s)) \, ds \right) dt
+ \sigma_1(\alpha(t) - \alpha^*)\dot{w}_1(t),
\]
\[
d\lambda(t) = \left( \frac{\beta \alpha(t)}{1 + q \kappa(t)} \int_0^h f(\lambda(t-s)) \, ds - a \lambda(t) - p \lambda(t) \kappa(t) \right) dt
+ \sigma_2(\lambda(t) - \lambda^*)\dot{w}_2(t),
\]
\[
d\kappa(t) = (c \dot{\lambda}(t) - b \kappa(t)) + \sigma_3(\kappa(t) - \kappa^*)\dot{w}_3(t).
\] (2)

Here, \( \dot{w}_i(t), i = 1, 2, 3 \) are Wiener processes defined on a filtered complete probability space, \( (\Omega, \mathcal{F}) \), with filtration \( \{\mathcal{F}_t\}_{t \geq 0} \), where \( \mathcal{F}_T \) satisfies the usual conditions of right continuity, increasing while \( \mathcal{F}_0 \) contains all the P-null sets and \( \sigma_i, i = 1, 2, 3 \) are noise coefficients with initial conditions

\[
\alpha(\theta) = \varphi_1(\theta), \quad \lambda(\theta) = \varphi_2(\theta), \quad \kappa(\theta) = \varphi_3(\theta),
\]
with \( \theta \in [-\tau, 0) \) and \( (\varphi_1, \varphi_2, \varphi_3) \in C_\mu \) such that \( \varphi_i(\theta) > 0, i = 1, 2, 3 \).

Here, \( C = C([-\tau, 0], \mathbb{R}_+^3) \) is a Banach space of continuous functions mapping from the interval \([-\tau, 0]\) into \( \mathbb{R}_+^3 \) equipped with the norm \( \|\varphi\| = \sup_{-\tau < \theta < 0} |\varphi(\theta)| \).

In addition, we assume the parameters in model system (2) viz., \( \beta, \gamma, \mu, q, a, p, c \) and \( b \) are all positive and noise factors \( (\dot{w}_1(t), \dot{w}_2(t), \dot{w}_3(t)) \) incorporated in system are mutually independent standard Wiener processes of Gaussian- white noise type with stochastic differential equations of system (2) understood in Itô’s sense. Stochastic perturbations techniques adapted in model (2) are standard methods proposed earlier in literature [34] and widely used in many analytical expeditions (see, for instance, [39] and references therein).

Contagious competencies of susceptible cells are high with regard to SARS-CoV-2 infections, as they actively transmit free virus particles by concealing themselves as RNA synthesized by cell DNA and complicate immune activities by astraying immune system in identifying infected cells thereby. Dynamical perspectives inferred from earlier studies on SARS-CoV-2 interpreted that virus entering susceptible cell either attempt to establish symbiotic relationship with cells exhibiting strong immunity or deploy cellular activities of weak victims. In former, they designate host cells as viral reservoirs to initiate secondary infections yet leaving their cellular metabolisms undisturbed and in latter either portray parasitic actions of accelerating cell death instantly after releasing free virus particles even before evoking any immune responses or exhibit abnormalities at time periods when immune actions may prove in vain, thereby hindering host immune actions afterward. Also, it is perceived from immunological studies that strong immune host cells tend to lose their immunity with continued virulent actions within the cell and display weaker immune behavior at later infectious stages.

Acknowledging the fact that host immune mechanisms tend to invade infections only when abnormalities are examined in metabolic activities of cells, the confounding nature of SARS-CoV-2 virus deceives immune actions. Thus, efforts to analyze infection dynamics in view of incubation periods exerted by infected cells will be an appropriate move at this juncture, to expose abnormalities in metabolic activities and their repercussions in infection progressions over time to discover chancy encounters of curing infections at advanced stages of infection, and to reduce risk of aggravating other infections therein.

Equivocally, evoking immune responses against all susceptible host cells will mount risks of killing normal cells and thus, significance of analyzing past state of cell metabolisms in view of their incubation periods becomes inevitable, to exercise responsive immune activities without exerting much damage. Modeling this phenomenon in (2), infection transmission rate took the form

\[
\frac{\beta \alpha(t)}{1 + q \kappa(t)} \int_0^h f(s)\lambda(t-s) \, ds
d\kappa(t) = (c \dot{\lambda}(t) - b \kappa(t)) + \sigma_3(\kappa(t) - \kappa^*)\dot{w}_3(t).
\] (2)

\[
\text{to introspect dynamical perspectives in light of incubation periods.}
\]

Dependence of incubation period on immune levels of infected cells, illustrates that the value of \( \tau \) may not be same for entire population but a distributed parameter over the interval \([0, h] \), \( h \in \mathbb{R}^+ \), the limit superior of incubation time period \( \tau \) in infected population. Thus, infection transmission rate \( \frac{\beta \alpha(t)}{1 + q \kappa(t)} \lambda(t - \tau) \) can be mathematical interpreted in the form as below

\[
\frac{\beta \alpha(t)}{1 + q \kappa(t)} \int_0^h f(\tau)\lambda(t-\tau) \, d\tau,
\]
where \( f \) is a non-negative, continuous distribution function of incubation periods \( \tau \) among the infected population such that

\[
\int_0^h f(\tau) \, d\tau = 1, \quad \int_0^h \tau f(\tau) \, d\tau < \infty
\] (4)
depiecting clear indications on positivity of infection transmission rates such that whenever the value of $1 + q_k(t)$ exceeds $\beta \alpha(t)$, the infection dies out gradually, reflecting infection-free dynamics. Here, active replication of virus is inhibited by immune system at the rate of $1 + q_k(t)$ while distributed time delay factor analyzes infection dynamics based on incubation period of virus to decrease the viral productivity and evade lethal risk factors. Hence, this model can be identified with those models developed to study SARS-CoV-2 dynamics.

In view of SARS-CoV-2 infections, significance of noise factors in each compartment of model system (2) are equivocal, and hence, we effectuate analytical exemplifications by analyzing their stochastic proportionality to deviations from equilibrium steady states, the key parameters in determining stability thresholds of any dynamical system. On similar lines, model structure (2) admits equilibrium steady states of two types viz., infection-free dynamics ($\alpha_1, \lambda_1, \kappa_1$) and positive endemic equilibrium ($\alpha^*, \lambda^*, \kappa^*$) which are assumed to be directly proportional to noise factors of model (2) and are given by

$$\alpha^* = \frac{(\alpha + p\alpha^*)(1 + q_k\alpha^*)}{\beta} = \frac{b\alpha'(1 + q_k\alpha^*)}{c\mu + (b\beta + c\mu)\alpha^*},$$

$$\lambda^* = \frac{bc^*}{c},$$

$$\kappa^* = \frac{-(pc\mu + ab\beta + ac\mu q)}{2(bpc\beta + c\mu pq)}$$

$$+ \sqrt{\left(pc\mu + ab\beta + ac\mu q\right)^2 - 4p\left(b\beta + c\mu q\right)(ac\mu - cy\beta)}.$$  \hspace{1cm} (5)

which is also a positive solution to system (1).

Here, equilibrium steady states are interpreted as non-negative in the sense of infection-free dynamics and positive in endemic steady states, thereby characterizing the existence of infection persistence in model (2).

With these interesting notions on SARS-CoV-2 infection dynamics, the rest of research executions are organized as follows: Following a brief note on SARS-CoV-2 infection dynamics and elaborate deliberation on model structure in section 1, an analytical forecast on dynamical perspectives of internal viral characterizations of SARS-CoV-2 virus is spotlighted in section 2. Analytical interpretations excerpted from section 2 are empirically substantiated with simulation techniques and visualized as graphical upshots in section 3 to render compendious account on salient features of SARS-CoV-2 infection dynamics in comparison with other modeling techniques and thereby effort to assert model system (2) as best fit.

Empirical substantiations are discussed in brief to contemplate its conformity with real dynamical phenomena and research executions are concluded with futuristic directions of study in section 4. An assiduity has been taken to place necessary requisites of study in Appendix as not to interrupt conceptual flow.

2. Model analysis

We begin our analytical investigations in this section by checking the biological viability of model system (2) after incorporating noise and time delay factors. As we deal with biological phenomena, it is significant to study the behavioral effects aftermath random perturbations for its compliance with investigation process (positivity) or adverse reactions. Hence, we infer these by inquiring the existence of unique positive global solutions in the consecutive section.

2.1. Existence of unique global solution

In this section, we attempt to identify suitable phase portrait in which unique positive solution to system (2) exists via following theorem.

**Theorem 1.** For any initial value $(\alpha(0), \lambda(0), \kappa(0)) \in \mathbb{R}^3_+$, model (2) admits a positive solution given by $(\alpha(t), \lambda(t), \kappa(t))$. \forall t \geq 0 which is unique globally and will remain in $\mathbb{R}^3_+$ with probability 1 viz., $(\alpha(t), \lambda(t), \kappa(t)) \in \mathbb{R}^3_+$, $\forall t \geq 0$ almost surely (a.s).

**Proof.** The proof of this theorem traces similar ideas as in [40] and thus, omitted here for precision.

A detailed study on existence of unique global solution to stochastic version of (2) can be found in [30]. \hspace{1cm} □

Next, we analyze the system (2) by adapting mathematical analogies in [39,41]. For deliberate studies, one can refer the works in [42–44].

Firstly, we centralize the system (2) around equilibrium steady states by substituting $u_1 = \alpha(t) - \alpha^*$, $u_2 = \lambda(t) - \lambda^*$, $u_3 = \kappa(t) - \kappa^*$. Take

$$Q(t) = \frac{2\kappa^2(t)(1 + q_k\kappa^*)^2 + qu_3(t)(1 + q_k\kappa^* + qu_1(t))}{q(1 + (\kappa^* + 1)\kappa^* + 1 + q_k(\kappa^* + q_k^*)^2)} > 0$$

and

$$I(u_2) = \int_0^b f(s)u_2(t - s)ds$$  \hspace{1cm} (6)

to rewrite model system (2) in the following form:

$$u_1(t) = -\mu u_1(t) - \frac{\beta u_1(t)}{1 + q_k\alpha^*}I(u_2) - \frac{\beta \alpha^*}{1 + q_k\alpha^*}I(u_2) + \beta \alpha^* Q(t)I(u_2) - \frac{2\beta \kappa^2 u_1(t)}{q(1 + (\kappa^* + 1)\kappa^* + 1 + q_k(\kappa^* + q_k^*)^2)}I(u_2) - \frac{2\beta \alpha^* \kappa^2}{q(1 + (\kappa^* + 1)\kappa^* + 1 + q_k(\kappa^* + q_k^*)^2)}I(u_2)$$
stability with M.

\[ u_2(t) = \frac{\beta u_1(t)}{1 + q\kappa^*} - \frac{2\beta\lambda^* u_1(t)}{q(1 + (\kappa^* - 1) + 2u_3\kappa^*)} \]

Then from the above system, we have

\[ u_1(t) = a_{11}u_1(t) - \frac{\beta u_1(t)}{m} (t) - \frac{2\beta\kappa^* u_1(t)}{q(1 + (\kappa^* - 1) + 2u_3\kappa^*)} (t) + Q(t)u_1(t) \]

\[ u_2(t) = a_{21}u_1(t) + a_{22}u_2(t) + \frac{\beta u_1(t)}{m} l(u_2) + \frac{2\beta\kappa^* u_1(t)}{q(1 + (\kappa^* + 1)(\kappa^* - 1) + 2u_3\kappa^*)} l(u_2) \]

Where \( m = 1 + q\kappa^* \) and

\[ a_{11} = -\mu - \frac{\beta\lambda^*}{m}; \quad a_{12} = 0; \quad a_{13} = 0; \]

\[ a_{21} = \frac{\beta\lambda^*}{m}; \quad a_{22} = -a -pk^*; \quad a_{23} = -p\lambda^*; \]

\[ a_{31} = 0; \quad a_{32} = c; \quad a_{33} = -b. \]

Thus, stability of equilibrium point of system (7) is equivalent to zero solution of system (8) is clear from [39] and tracing those ideas, we linearize system (8) by neglecting non-linear terms and is given in following form,

\[ v_1(t) = a_{11}v_1(t) - \frac{\beta\alpha^*}{m} l(v_2_1) + \sigma_1v_1(t) \]

\[ v_2(t) = a_{21}v_1(t) + a_{22}v_2(t) + a_{23}v_3(t) + \frac{\beta\alpha^*}{m} l(v_2_3) \]

2.2. Stability Analysis

Stability analysis of system (2) is propounded with ideologies adapted from works of Shaikh et al. [41] in this section. By identifying stability thresholds for SARS-CoV-2 infections, we attempt to presume the progression of infection dynamics around equilibrium steady states viz., feasible conditions expounded to evade infections in host cells either to harmless levels such that their presence in minuscule will not generate any abnormalities in health of individuals (infection persistence) or attaining completely infection - free state such that any possibilities of reinfections will be attenuated instantaneously by host immune mechanisms to ensure total immunity against SARS-CoV-2 infections throughout life span of infected individual.

\[ v_3(t) = a_{31}v_2(t) + a_{32}v_3(t) + a_{33}v_3(t) \]

with initial conditions given by (3). We see that the non-linear system (8) has non-linearity higher than 1, hence the sufficient conditions for asymptotic mean square stability of the zero solution of the linear system (8) are sufficient conditions for stability in probability of the zero solution of the non-linear system (10) and henceforth are sufficient conditions for stability in probability of the equilibrium solution of system (7).

We establish this idea of analyzing stability behavior in the following section.
In this section, we begin our execution for stability perspectives by rewriting system (10) in the form
\[ \dot{v}(t) = Av(t) + B(v(t)) + \sigma(\nu(t))\dot{\nu}(t). \] (11)
where, \( \nu(t) = (v_1(t), v_2(t), v_3(t))^T \); \( w(t) = (w_1(t), w_2(t), w_3(t))^T \);
\[ B(v_1) = \left( -\frac{\beta a_s}{m} I(v_2), \frac{\beta a_s}{m} I(v_2), 0 \right)^T, \]
to get sufficient conditions for asymptotic mean square stability of the zero solution of the system (10).

Proceeding with the construction of Lyapunov functional as discussed in [39,41] for stability investigation of system (11), we consider the auxiliary equation without memory (i.e., without delay terms as below)
\[ \dot{g}(t) = Ag(t) + \sigma(g(t))\dot{\nu}(t) \] (13)
By Routh-Hurwitz criterion, the zero solution of the system (13) without randomness, is asymptotically stable if
\[ a_0 > 0, \Delta_1 = a_1 > 0, \Delta_2 = \frac{a_1 a_0 - a_1 a_2}{a_1} > 0; \]
where
\[ a_0 = m, a_1 = \beta \lambda + m(a + b + pk + \mu), a_2 = (\beta \lambda + m\mu)(pk + a + b) + m(bpk + ab + cp\lambda), a_3 = (\beta \lambda + m\mu)(bpk + ab + cp\lambda) \]
are coefficients of the characteristic equation corresponding to (13) without random factors obtained by solving det(\( A - \gamma I \)) and given by
\[ \gamma^3 + m(\beta \lambda + m(a + b + pk + \mu)) + \gamma^2(\beta \lambda + m\mu)(pk + a + b) + m(bpk + ab + cp\lambda) + (\beta \lambda + m\mu)(bpk + ab + cp\lambda) \].

Thus, the auxiliary system (13) without memory and random factors (i.e.,) the deterministic system satisfy the Routh-Hurwitz stability criterion and we try to substantiate with numerical values excerpted from [30] in support of our theoretical results via following remark.

**Remark 1.** We try to give empirical support to our assertions above by taking parameters values as \( \gamma = 15 \) cells per ml per virion per day; \( \beta = 0.05 \) per ml per day; \( a = 0.8 \) per day; \( \mu = 0.5 \) per day; \( p = 0.04 \) per ml per cell; \( q = 0.007 \) per cell per day; \( b = 0.31 \) cell per per day; \( c = 0.45 \) cell per day. we observe \( a_0 = 1.0413; \ a_1 = 2.1256; \ a_2 = 1.3850; \ a_2 = 0.2855. \)

Thus, the system without delay satisfies Routh-Hurwitz stability criterion. Here,
\[ \text{Tr}(A) = a_{11} + a_{22} + a_{33} \]
\[ = -\mu - \frac{\beta \lambda}{m} - a - pk - b < 0; \]
\[ \text{det}(A) = a_{11}(a_{22}a_{33} - a_{23}a_{32}) \]
\[ = \left(-\mu - \frac{\beta \lambda}{m}\right)[(-a - pk)(-b) - (-p\lambda)(c)] < 0. \]
We see that \( \text{Tr}(A) = -2.0412 < 0 \) and \( \text{det}(A) = -0.2741 < 0. \)

Next, we analyze our model (2) to study the stability behavior around its equilibrium solution by adapting analytical approach in [39]. Biologically, we try to identify thresholds of viral dynamics exhibited by SARS-CoV-2. (i.e.), we attempt to exemplify conditions under which infections may subside partially exhibiting infection persistence in form of endemic dynamics or completely free from infection by attaining infection-free steady states. To begin with this execution, we prove the following lemma.

**Lemma 1.** Let us take \( \delta_i = \frac{1}{2}\sigma_i^2, \) \( \bar{a}_{ii} = a_{ii} + \delta_i; \ i = 1, 2, 3 \) and if
\[ \bar{a}_{ii} < 0; \ i = 1, 2, 3. \] (14)
then the zero solution of the system (13) is asymptotically mean square stable.

**Proof.** Let \( P \) be a positive definite solution of the matrix equation
\[ A^TP + PA + P = -C \] (15)
where
\[ P = \begin{pmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{pmatrix}; \ P_\sigma = \begin{pmatrix} p_{11}\sigma_1^2 & 0 & 0 \\ 0 & p_{22}\sigma_2^2 & 0 \\ 0 & 0 & p_{33}\sigma_3^2 \end{pmatrix}; \ C = \begin{pmatrix} c_1 & 0 & 0 \\ 0 & c_2 & 0 \\ 0 & 0 & c_3 \end{pmatrix} \] (16)
\[ c_i > 0; \ i = 1, 2, 3. \] the matrix \( A \) is as defined in (9) and (12).

Let \( C \) be the generator of (13) and \( V(g) = \sigma(P)g, \) then from (15), we have
\[ Lg = g^T(A^TP + PA + P_\sigma)g = -g^TCg \] (17)
From [39,41], we infer that if the matrix \( P \) is positive definite, then zero solution of (11) is asymptotically mean square stable. Hence, to prove asymptotic mean square stability, it is enough to show \( P \) is positive definite.

To check positive definiteness, we represent matrix equation (13) given by (15) in the following form of equation systems:
\[ 2(a_{11}p_{11} + a_{21}p_{21}) + p_{11}\sigma_1^2 = -c_1; \]
\[ a_{22}p_{12} + a_{11}p_{12} + a_{32}p_{13} + a_{21}p_{22} = 0; \]
\[ a_{33}p_{33} + a_{23}p_{33} + a_{31}p_{31} + a_{21}p_{32} = 0; \]
\[ a_{23}p_{12} + a_{33}p_{13} + a_{11}p_{13} + a_{21}p_{23} = 0; \]
\[
2(a_{22}p_{22} + a_{12}p_{23}) + p_{22}s_2^2 = -c_2; \]
\[ a_{11}p_{21} + a_{22}p_{21} + a_{21}p_{22} + a_{12}p_{31} = 0; \]
\[ a_{23}p_{22} + a_{33}p_{23} + a_{22}p_{23} + a_{22}p_{33} = 0; \]
\[
2(a_{23}p_{23} + a_{33}p_{31}) + p_{33}s_3^2 = -c_1; \]
\[ a_{11}p_{31} + a_{33}p_{31} + a_{21}p_{32} + a_{23}p_{21} = 0; \]
\[ a_{22}p_{32} + a_{32}p_{33} + a_{23}p_{22} + a_{33}p_{22} = 0; \]

From (18), we get
\[
p_{11} = -\frac{c_1 + 2a_{21}p_{21}}{2\bar{a}_{11}}; \]
\[
p_{22} = -\frac{c_2 + 2a_{12}p_{23}}{2\bar{a}_{22}}; \]
\[
p_{33} = -\frac{c_3 + 2a_{23}p_{23}}{2\bar{a}_{33}}. \]

and
\[
p_{12} = -\frac{a_{21}p_{22} + a_{32}p_{12}}{(a_{11} + a_{22})}; \]
\[
p_{13} = -\frac{a_{23}p_{12} + a_{12}p_{23}}{(a_{11} + a_{23})}; \]
\[
p_{23} = -\frac{a_{12}p_{13} + a_{22}p_{23}}{(a_{22} + a_{33})}. \]

Next, by substituting \( p_{13} \) and \( p_{22} \) in \( p_{23} \),
\[ p_{23} = \frac{\bar{a}_{22}\bar{a}_{23}a_{c_1} + \bar{a}_{33}a_{23a_2}}{2(\bar{a}_{22}\bar{a}_{23}(a_{12} + a_{23}) - a_{23}a_{22}(a_{22} + a_{33}))} \]
\[ \text{or} \quad p_{23} = \frac{\bar{a}_{22}a_{23a_1} + \bar{a}_{33}a_{23a_2}}{2\bar{Z}_1}. \]

where, \( Z_1 = [\bar{a}_{22}\bar{a}_{23}(a_{12} + a_{23}) - a_{23}a_{22}(a_{22} + a_{33})] \).

Now, subs \( p_{23} \) in \( p_{13} \),
\[ p_{13} = \frac{a_{23}(\bar{a}_{22}a_{c_2} + (a^2_{22} + 2\bar{a}_{23}(a_{11} + a_{22})))p_{23}}{2\bar{a}_{22}(a_{11} + a_{23})(a_{12} + a_{22}) - a^3_{22}}. \]

Subs \( p_{13} \) in \( p_{12} \), we get
\[ p_{12} = \frac{a_{21}a_{23a_2}((a_{11} + a_{33}) + 2\bar{a}_{22}) + c_2a_{23}(a_{11} + a_{33})}{2\bar{a}_{22}(a_{11} + a_{33})(a_{12} + a_{22}) - a^3_{22}}, \]
\[ \text{or} \quad p_{12} = \frac{a_{21}a_{23a_2}((a_{11} + a_{33}) + 2\bar{a}_{22}) + c_2a_{23}(a_{11} + a_{33})}{2\bar{a}_{22}Z_2}. \]

where \( Z_2 = (a_{11} + a_{33})(a_{12} + a_{22}) - a^2_{23} \).

Now, upon substituting \( p_{23} \) in \( p_{22} \), \( p_{33} \), we get
\[ p_{22} = -\frac{c_2Z_1 + a_{23a_1E}}{2\bar{Z}_1\bar{a}_{22}}, \]
\[ \text{where} \quad E = \bar{a}_{23}a_{32a_3} + \bar{a}_{33}a_{23a_2} < 0. \]
\[ p_{33} = -\frac{c_3Z_1 + a_{23a_1E}}{2\bar{Z}_1\bar{a}_{33}}. \]

Upon substitution by (23), \( p_{11} \) becomes
\[ p_{11} = \frac{Z_1Z_2\bar{a}_{22}a_{c_1} + a^2_{21}(a_{23a_1E}(\bar{a}_{23}a_{11}E + \bar{a}_{23}a_{11}E(\bar{a}_{22} + 2\delta_2) + a_{23a_1E}Z_1)) + 2Z_1c_2(a_{11} + a_{33})}{2Z_1Z_2Z_1\bar{a}_{11}a_{22}}. \]

Let us show that \( p_{11} > 0 \), \( p_{22} > 0 \), \( p_{33} > 0 \) for some arbitrary \( a_1, a_2, a_3 \).

We know, \( Z_1 = \bar{a}_{23}Z_3(a_{22} + a_{33}) - a_{23}a_{32}(a_{22} + a_{33}). \) Now,
\[ Z_1 = (a_{22} + \delta_2)(a_{33} + \delta_3)[\bar{a}_{23}a_{11} - a_{23}a_{32}(a_{22} + \delta_2) + (a_{33} + \delta_3)], \]
\[ = a^2_{23}(a_{33} + \delta_3) + a^2_{32}a_{22} + \frac{\det(A)\delta_3}{a_{11}} + \frac{\det(A)\delta_2}{a_{11}} - a_{23}a_{32}(a_{22} + a_{33}), \]
\[ = a^2_{23}(a_{33} + \delta_3) + a^2_{32}a_{22} + \frac{\det(A)\delta_3}{a_{11}} + \frac{\det(A)\delta_2}{a_{11}} - a_{23}a_{32}a_{11} \]
\[ - a_{32}a_{23a_2} - a_{32}a_{23a_3} + a_{11}a_{12}a_{23} \]
\[ = \frac{\det(A)(\bar{a}_{22} + \bar{a}_{33}) + a_{11}(a^2_{22}\delta_2 - 2\det(A))}{a_{11}}. \]
Thus, from (9) and Remark 1, we see $Z_1 < 0$.
Consider $Z_2 = (a_{11} + a_{33})(a_{11} + a_{22}) - a_{23}^2$,

$$
Z_2 = (\text{Tr}(A) - a_{22})(\text{Tr}(A) - a_{33}) - a_{23}^2,
$$

$$
= (\text{Tr}(A))^2 - a_{11}a_{11} - a_{12}a_{22} - a_{13}a_{33} - a_{22}a_{11} - a_{23}^2 - a_{22}a_{33} + a_{22}a_{33} - a_{23}^2,
$$

$$
= (\text{Tr}(A))^2 - a_{11}\text{Tr}(A) + a_{11}^2 - a_{22}a_{33} - a_{33}^2 - a_{22}^2 - a_{23}^2.
$$

(28)

From (9) and Remark 1, we see $Z_2 < 0$.
Thus, $p_{11} > 0$, $p_{22} > 0$, $p_{33} > 0$ as it is evident from (24), (25), (26) and (27), (28) if $\hat{a}_{ii} < 0, i = 1, 2, 3$.
To show $P$ is positive definite, it remains to prove

$$
p_{11}p_{22}p_{33} - p_{12}^2p_{33} - p_{13}^2p_{22} - p_{23}^2p_{11} > 0.
$$

(29)

Substituting respective values, we get

$$
8Z_1^2Z_2\hat{a}_{11}\hat{a}_{22}^2\hat{a}_{33}p_{11}p_{22}p_{33} > -[p_{12}^2(c_1z_1 + a_{23}a_{11}E)(4Z_1^2Z_2\hat{a}_{11}\hat{a}_{22})]
$$

$$
+ [p_{23}^2(Z_1Z_2\hat{a}_{22}c_1 + a_{23}^2a_{11}E(\text{Tr}(A))
$$

$$
+ a_{22} + 2\delta_2)] + 2Z_1c_1(a_{11} + a_{33})(4\hat{a}_{11}\hat{a}_{22}Z_1^2)
$$

$$
+ [p_{13}^2(c_2Z_1 + a_{32}a_{11}E)(4Z_1^2\hat{a}_{11}\hat{a}_{22}Z_1^2)].
$$

Upon substitution and simplification,

$$
p_{11}p_{22}p_{33} - p_{12}^2p_{33} - p_{13}^2p_{22} - p_{23}^2p_{11} = Z_1Z_2\hat{a}_{22}c_1 + a_{23}^2a_{11}E\text{Tr}(A)
$$

$$
+ a_{22} + 2\delta_2 + 2Z_1c_1(a_{11} + a_{33})(4\hat{a}_{11}\hat{a}_{22}Z_1^2)
$$

$$
+ 2a_{23}^2Z_1c_2\text{Tr}(A) - 2a_{23}^2Z_1c_2\hat{a}_{22} > 0.
$$

(30)

From (27), (28) and (30), we proved (29). The proof completes here as the matrix $P$ is positive definite for some arbitrary $c_1 > 0, c_2 > 0, c_3 > 0$. □

We try to render supportive evidences for the above theory via following remark.

Remark 2. From the parameter values as in Remark 1, we get $a_{11} = -0.6952; a_{21} = 0.1952; a_{22} = -0.3060; a_{23} = -0.1626; a_{32} = 0.4505; a_{33} = -0.3100; a_{11} = -0.5702; a_{22} = -0.10356; a_{33} = -0.2900; E = -0.0602; Z_1 = -0.5012; Z_2 = 1.7138; p_{11} = 0.2509; p_{12} = 0.1848; p_{13} = 0.0332; p_{21} = 0.1848; p_{22} = 0.4591; p_{23} = 0.6000; p_{31} = 0.0332; p_{32} = 0.6000; p_{33} = 1.7073.$

We know that for a matrix to be positive definite, Eigen values also should be positive. Eigen values of the matrix $P$ under the assumed parameter values are $0.1516, 0.5909, 1.7115$. Also, we can see the condition (29) is satisfied with value $0.1526 > 0$. Thus, the zero solution of the system (13) is asymptotically mean square stable.

In the follow up process, we try to lit up more analysis on stability in probability (Appendix) of our system (2) by the following theorem.

Theorem 2. If the condition (14) holds and if for some positive constants $c_1, c_2, c_3$, the following condition holds,

$$
\frac{\beta \alpha^*}{m} |p_{12} - p_{11}|y_1 < c_1;
$$

$$
\left(2\frac{\beta \alpha^*}{m} |p_{22} - p_{12}| + \frac{\beta \alpha^*}{m} |p_{12} - p_{11}|y_1^{-1} + \frac{\beta \alpha^*}{m} |p_{23} - p_{13}|y_2^{-1} \right) < c_2;
$$

$$
\frac{\beta \alpha^*}{m} |p_{23} - p_{13}|y_2 < c_3.
$$

(31)

then the equilibrium solution of the system (2) is stable in probability.

Proof. By the methods for constructing Lyapunov functionals in [39], let us consider Lyapunov functional of the form $V = V_1 + V_2$, where $V_1$ is taken as $V_1 = v^TPv_1$ and $v = (v_1, v_2, v_3)^T$. Here, $P$ is the positive definite solution of system (18) with entries as in (19) & (20) and we will choose $V_2$ later. Let $C$ be the generator of system (10). Then by (10) and (18), we have

$$
\mathcal{L}V_1 = 2[v_1p_{11} + v_2p_{12} + v_3p_{13}](a_{11}v_1(t) - \frac{\beta \alpha^*}{m} I(v_2))
$$

$$
+ p_{11}\sigma_1^2v_1^2(t) + 2(v_2p_{22} + v_1p_{12} + v_3p_{23})
$$

$$
\left(a_{22}v_1(t) + a_{23}v_2(t) + a_{33}v_3(t) + \frac{\beta \alpha^*}{m} I(v_2)\right) + p_{22}\sigma_2^2v_2^2(t)
$$

$$
+ 2[v_3p_{31} + v_2p_{13} + v_2p_{23}]p_{32}(a_{32}v_2(t) + a_{33}v_3(t)) + p_{33}\sigma_3^2v_3^2(t)
$$

$$
\mathcal{L}V_1 = 2[v_1p_{11} + v_2p_{12} + v_3p_{13}](a_{11}v_1(t) - \frac{\beta \alpha^*}{m} I(v_2))
$$

$$
+ 2(a_{23}p_{23} + a_{33}p_{33} + p_{33}\delta_3)v_3^2(t) - v_1p_{11}\frac{\beta \alpha^*}{m} I(v_2)
$$

$$
+ p_{11}\sigma_1^2v_1^2(t) + 2(v_2p_{22} + v_1p_{12} + v_3p_{23})
$$

$$
\left(a_{22}v_1(t) + a_{23}v_2(t) + a_{33}v_3(t) + \frac{\beta \alpha^*}{m} I(v_2)\right) + p_{22}\sigma_2^2v_2^2(t)
$$

$$
+ 2[v_3p_{31} + v_2p_{13} + v_2p_{23}]p_{32}(a_{32}v_2(t) + a_{33}v_3(t)) + p_{33}\sigma_3^2v_3^2(t)
$$

$$
+ 2[a_{23}p_{23} + a_{33}p_{33} + p_{33}\delta_3]v_3^2(t) - v_1p_{11}\frac{\beta \alpha^*}{m} I(v_2)
$$

8
Thus, by (4) and (6), we have

\[ 2v_1(t)I(v_2) \leq y_1 v_1^2(t) + y_1^{-1}I(v_2^2), \]
\[ 2v_2(t)I(v_1) \leq v_2^2(t) + l(v_1^2), \]
\[ 2v_3(t)I(v_2) \leq v_3 v_2^2(t) + y_2^{-1}I(v_2^2). \]

(33)

for some positive \( y_1, y_2 \) and using the above inequalities, we get

\[
\mathcal{L}V_1 \leq \left[ \frac{\beta \alpha^*}{m} |p_{12} - 1| |y_1 - c_1| \right] v_1^2(t) + \left[ \frac{\beta \alpha^*}{m} |p_{22} - p_{12}| - c_2 \right] v_2^2(t) \\
+ \left[ \frac{\beta \alpha^*}{m} |p_{23} - p_{13}| y_2 - c_2 \right] v_3^2(t) + r I(v_2^2),
\]

where \( r = \frac{\beta \alpha^*}{m} \left[ |p_{12} - p_{11}| y_1^{-1} + |p_{22} - p_{12}| + |p_{23} - p_{13}| y_2^{-1} \right]. \)

(34)

Now, choose Lyapunov functional \( V_2 \) as

\[ V_2 = \int_0^h f(s) \int_{s-\varepsilon}^s v_2^2(\theta)d\theta ds, \]

and from (4) & (6), we get, \( \mathcal{L}V_2 = r(v_2^2(t) - I(v_2^2)). \)

Thus, via (34), we have

\[
\mathcal{L}V \leq \left[ \frac{\beta \alpha^*}{m} |p_{12} - 1| |y_1 - c_1| \right] v_1^2(t) + \left[ \frac{\beta \alpha^*}{m} |p_{23} - p_{13}| y_2 - c_2 \right] v_3^2(t) \\
+ \left[ 2 \frac{\beta \alpha^*}{m} |p_{22} - p_{12}| + \frac{\beta \alpha^*}{m} |p_{12} - p_{11}| y_1^{-1} + \frac{\beta \alpha^*}{m} |p_{23} - p_{13}| y_2^{-1} - c_2 \right] v_2^2(t),
\]

(35)

Thus, as in [41], the zero solution of (10) is asymptotically mean square stable if

\[ \frac{\beta \alpha^*}{m} |p_{12} - p_{11}| y_1 \quad \left( 2 \frac{\beta \alpha^*}{m} |p_{22} - p_{12}| + \frac{\beta \alpha^*}{m} |p_{12} - p_{11}| y_1^{-1} + \frac{\beta \alpha^*}{m} |p_{23} - p_{13}| y_2^{-1} \right) \quad < \quad c_1; \]
\[ \frac{\beta \alpha^*}{m} |p_{23} - p_{13}| y_2 \quad \frac{\beta \alpha^*}{m} |p_{22} - p_{12}| + \frac{\beta \alpha^*}{m} |p_{12} - p_{11}| y_1^{-1} + \frac{\beta \alpha^*}{m} |p_{23} - p_{13}| y_2^{-1} - c_2 \quad < \quad c_2; \]
\[ \frac{\beta \alpha^*}{m} |p_{23} - p_{13}| y_2 \quad < \quad c_3. \]

(36)

From (36), we see that

\[ y_1 < \frac{mc_1}{\beta \alpha^* |p_{12} - p_{11}|} \quad y_2 < \frac{mc_3}{\beta \alpha^* |p_{23} - p_{13}| y_2}. \]

(37)

Thus, if for some positive constants \( c_1, c_2, c_3 \), the condition (31) holds, then there exists \( y_1 > 0 \), \( y_2 > 0 \) such that (37) too hold and so zero solution of system (10) is asymptotically mean square stable and it follows from [39] that zero solution of system (8) is also asymptotically stable. Henceforth, equilibrium point \((\alpha^*, \lambda^*, \kappa^*)\) of system (2) is stable in probability which completes the proof. \( \square \)

In view of theorem above, we have identified thresholds of stability with a general notion and infer that system (2) ensures stability around equilibrium steady states, throwing lights on feasibility of either infection extinction or persistence so that control strategies can be developed in accordance with infection dynamics over time.

In biological terminologies, we have identified infection dynamics thresholds for SARS-CoV-2 infections to portray stable behavior around infection-free state and permanence of infections in the course of dynamics. In alternate words, we have identified conditions under which host cells may either exhibit total immunity against SARS-CV-2 infections by stimulating appropriate anti-viral activity with combined actions of innate and adaptive immunity or leaving some imprints of infection in host cells permanently yet not detrimental has been ensured via the theorem above.
Empirical evidences that strengthens above conditions are given in remark that follows immediately.

**Remark 3.** From 2, we find for the choice of $c_1 = 0.25; c_2 = 0.7; c_3 = 0.2$, with parameter values as in remarks 1, the condition (35) is met for $0.2738 < y_1 < 3.6530; 0.1388 < y_2 < 7.2033$, thereby (34) is negative definite as $\mathcal{L}V \leq -0.1891r^2(t) - 0.0019r^2(t) - 0.1793r^2(t)$.

Biologically, the host cells exposed or at the risk of exposing to infections will show steady dynamics under assumed conditions to promulgate immune actions deployed by host immune system to mitigate infection levels or evade completely.

Analytical perspectives discussed on stability behavior can be given only partial credit hitherto and an comprehensive view on realistic account can be uphold with empirical substantiations to visualize dynamical perspectives ensuring its adherence with reality.

Thus, in forthcoming section, we render empirical support to our theoretical establishments by simulating model system (2) with numerical techniques.

### 3. Empirical support

In this section, we simulate our model (2) using Euler-Theta method as in [45] to encounter the compliance of anticipated internal viral dynamics exhibited by SARS-CoV-2 infections in theoretical ideologies with reality and visualizations are presented via graphs.

Firstly, we discretize system (2) based on the works in [46–52] as follows:

$$\alpha_{n+1} = \alpha_n + \left( \frac{\gamma - \mu}{1 + \theta} \right) \left( 1 - \alpha_n \lambda_{n-N+1} + (1 - \theta) \lambda_{n-N} \right) \Delta W_{1n} + \sigma_1 \left( \alpha_n - \alpha^* \right) \Delta W_{1n}$$

$$\lambda_{n+1} = \lambda_n + \left( \frac{\beta}{1 + \theta} \right) \left( 1 - \theta \lambda_{n-N+1} + (1 - \theta) \lambda_{n-N} \right) - q \lambda_n - p \lambda_n \Delta W_{2n} + \sigma_2 \left( \lambda_n - \lambda^* \right) \Delta W_{2n}$$

$$\kappa_{n+1} = \left( \kappa_n + \frac{c_3 \lambda_n - b \kappa_n}{\theta} \right) \Delta W_{3n} + \sigma_3 \left( \kappa_n - \kappa^* \right) \Delta W_{3n},$$

where $\theta \in (0,1)$ and $\Delta W_{1n} = W_{1(n+1)} - W_{1n}$, for $n \in \mathbb{N}$ and $k = 1, 2, 3$ is the discretized Wiener process and $h$ is the step size.

For simulation purposes, the delay factor $\int_0^T f(s) \lambda(t - s) ds$ has been considered in discrete form as $\int_0^T f(s) \lambda(t - s) ds = \lambda(t - T)$. $T = nh$ and all numerical simulations have been carried out with value of $\theta = 0.5$. The choice of $\theta$ is justified by referring to methodologies in [53] and is omitted here for brevity.

With numerical simulations, we endeavor to portray an incocular view on dynamical perspectives of SARS-CoV-2 virus in following lanes.

- To enunciate behavioral dynamics around equilibrium steady states in light of varying incubation periods.
- To emphasize key role played by noise factors in presuming viral dynamics and visualize impacts of analyzing epidemic dynamics inclusive of factors representing their past states to foresee their progression dynamics.
- To investigate compatibility of system (36) in depicting real dynamical interpretations over other modeling approaches and forecast infection progression over time.
- To probe feasible strategies to mitigate SARS-CoV-2 infections from visualizations representing analytical interpretations.

As incubation periods of SARS-CoV-2 virus are approximated around 3 – 14 days, we attempted to sketch dynamical perspectives with choice of values for $\tau = 3, 5, 9$, and 14 days.

We attempted to effectuate empirical supplements by drawing comparative analytical accounts between model dynamics exhibited by different model structures viz., DDE, SDE and SDDE systems, to render numerical support to discussed theoretical exponents and visualize infection dynamics.

Meticulous efforts have been taken in choosing parameter values such that they depict realistic picture on internal viral dynamics of SARS-CoV-2 virus.

Researchers gravitate their reliance on data from other works in the absence of precise account pertaining to their work and effort to interpret dynamics from them. Adapting the same ideology, we have used numerical data from well established works of other researchers to analyze SARS-CoV-2 dynamics.

The parameter values used in simulations are meticulously chosen from works in [30] such that they give proper manifestations to the mathematical theory discussed earlier.

As compatibility of models in depicting real dynamics is crucial in mathematical analysis, in particular when we rely on data inferred from other research studies and thus, advancing towards numerical investigations of system (38), we begin with check on model compatibility to comply with the criteria of recreating reality in artificial arena.

Biological vulnerability of model (38) is scrutinized by analyzing infection dynamics with different infection transmission rates to emphasize their imperative role in deciding course of dynamics over time. A vivid picture on model compatibility can be explored if infections increases with increase in infection transmission rates.

With this summary, we begin our empirical investigations by examining model compatibility of system (38) with different infection transmission rates $\beta$ as follows.

We tabulate parameter values used in simulating model (38) as below.

#### 3.1. Compatibility of SDDE model (38) with real dynamics

We incline on infection transmission rate $\beta$ to portray model compatibility to ease views on compatibility of system (38) in its compliance with reality in absence of real data values.

#### 3.2. SDDE vs DDE : A comparative analysis

Impacts of noises in delay system are evinced around endemic equilibrium via following graph.

#### 3.3. SDDE vs SDE: A comparative study

In this section, we draw out an analysis with SDE and SDDE model approaches and the outcomes are depicted via figures (4) and (5).

**Dynamics of SARS-CoV-2 virus for permanence in infection-delay impacts**

Research on clinical data studies reveal that infectious effects of SARS-CoV-2 virus in host stay inactive for a maximum period of 14 days only. Thus, we investigated impacts of extending incubation period for 14 days and Fig. 6 represents SARS-CoV-2 viral dynamics around equilibrium steady states.

**Dynamics of SARS-CoV-2 virus around equilibrium solutions for $\tau = 14$.**

Privilege of noise-delay modeling techniques in interpreting dynamical prospects of biological systems is illustrated by simulating system (38) with parameter values taken from [31] in which similar study on viral infections are analyzed with Lévy noises.

**Impacts of delay in SARS-CoV-2 viral dynamics for $\tau = 5$.**

We attempt to ensure observations on infection dynamics sketched with empirical manifestations in following section.
3.4. Observations

We enunciate behavioral dynamics of SARS-CoV-2 virus in host cells around equilibrium solutions based on our empirical investigations in this section. Simulated outcomes of system (38) makes it clear that incorporation of noise and delay in biological systems have great impact on dynamical interpretations. Relying upon empirical evidences, we intend to spotlight following observations and discuss the backing phenomena.

- In Fig. 1, the amicability of model (38) is visualized with choice of different infection transmission rates $\beta$. It is observed that infection transmission increases with increase in $\beta$ values. In epidemic outbreaks, disease spread will escalate with increase in rate of transmission and thus, our model complies with natural phenomenon. Henceforth, we can assert that simulated results of system (38) will befit with the boundaries of reality. We chose $\beta$ rates to trace the compatibility to emphasize our goal in mitigating progress of SARS-CoV-2 infections at intercellular level and effectuate feasible control strategies.

- Figs. 2 & 3 display effects of noises in determining infection progressions of SARS-CoV-2 infections at intercellular level over time with different values of $\tau = 39, 14$. We can examine that curves in figures depicting viral dynamics are smooth upon simulating delay models and erratic in case of noise-delay model simulations asserting natural fact, dynamical system behaviors cannot be smooth and displays advantages of noise-delay analytic approach over delay methodology thereafter.

- Now, next inquisitive is about impacts of delay in a noisy model. Even though noisy models are better modeling approaches to analyze dynamical perspectives of infections, incorporation of delay draws more realism and gives an opportunity to execute investigations on futuristic characteristics of infection. For instance, for small delay values viz., $\tau = 3, 9$, empirical expounds are almost similar with minimum disparity as examined in SDDE vs SDE comparative analysis of (38). However, infection dynamics differs widely for relatively large value $\tau = 14$ and can be witnessed in Fig. 6 forming evidences for effects of delay in noisy models.

- Final set of simulations are carried out with parameter values taken from [31] in which analytic studies are based on Lévy noises in [37] model (a model from which system (2) is formulated) and results viewed in Fig. 7 are evident that our system (38) is better fit in showcasing real scenario.

**Remark 4.** On an interesting note, we can view that our system shows steady dynamics around both infection - free and endemic equilibrium solutions rendering hope that SARS-CoV-2 infections can be curbed if properly treated with care to prevent aggrava-

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**Table 1**

| Parameter | Value |
|-----------|-------|
| $\gamma$ | 15 cells per ml per day |
| $\beta$  | 0.02 per ml per virion per day |
| $q$      | 0.007 ml per cell |
| $p$      | 0.04 ml per cell per day |
| $c$      | 0.45 cell per virion per day |

**Table 2**

| Parameter | Value |
|-----------|-------|
| $\gamma$ | 15 cells per ml per day |
| $\beta$  | 0.05 per ml per virion per day |
| $q$      | 0.007 ml per cell |
| $p$      | 0.04 ml per cell per day |
| $c$      | 0.45 cell per virion per day |

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**Fig. 1.** For the values of $\beta = 0.14, 0.18, 0.22$, the dynamics exhibited by (38) for $\tau = 5$ days upon simulating with parameter values as in [31] $\gamma = 4$. $a = 0.2$, $\mu = 0.4$, $p = 0.05$, $q = 0.01$, $b = 0.1$. $c = 0.0805$, for the initial values $(\alpha_0, \lambda_0, \kappa_0) = (7, 2, 3)$. **Note** In any epidemics, the infection rates are expected to increase with increase in the infection transmission rates and simulated results reveal that our model found to comply with the criteria briefed above and Fig. 1 enunciates it. In forthcoming section, we demonstrate the prominent role of noise factors in deliberating SARS-CoV-2 viral dynamics by simulating system (38) and draw comparative account with DDE outputs.

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A crystalline and panoramic view on the internal viral dynamics of SARS-CoV-2 is showcased by adapting a comparative approach on different modeling techniques existing in mathematical theory and how their manifestations draw realism into the dynamics of epidemic outbreaks.
Fig. 2. The simulations for infection-free equilibrium are carried out with parameter values taken from Table 1 for \( \tau = 3, 9, 14 \).

Thus, we observe that the simulations for infection-free equilibrium are carried out with parameter values taken from Table 1 for \( \tau = 3, 9, 14 \). The left column in each set of graphs represents the simulations for infection-free equilibrium with noise and delay, the middle column represents the simulations for infection-free equilibrium with delay alone, and the right column represents the simulations for infection-free equilibrium with noise and delay.

It is observed that the simulations for infection-free equilibrium are carried out with parameter values taken from Table 1 for \( \tau = 3, 9, 14 \). The left column in each set of graphs represents the simulations for infection-free equilibrium with noise and delay, the middle column represents the simulations for infection-free equilibrium with delay alone, and the right column represents the simulations for infection-free equilibrium with noise and delay.

We discuss the biological interpretations of numerical manifestations and conclude this work on internal viral dynamics of SARS-CoV-2 with some future prospects in consecutive section.
Fig. 3. The parameter values for this simulation are taken from Table 2 with \( r = 3, 9, 14 \). A natural question on effects of delay incorporation in noisy biological models is momentary and thus, we sketch those effects in forecoming analysis.

### 4. Discussions and Concluding remarks with future scope

Ensuing empirical investigations on behavioral perspectives of internal viral dynamics exhibited by SARS-CoV-2 infections in host cells as in aforementioned section, we endeavor to integrate theoretical visualizations with biological perspectives to facilitate crystalline view on the course of viral dynamics exhibited by (38) and its compatibility to analyze COVID-19 infections in this section followed by concluding remarks with futuristic scopes.

We focus our biological interpretations with simulated outcomes drawn from compendious comparative analysis on SDE and SDDE models as noisy model structures with or without delay...
incorporation are acknowledged as better fit in depicting reality of dynamical interpretations than DDE model systems as evinced by Figs. 2 and 3, henceforth, backing up such forms of model structures (2) and (38) as best fits in presuming epidemiological dynamics.

Consecutively, transmission rates are higher in SARS-CoV-2 infections as mode of infection transmission are palpable and straightforward. Viral behaviors of SARS-CoV-2 within host cells are highly complex even though they are cell specific at early stages of infection. Upon attempting to analyze infection progression by extending incubation period of virus by few hours, we examined that impacts in mitigating infection spread are minimal owing to confounding nature of SARS-CoV-2 virus attributing the fact of concealing themselves as RNA synthesized by host cell DNA and exhibit entirely different behaviors even at inactive state.

However, we can visualize those minimal impacts in Figs. 4 & 5 showing promising signs that extending incubation period has positive impacts at permanency in infection but achieving infection - free steady states are arduous as infection spread might have been progressing towards advanced stages with aggravated level of other infections with longer incubation periods. Thus, for small extensions though infections cannot be completely evaded but their levels can be stabilized at certain level thus, immune mechanisms can be deployed to aggravate effective actions against those detectable antigens is evident from Figs. 4, 5.

Time taken to achieve stability by noisy-delay model when compared with noisy approach may lead to conclusions that noisy approach suits as better analytic approach and extending incubation periods shows adverse impacts. In reality, this is not true with COVID-19 infections because in inactive cases, time taken by immune mechanisms of host cells will be more than usual to detect and evade infection and thus, infections will remain for relatively long time in host cells. By extending incubation period, we make efforts to stabilize viral load from spreading infections further. Also, at advanced infection stages, infections from other antigens get aggravated and immune mechanisms need to be strengthened greatly to fight against new aggravations. Hence, infection
levels will remain high despite higher immune actions and cannot be brought down immediately as seen in simulated outputs from noisy models.

For instance, consider visual representations inferred from Fig. 6 wherein achieving infection permanency is rapid as immune mechanisms are attenuated to inhibit viral replication but achieving infection-free state is difficult as infected cells takes more time to display abnormalities in their cellular metabolic activities, thereby failing to heed immune actions in short period.

An imperative assertion shows that immune mechanisms cannot be lethal only to antigens always because over actions deployed by immune systems due to higher infection levels can lyse own cells of host like enunciating cytokine release syndrome as witnessed in SARS-CoV-2 viral infections, augmenting opportunities of susceptible cells being killed by immune actions with increased activities. Also, an over responsive immune action is anticipated in case of SARS-CoV-2 infections as they aggravate other infections in host cells and henceforth, curves representing susceptible cell population remains mostly erratic at both infection states and illustrate much higher erratic behavior when we examine infection-free states with possibilities of re-infections.

Another significant viral dynamics is observed in SARS-CoV-2 infections is that viral dynamics exhibited by model system (38) is almost same when simulations are performed with \( \tau \) values greater than 14 highlighting the apparent natural phenomena of SARS-CoV-2 virus, actively transmitting infection for a maximum period of 14 days and may tend to subside with permeating immune actions from both innate and adaptive immunity by meeting either natural or immune related death thereafter. Thus, an inocular view on internal viral dynamics of SARS-CoV-2 infections are presumed from simulated outcomes of our model (38), sketching anticipated behavior in host cells.

Furthermore, we can observe from simulated outputs of system (38), with increase in infection levels immune responses tend to get stronger in evading infection which is a natural phenomenon in any viral infection, such that SARS-CoV2 infections
can also be minced by immune systems like in cases of cold, flu etc.

Recent reports on COVID-19 infections affirm possibilities of secondary infections in infected hosts by SARS-CoV-2 virus as they undergo mutation like other corona viruses. As World Health Organization (WHO) suggests, persistence of infection in host may take more than 250 days to subside partially and complete eviction cannot be possible in the absence of effective vaccine that may stimulate immune responses against all feasible mutant variants of SARS-CoV-2 virus. Simulated outcomes of our system (38) complying with this assertion can be witnessed from empirical manifestations in aforementioned section.

Thus concluding our research executions on SARS-CoV-2 infections, we emphasize shorter incubation periods to evade infections at early infection stages to avert severe lethal complications thereafter and effective vaccinations at pertinent time intervals to achieve total immunity against future infections. Based on reminiscence inferred from research studies, incubation periods of host individuals as well as host cells play conspicuous role in infection dynamics by exhibiting different behavior and thus, efforts to mince infection spread can be adhered to above assertion as witnessed from our empirical investigations. Also, our endeavors to exemplify behaviors of SARS-CoV-2 virus at intercellular level have depicted optimal results in explicating effects of incubation period to expedite the process of epidemic control and analytical investigations by simulating model (2) is found to comply with clinical data studies carried out previously in this direction.

Summarizing our research executions in this analytical study, we exerted to give an overview on internal viral dynamics of

Fig. 6. Viral dynamics exhibited for $\tau = 14$ around both infection - free and endemic equilibrium solutions for parameter values taken from Tables 1 & 2.
SARS-CoV-2 virus and approximations on effects of chemotherapeutic procedures. However, future works will rely upon in expediting analytical interpretations to identify explicit conditions for extinction of epidemics and analyzing COVID-19 dynamics with similar analytic approaches to probe strategies in developing effective vaccine devoid of any side effects and preventing secondary infections thereby. Furthermore, we aim to pay heed on bringing out a comprehensive analytical account on some explicit factors that may give almost exact information to decide upon type of treatment to be given for different stages of infections coping up with behavioral differences of mutant variants.

Declaration of Competing Interest

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

CRediT authorship contribution statement

M. Pitchaimani: Investigation, Supervision, Data curation, Writing – review & editing. M. Brasanna Devi: Conceptualization, Methodology, Visualization, Investigation, Software, Writing – original draft, Writing – review & editing.

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Appendix

A1

Definition. Cytokine storm or Cytokine release syndrome. The phenomena of flooding blood stream with inflammatory proteins called cytokines is known as Cytokine storm or Cytokine release syndrome. This happens when an infection triggers the immune system of the host and cytokine storm can kill tissue and damage organs.

Definition. Incubation Period. The time taken by host individuals to become infectious and exhibit onset of symptoms in response to infection.

A2

Consider the stochastic delay differential equation of the following type

\[ dx(t) = a(t, x_t)dt + b(t, x_t)dw(t), \quad x_0 = \varphi \in H, \quad (39) \]

where the function \( a(t, x_t) \) is defined in \([t_0, \infty) \times \mathbb{R}^n \) and \( b(t, x_t) \) is an \( n \times m \) matrix.

Let us define \( \{\Omega, \sigma, \mathbb{P}\} \) to be the probability space, \( \{f_s, t \geq 0\} \) be the family of \( \sigma - \) algebras, \( f_s \in \sigma \) and \( H \) be the space of \( f_0 \) adapted functions \( \varphi(s) \in \mathbb{R}^n, \quad s \leq 0, \quad \|\varphi\|_0 = \sup_{s \leq 0} |\varphi(s)|, \quad \|\varphi\|_2 = \sup_{s \leq 0} E|\varphi(s)|^2 \). \( \mathbb{E} \) is the mathematical expectation, \( x_t(s) = x(t+s) \) with \( s \leq 0 \) and \( w(t) \) is an \( m- \) dimensional \( f_t \)- adapted Wiener process.

We assume that \( x = 0 \) is the zero solution of the system (39), \( (i.e.,) \ a(t, 0) = 0, \ b(t, 0) = 0 \) for all \( t \geq t_0 \).

Let \( V : [0, \infty) \times H \to \mathbb{R} \) be a functional defined for \( t \geq 0, \ \varphi \in H \) and generating operator \( L \) is defined by

\[ L\mathbb{E}_t \mathbb{E}V(t, \varphi) = \lim_{\Delta \to 0} \frac{\mathbb{E}_t \mathbb{E}V(t + \Delta, \varphi_{t+\Delta}) - V(t, \varphi)}{\Delta} \]

Here, scalar functional \( V(t, \varphi) \) is defined by \( t \geq 0, \ \varphi \in H \) and \( x(s) \) is the solution of Eq. (39) for \( s \leq t \) with initial function \( x_0(s) = \varphi(s) \).

Let us define a class of functionals \( V(t, \varphi) \) for which the operator \( L \) can be calculated in final form. By reducing arbitrary functional \( V(t, \varphi) \), \( t \geq 0, \ \varphi \in H \) to the form \( V(t, \varphi) = V(t, \varphi(0), \varphi(s), s \leq 0 \), we define the function

\[ V_0 = V(t, \varphi) = V(t, x_t) = V(t, x(t+s)), \quad s \leq 0, \ \varphi = x_t, \quad x = \varphi(0) = x(t). \]

Let \( D \) be a class of functionals \( V(t, \varphi) \) for which function \( V_0(t, x) \) has two continuous derivations with respect to \( x \) and one bounded derivative with respect to \( t \), for almost all \( t \geq 0 \). For functionals from \( D \) the generating operator \( L \) of Eq. (39) is defined and is equal to

\[ L\mathbb{E}_t \mathbb{E}V(t, x_t) = \frac{\partial V_0(t, x)}{\partial t} + a'(t, x_t) \frac{\partial V_0(t, x)}{\partial x} + \frac{1}{2} \text{Tr} \left[ b'(t, x_t) \frac{\partial^2 V_0(t, x)}{\partial x^2} b(t, x_t) \right]. \]

Next we present some definitions and theorems that forms prerequisites to comply with stability theory discussed in the article.
Theorem. The zero solution of the Eq. (39) is said to be mean square stable if for any $\varepsilon > 0$ there exists a $\delta > 0$ such that $\mathbb{E}(\langle x(t) \rangle^2) < \varepsilon$ for any $t \geq 0$ provided that $\|\phi\|_2 < \delta$.

Definition (Asymptotically mean square stable). The zero solution of the Eq. (39) is said to be asymptotically mean square stable if it is mean square stable and $\lim_{t \to \infty} \mathbb{E}(\langle x(t) \rangle^2) = 0$.

Definition (Stable in Probability). The zero solution of the Eq. (39) is said to be stable in probability if for any $\varepsilon_1 > 0$ and $\varepsilon_2 > 0$, there exists $\delta > 0$ such that the solution $x(t) = x(t, \varphi)$ of Eq. (39) satisfies

$$\mathbb{P}\{\|x(t, \varphi)\| > \varepsilon_1\} < \varepsilon_2$$

for any initial function $\varphi \in H$ such that $\mathbb{P}(\|\varphi\| \leq \delta) = 1$. Here, $\mathbb{P}\{}$ is the probability of the event enclosed in braces.

Theorem. Let there exist the functional $V(t, \varphi) \in D$ such that $c_1 \mathbb{E}(\langle x(t) \rangle^2) \leq V(t, \varphi) \leq c_2 \|x(t)\|_2^2$, $\mathbb{E}V'(t, \varphi) \leq -c_3 \mathbb{E}(\langle x(t) \rangle^2)$, $c_1 > 0$. Then the zero solution of the Eq. (39) is asymptotically mean square stable.

Theorem. Let there exist a functional $V(t, \varphi) \in D$ such that $c_1 \mathbb{E}(\langle x(t) \rangle^2) \leq V(t, \varphi) \leq c_2 \|x(t)\|_2^2$, $\mathbb{E}V'(t, \varphi) \leq 0$, $c_1 > 0$, for any function $\varphi \in H$ such that $\mathbb{P}(\|\varphi\| \leq \delta) = 1$, where $\delta > 0$ is sufficiently small. Then the zero solution of Eq. (39) is stable in probability.

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