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# Stationary distribution and extinction in the stochastic model of human immune system response to COVID-19 virus under regime switching

**Marija Krstić, Vuk Vujović, Milica Marković**

**Abstract**

In this paper, in order to study effects of the human immune system response to spread of COVID-19 virus, we establish a stochastic competition model between immune cells and COVID-19 particles by introducing both white and coloured noise. We first prove the existence and uniqueness of the global positive solution of the system under consideration. Furthermore, the stationary distribution and ergodicity of the system are investigated in order to prove weak persistence in mean. We also obtain the conditions for extinction of the disease. The obtained results are related to basic reproduction number of the corresponding deterministic analogue of the system. Finally, we provide numerical simulations with real life data to support theoretical conclusions obtained in the paper.

## 1 Introduction and motivation

Since it first appeared in Wuhan, China, in December 2019, coronavirus pandemic (COVID-19) has spread to more than 197 countries and threatened the health and lives of many people all over the world. Therefore, it was necessary

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to develop treatment methods for such infectious disease in order to prevent and control its further spread.

The pandemic has united the world scientific community in solidarity and sharing knowledge so that effective vaccines could be produced quickly, and now we have vaccines which are available to majority of population. However, the disease is changing rapidly and new strains, for which existing vaccines are not effective, are constantly appearing. Thus, it is important to study the role that immune system may have, by preventing the disease from progressing to the acute phase that may eventually lead to the patient's death. In innate immune system natural killer cells (NK) are considered the primary defence lymphocytes against virus-infected cells. Preliminary studies in COVID-19 patients with severe disease symptoms suggest a reduction in the number and function of NK cells, which results in decreased clearance of infected and activated cells. Restoring the effector functions of NK cells has the potential to correct the delicate immune balance needed to effectively overcome COVID-19 infection. On the other hand, the authors in [7] investigate the role of T-cells in severe COVID-19 disease, protection, and long term immunity. They highlighted that one of the best known recorded symptoms observed in hospitalized COVID-19 patients is lymphopenia in the blood. The absolute number of T-cells, which are part of adoptive immune system, was decreased within all of the studied COVID-19 patients compared to healthy individuals. The decline in T lymphocytes was especially strong within the more severe cases. In hospitalized COVID-19 patients, an increase in the T-cells, was strongly associated with a successful treatment, while no significant increase in T-cell numbers was observed in failed treatments. These observations show that the amount of T cells in the blood is associated with disease outcome. For more details we refer reader to [7] and references cited therein.

In epidemiology and immunology, mathematical models (deterministic and stochastic) are used to understand the dynamics of infectious diseases (see [2], [12]–[15], [17], [18], [22], [23], for instance). Due to the fact that it affected the lives of many people, COVID-19 is, in addition to medical, one of the most dominant topics in mathematical literature, too. Lately, many authors proposed to describe the dynamics of the COVID-19 in terms of standard and stochastic epidemiological models (see [3, 11, 19, 20], among the others).

However, there are few papers that deal with interaction of humans immune system and COVID-19 particles. In paper [6], the authors propose to develop a fractional-order mathematical model for the immune system response to the virus in COVID-19 patients. They consider interaction of the COVID-19 particles ($S$), a cell population of the NK cells ($N$), and a cell population of the cytotoxic (CD8+) T-cells ($T$). The assumptions of the model are: the population of COVID-19 particles in the absence of an immune response

grows logistically; the infected virus can be cleared by both NK and T-cells; the virus promotes an initial activation of NK and T-cells at the beginning of the disease; the total number of NK cells was decreased in patients after some number of encounters with coronavirus particles. Thus, the system of fractional differential equations for representing interactions of the COVID-19 particles and the immune system is given by

$$\begin{aligned} D^{\alpha}S(t) &= a_1 S(t)\,(1-bS(t)) - d_{st}S(t)\mathcal{F}(S,T) - d_{sn}S(t)N(t) - d_1 S(t) \\ D^{\alpha}T(t) &= b_t + r\mathcal{G}(S)T(t) + e_1 N(t)S(t) - qT(t)S(t) - d_t T(t) \\ D^{\alpha}N(t) &= b_n + k\mathcal{G}(S)N(t) - d_{ns}N(t)S(t) - d_n N(t), \end{aligned} \tag{1}$$

with initial condition $S(0) = S_0$, $T(0) = S_0$, $N(0) = S_0$, while $D^{\alpha} = \frac{d^{\alpha}}{dt^{\alpha}}$ is derivative defined in Caputo sense. Function $\mathcal{F}(S,T) = \frac{(T/S)^{\alpha}}{z+(T/S)^{\alpha}}$ represents viral clearance rate of rational form by activated T-cells, while $0 < \alpha \leq 1$ is derivative order, or fractional virus kill power and $z$ is steepness coefficient of virus lysis by T-cells. Also, $\mathcal{G}(S) = \frac{S^n}{c_1+S^n}$ is a modified Michaelis-Menten term for T-cells activation and NK cell recruitment by COVID-19 virus particles, where $n$ represents Michaelis-Menten order, while $c_1$ is steepness coefficient of NK cels recruitment. In this paper we will assume that $n = 2$. Model parameters of system (1) are given in the following table.

| Parameter | Biological interpretation |
|---|---|
| $a_1$ | replication rate of COVID-19 particles |
| $\frac{1}{b}$ | carrying capacity of COVID-19 particles |
| $d_{st}$ | rate of virus lysis by T-cells |
| $d_{sn}$ | rate of virus death due to NK cells |
| $d_1$ | natural death rate of virus particles |
| $d_t$ | natural death rate of T-cells |
| $d_n$ | natural death rate of NK cells |
| $b_t$ | T-cells proliferation |
| $b_n$ | NK cells proliferation |
| $r$ | T-cells activation rate |
| $k$ | NK cells activation rate |
| $e_1$ | recruitment rate of T-cells by virus lysed by NK cells |
| $q$ | inactivation rate of T-cells by virus |
| $d_{ns}$ | inactivation rate of NK cells by virus |

Table 1: Biological interpretation of the parameters of system (1)

All populations in nature are inevitably influenced by environmental interference from factors, such as temperature, radiation, oxygen supply, nutrients, etc. They affect activity of enzymes, and therefore growth of cells and their activation, among other processes related to cell population. Thus, in order to

take influence of random variations into account, we suppose that they affect activation rates of immune cells, and perturb them by linear functions of white noise, i.e. $r \to r + \sigma_1 \dot{w}_1(t)$ and $k \to k + \sigma_2 \dot{w}_2(t)$. On the other hand, depending on the variations in the virus strain, the different virus flow (virus isolation and prevention measures) as well as the degree of immunity of the population, the result of the interaction between the virus and the population may be different. When talking about mutual income, one should take into account the tendency towards seasonal oscillations in the spread of the COVID-19 virus. As the majority of human respiratory viral infections occur in winter, it is expected that the COVID-19 virus will follow this pattern. Also, an increased number of infected people was noticed after the annual holidays, which corresponds to the period of late summer and early autumn. In order to take into account seasonal effect on interaction between immune cell and virus particles, besides the Gaussian white noise, we introduce coloured or telegraphic noise, which will be represented by right-continuous Markov chain $\{\xi(t), t \geq 0\}$, defined on complete probability space $(\Omega, \mathcal{F}, \mathbb{P})$ with the filtration $\{\mathcal{F}_t\}_{t\geq 0}$ satisfying the usual conditions (it is right continuous and increasing, while $\mathcal{F}_0$ contains all $\mathbb{P}$-null sets), independent of Brownian motions $w_1(t)$ and $w_2(t)$ and taking values in a finite space $\mathbb{S} = \{1, 2, \ldots, \bar{M}\}$. Hence, system (1) becomes

$$\begin{aligned}
dS(t) &= \Big[a_1(\xi(t))S(t)(1-b(\xi(t))S(t)) - d_{st}(\xi(t))S(t)\mathcal{F}(S,T) - d_{sn}(\xi(t))S(t)N(t) \\
&\quad - d_1(\xi(t))S(t)\Big]dt \\
dT(t) &= \Big[b_t(\xi(t)) + r(\xi(t))\mathcal{G}(S)T(t) + e_1(\xi(t))N(t)S(t) - q(\xi(t))T(t)S(t) \\
&\quad - d_t(\xi(t))T(t)\Big]dt + \sigma_1(\xi(t))\mathcal{G}(S)T(t)dw_1(t) \qquad (2) \\
dN(t) &= [b_n(\xi(t)) + k(\xi(t))\mathcal{G}(S)N(t) - d_{ns}(\xi(t))N(t)S(t) - d_n(\xi(t))N(t)]dt \\
&\quad + \sigma_2(\xi(t))\mathcal{G}(S)N(t)dw_2(t), \ t \geq 0,
\end{aligned}$$

with initial condition

$$S(0) = S_0, T(0) = T_0, N(0) = N_0, \xi(0) \in \mathbb{S}, \qquad (3)$$

and for any $i \in \mathbb{S}$, coefficients $a_1(i)$, $b(i)$, $d_{st}(i)$, $d_{sn}(i)$, $d_1(i)$, $b_t(i)$, $r(i)$, $e_1(i)$, $q(i)$, $d_t(i)$, $b_n(i)$, $k(i)$, $d_{ns}(i)$, $d_n(i)$, $\sigma_1(i)$, and $\sigma_2(i)$ are positive.

The infinitesimal generator matrix $\Gamma = [\gamma_{ij}]_{\bar{M}\times\bar{M}}$ is defined by

$$P\{\xi(t+\Delta) = j | \xi(t) = i\} = \begin{cases} \gamma_{ij}\Delta + o(\Delta), & i \neq j, \\ 1 + \gamma_{ii}\Delta + o(\Delta), & i = j, \end{cases}$$

where $\gamma_{ij} \geq 0$ is the transition rate from state $i$ to state $j$ if $i \neq j$, while $\gamma_{ii} = -\sum_{j\neq i}\gamma_{ij}$. We assume that $\gamma_{ij} > 0$ for $i, j = 1, 2, \ldots, \bar{M}$ with $i \neq j$. This

assumption provides that the Markov chain $\xi(t)$ is irreducible, i.e. there exists a unique stationary distribution $\pi = (\pi_i)_{1\times \bar{M}}$ such that $\pi\Gamma = 0$, $\sum_{i=1}^{\bar{M}} \pi_i = 1$ and $\pi > 0$ for any $i \in \mathbb{S}$.

For discussion convenience, let us define $\hat{\rho}=\min_{i\in\mathbb{S}} \rho(i)$ and $\check{\rho}=\max_{i\in\mathbb{S}} \rho(i)$.

The rest of the paper is arranged as follows. In Section 2 we provide auxiliary definitions and lemmas which will be used for proving main results. Section 3 is devoted to verification of the existence and uniqueness of the global positive solution of system (2). In Section 4, we give sufficient conditions under which there exists unique stationary distribution in order to prove weak persistence in mean of system (2). Results on extinction are presented in Section 5. In Section 6, we illustrate the theoretical results using real data from virological analysis on nine COVID-19 patients who were hospitalized in the hospital in Munich. We close the paper with a conclusion section.

## 2 Preliminaries

Let $\{(x(t), \xi(t)), t \geq 0\}$ be the diffusion Markov process which satisfies the following equation

$$dx(t) = f(x(t), \xi(t))dt + g(x(t), \xi(t))dw(t), \quad t \geq 0, \tag{4}$$

with the initial condition

$$x(0) = x_0 \in \mathbb{R}^d, \quad \xi(0) = \xi_0 \in \mathbb{S},$$

where $f : \mathbb{R}^d \times \mathbb{S} \to \mathbb{R}^d, g : \mathbb{R}^d \times \mathbb{S} \to \mathbb{R}^{d\times m}$, while $A(x,k)=g(x,k)\cdot g^{\mathbf{T}}(x,k)$ $=(a_{ij}(x,k)), i,j = 1,\ldots,d$, is a diffusion matrix of process $\{(x(t),\xi(t)), t \geq 0\}$. For each $k \in \mathbb{S}$, let $V(\cdot,k)$ be any twice continuously differentiable function. The differential operator $L$ of Eq. (4) is defined by

$$L(x,k) = \sum_{i=1}^{d} f_i(x,k)\frac{\partial V(x,k)}{\partial x_i} + \frac{1}{2}\sum_{i=1}^{d} a_{ij(x,k)}\frac{\partial^2 V(x,k)}{\partial x_i \partial x_j} + \sum_{l=1}^{\bar{M}} \gamma_{kl} V(x,l),\ k \in \mathbb{S}.$$

In the sequel we formulate lemma which will be used to prove the main results of this paper.

**Lemma 2.1.** *If the following conditions are satisfied:*
*(C.1)* $\gamma_{ij} > 0$, *for any* $i \neq j$;
*(C.2) there exist some* $i \in \{1,2,\ldots,d\}$ *and positive constant* $\kappa$ *such that*

$$a_{ii}(x) \geq \kappa, \quad \textit{for any} \quad x \in \mathcal{D} \subset \mathbb{R}^d,$$

*where* $\mathcal{D}$ *represents a nonempty open set with compact closure;*

*(C.3) there exists a nonempty open set $\mathcal{D}$ with compact closure, satisfying that, for each $k \in \mathbb{S}$ there exists nonegative function $V : \mathcal{D}^c \to \mathbb{R}$ which is twice continuously differentiable, and that for some $\theta > 0$,*

$$LV(x) < -\theta, \qquad (x,k) \in \mathcal{D}^c \times \mathbb{S},$$

*then $\{(x(t), \xi(t)), t \geq 0\}$ is positive recurrent and ergodic. Namely, there exists a unique stationary distribution $\pi(\cdot,\cdot)$ such that for any Borel measurable function $\varphi : \mathbb{R}^d \times \mathbb{S} \to \mathbb{R}$, satisfying $\sum_{k\in\mathbb{S}} \int_{\mathbb{R}^d} |\varphi(x,k)|\pi(dx,k) < \infty$, we have*

$$\mathbb{P}\left\{\lim_{t\to\infty} \frac{1}{t}\int_0^t \varphi(x(s),\xi(s))ds = \sum_{k\in\mathbb{S}} \int_{\mathbb{R}^d} |\varphi(x,k)|\pi(dx,k)\right\} = 1.$$

**Remark 1.** *Conditions (C.1), (C.2) and (C.3) in Lemma 2.1 represent different variants of sufficient conditions for the existence of a unique stationary distribution (see [1], [4], [5], [10], [21], [26], for instance).*

## 3 Existence and uniqueness of positive solution

Since $S(t), T(t), N(t), t \geq 0$, in system (2) represent the number of virus particles, T-cells and NK cells, respectively, it is natural to consider only positive global solution of system (2).

**Theorem 3.1.** *For any initial value (3), system (2) has unique global solution $(S(t), T(t), N(t))$, for all $t \geq 0$. Moreover, the solution remains in $\mathbb{R}^3_+$ with probability 1.*

*Proof.* Since the coefficients of system (2) are locally Lipshitz continuous for any initial condition (3) in $\mathbb{R}^3_+$, then system (2) has a unique local positive solution for $t \in [0, \tau_\varepsilon)$, where $\tau_\varepsilon$ represents explosion time [16]. To prove the globality of the solution, it only needs to be shown that the solution does not explode in a finite time, i.e. that $\tau_\varepsilon = \infty$ almost surely.

Thus, let $k_0 > 0$ be sufficient large number such that the values $S_0, T_0, N_0$ are lying within the interval $\left[\frac{1}{k_0}, k_0\right]$. For each integer $k \geq k_0$, define the stopping time

$$\tau_k = \inf\left\{t \in [0,\tau_\varepsilon) : S(t) \notin \left(\frac{1}{k}, k\right) \text{ ili } T(t) \notin \left(\frac{1}{k}, k\right) \text{ ili } N(t) \notin \left(\frac{1}{k}, k\right)\right\},$$

where we fix $\inf \emptyset = \infty$ ($\emptyset$ is the empty set).

Apparently, when $k \to \infty$ then $\tau_k$ is increasing. Let $\tau_\infty = \lim_{k\to\infty} \tau_k$. Then $\tau_\infty \leq \tau_\varepsilon$ almost surely. If $\tau_\infty = \infty$ almost surely, then $\tau_\varepsilon = \infty$ and

$(S(t), T(t), N(t)) \in \mathbb{R}^3_+$ almost surely for $t \geq 0$. Hence, let us prove that $\tau_\infty = \infty$ almost surely. If this were not true, then there exist a pair of positive constants $\mathcal{T} > 0$ and $\varepsilon \in (0,1)$ such that $\mathbb{P}\{\tau_\infty \leq \mathcal{T}\} > \varepsilon$. Therefore, there exists an integer $k_1 \geq k_0$, such that

$$\mathbb{P}\{\tau_\infty \leq \mathcal{T}\} \geq \varepsilon \text{ for every } k \geq k_1. \tag{5}$$

In addition we define function $V \in C^2(\mathbb{R}^3_+, \mathbb{R}_+)$ as

$$V(S,T,N) = S - 1 - \ln S + A(T - 1 - \ln T) + N - 1 - \ln N,$$

where $A$ is positive constant to be determined later. By applying the Itô formula

$$dV(S,T,N) = LV(S,T,N)dt + A\sigma_1(\xi)(T-1)\mathcal{G}(S)dw_1 + A\sigma_2(\xi)(N-1)\mathcal{G}(S)dw_2,$$

where

$$\begin{aligned}
LV(S,T,N) = &\left(1-\frac{1}{S}\right)[a_1(\xi)S(1-b(\xi)S) - d_{st}(\xi)S\mathcal{F}(S,T) - d_{sn}(\xi)SN - d_1(\xi)S] \\
&+ A\left(1-\frac{1}{T}\right)[b_t(\xi) + r(\xi)\mathcal{G}(S)T + e_1(\xi)NS - q(\xi)TS - d_t(\xi)T] \\
&+ \left(1-\frac{1}{N}\right)[b_n(\xi) + k(\xi)\mathcal{G}(S)N - d_{ns}(\xi)NS - d_n(\xi)N] \\
&+ \frac{A}{2}\sigma_1^2(\xi)\mathcal{G}^2(S) + \frac{\sigma_2^2(\xi)}{2}\mathcal{G}^2(S) \\
= &a_1(\xi)S - a_1(\xi)b(\xi)S^2 - d_{st}(\xi)S\mathcal{F}(S,T) - d_{sn}(\xi)SN - d_1(\xi)S \\
&- a_1(\xi) + a_1(\xi)b(\xi)S + d_{st}(\xi)\mathcal{F}(S,T) + d_{sn}(\xi)N + d_1(\xi) + Ab_t(\xi) \\
&+ Ar(\xi)\mathcal{G}(S)T + Ae_1(\xi)NS - Aq(\xi)TS - Ad_t(\xi)T - Ar(\xi)\mathcal{G}(S) \\
&- Ae_1(\xi)\frac{NS}{T} + Aq(\xi)S + Ad_t(\xi) + \frac{A}{2}\sigma_1^2(\xi)\mathcal{G}^2(S) + b_n(\xi) \\
&+ k(\xi)\mathcal{G}(S)N - d_{ns}(\xi)SN - d_n(\xi)N - \frac{b_n(\xi)}{N} - k(\xi)\mathcal{G}(S) \\
&+ d_{ns}(\xi)S + d_n(\xi) + \frac{\sigma_2^2(\xi)}{2}\mathcal{G}^2(S).
\end{aligned}$$

If we remove some nonpositive terms, we get

$$\begin{aligned}
&LV(S,T,N)\\
&\quad\le d_{st}(\xi)+d_1(\xi)+b_n(\xi)+d_n(\xi)+A(b_t(\xi)+d_t(\xi))+A\frac{\sigma_1^2(\xi)}{2}+\frac{\sigma_2^2(\xi)}{2}\\
&\qquad+(a_1(\xi)+a_1(\xi)b(\xi)+d_{ns}(\xi)+Aq(\xi))S+(d_{sn}(\xi)+k(\xi))\,N+Ar(\xi)T\\
&\qquad+(Ae_1(\xi)-(d_{ns}(\xi)+d_{sn}(\xi)))SN\\
&\quad\le \check{d}_{st}+\check{d}_1+\check{b}_n+\check{d}_n+A(\check{b}_t+\check{d}_t)+A\frac{\check{\sigma}_1^2}{2}+\frac{\check{\sigma}_2^2}{2}+\left(\check{a}_1+\check{a}_1\check{b}+\check{d}_{ns}+A\check{q}\right)S\\
&\qquad+\left(\check{d}_{sn}+\check{k}\right)N+A\check{r}T+(A\check{e}_1-(\hat{d}_{ns}+\hat{d}_{sn}))SN\\
&\quad\le K_1+K_2(S+AT+N)
\end{aligned}$$

where $K_1=\check{d}_{st}+\check{d}_1+\check{b}_n+\check{d}_n+A(\check{b}_t+\check{d}_t)+A\frac{\check{\sigma}_1^2}{2}+\frac{\check{\sigma}_2^2}{2}$ and $K_2=\max\left\{\check{a}_1+\check{a}_1\check{b}+\check{d}_{ns}+A\check{q},\check{d}_{sn}+\check{k},\check{r}\right\}$, while constant $A$ is chosen to annul the term in the bracket that multiplies $SN$, i.e. $A=\frac{\hat{d}_{ns}+\hat{d}_{sn}}{\check{e}_1}$.

By using inequality $x<2(x-1-\ln x+1)$, $x>0$, and recalling the form of function $V(S,T,N)$, the last estimation for $LV(S,T,N)$ becomes

$$\begin{aligned}
LV(S,T,N)&\le K_1+2K_2(S-1-\ln S+A(T-1-\ln T)+N-1-\ln N+2+A)\\
&=K_1+2K_2(2+A)+2K_2V(S,T,N).
\end{aligned}$$

Consequently,

$$\begin{aligned}
dV(S,T,N)&=LV(S,T,N)+A\sigma_1(\xi)(T-1)\mathcal{G}(S)dw_1+\sigma_2(\xi)(N-1)\mathcal{G}(S)dw_2\\
&\le (K_1+2K_2(2+A)+2K_2V(S,T,N))dt\\
&\quad+A\sigma_1(\xi)(T-1)\mathcal{G}(S)dw_1+\sigma_2(\xi)(N-1)\mathcal{G}(S)dw_2. \qquad (6)
\end{aligned}$$

Integrating (6) from 0 to $\tau_k\wedge\mathcal{T}$, and then taking the expectation on both sides, we obtain

$$\begin{aligned}
&\mathbb{E}V(S(\tau_k\wedge\mathcal{T}),T(\tau_k\wedge\mathcal{T}),N(\tau_k\wedge\mathcal{T}))\\
&\le V(S_0,T_0,N_0)\\
&\quad+\int_0^{\mathcal{T}}(K_1+2K_2(2+A)+2K_2EV(S(\tau_k\wedge\mathcal{T}),T(\tau_k\wedge\mathcal{T}T),N(\tau_k\wedge\mathcal{T})))dz\\
&=V(S_0,T_0,N_0)+(K_1+2K_2(2+A))\mathcal{T}\\
&\quad+2K_2\int_0^{\mathcal{T}}(EV(S(\tau_k\wedge\mathcal{T}),T(\tau_k\wedge\mathcal{T}),N(\tau_k\wedge\mathcal{T})))\,dz.
\end{aligned}$$

The Gronwall-Belman inequality implies

$$\mathbb{E}V(S(\tau_k\wedge\mathcal{T}),T(\tau_k\wedge\mathcal{T}),N(\tau_k\wedge\mathcal{T}))\le\left[V(S_0,T_0,N_0)+(K_1+2K_2(2+A))\mathcal{T}\right]e^{2K_2\mathcal{T}}. \qquad (7)$$

Let $\Omega_k = \{\tau_k \leq \mathcal{T}\}$ for $k \geq k_1$. According to (5), we get $\mathbb{P}(\Omega_k) \geq \varepsilon$. Obvious, for $\omega \in \Omega_k$, there is at least one of $S(\tau_k, \omega)$, $T(\tau_k, \omega)$ or $N(\tau_k, \omega)$ equaling either $\frac{1}{k}$ or $k$, such that

$$V(S(\tau_k), T(\tau_k), N(\tau_k)) \geq (k - 1 - \ln k) \vee \left(\frac{1}{k} - 1 - \ln \frac{1}{k}\right).$$

By using (7) and the last inequality, yields

$$\begin{aligned} \infty &> [V(S_0, T_0, N_0) + (K_1 + 2K_2(2+A))\mathcal{T}]\, e^{2K_2\mathcal{T}} \\ &\geq \mathbb{E}[I_{\Omega_k(\omega)} V(S(\tau_k), T(\tau_k), N(\tau_k))] \\ &\geq \varepsilon \left[(k - 1 - \ln k) \vee \left(\frac{1}{k} - 1 - \ln \frac{1}{k}\right)\right], \end{aligned}$$

where $I_{\Omega_k}$ is the indicator function of $\Omega_k$. When $k \to \infty$, then

$$\infty > [V(S_0, T_0, N_0) + (K_1 + 2K_2(2 + A))\mathcal{T}]\; e^{2K_2\mathcal{T}} \geq \infty,$$

which leads to a contradiction, from what follows $\tau_\infty = \infty$ almost surely, which proves the theorem. □

By using Theorem 3.1 it can be shown that the set

$$\Theta = \{(S, N, T) \in \mathbb{R}^3_+ | 0 < S(t) \leq \frac{\check{a}_1}{\hat{b}\hat{a}_1}, N > 0, T > 0\} \tag{8}$$

is positively invariant for system (2).

**Theorem 3.2.** *The region $\Theta$ is almost surely positively invariant set of system (2), i.e. if $(S_0, T_0, N_0) \in \Theta$ then*

$$\mathbb{P}((S(t), T(t), N(t)) \in \Theta) = 1,$$

*for all $t \geq 0$.*

*Proof.* Let $(S_0, T_0, N_0) \in \Theta$. In view of Theorem 3.1, for the first equation of system (2) we obtain

$$dS(t) \leq (\check{a}_1 S(t) - \hat{a}_1 \hat{b} S^2(t))dt, \quad t \geq 0.$$

Equation

$$dX(t) = (\check{a}_1 - \hat{a}_1 \hat{b} X(t))X(t)dt, \quad t \geq 0,$$

with initial condition $X(0) = S_0$, has a solution

$$X(t) = \frac{1}{\frac{\check{a}_1 - \hat{a}_1 \hat{b} S_0}{S_0} e^{-\check{a}_1 t} + \frac{\hat{b}\hat{a}_1}{\check{a}_1}}, \; t \geq 0.$$

Bearing in mind the assumption $S_0 \in \Theta$, we get the following estimation

$$X(t) \leq \frac{\check{a}_1}{\hat{b}\hat{a}_1}, \quad t \geq 0.$$

Applying the Comparison theorem for differential equations, we have

$$S(t) \leq \frac{\check{a}_1}{\hat{b}\hat{a}_1}, \quad t \geq 0,$$

which completes the proof. □

## 4 Existence of stationary distribution

In this section we discuss the existence of the ergodic stationary distribution of system (2). From biological point of view the existence of stationary distribution indicates the prevalence of the disease in population, (see [24]). Also, this means that the stochastic system oscillates around the endemic equilibrium of the corresponding deterministic system.

For simplicity, in the sequel we use the following notation

$$\mathcal{J} = \frac{\sum_{l=1}^{\bar{M}} \pi_l \Lambda(l)}{\sum_{l=1}^{\bar{M}} \pi_l u(l) \sum_{l=1}^{\bar{M}} \pi_l v(l) \sum_{l=1}^{\bar{M}} \pi_l b_t(l) \sum_{l=1}^{\bar{M}} \pi_l b_n(l)},$$

where $\Lambda(l) = b_t(l)b_n(l)(d_t(l) - r(l))(d_n(l) - k(l))$, $u(l) = \frac{\check{a}_1}{\hat{b}\hat{a}_1} q(l) + d_t(l) + \frac{\sigma_1^2(l)}{2}$, while $v(l) = \frac{\check{a}_1}{\hat{b}\hat{a}_1} d_{ns}(l) + d_n(l) + \frac{\sigma_2^2(l)}{2}$, for all $l \in \mathbb{S}$.

**Theorem 4.1.** *Let parameters of system (2) satisfy the condition $\mathcal{J} > 1$ as well as conditions*

$$\hat{d}_t > \check{r}, \tag{9}$$

$$\hat{d}_n > \check{k}, \tag{10}$$

$$\check{e}_1 \check{b}_n < \hat{d}_{ns} \hat{b}_t. \tag{11}$$

*Then, the solution $(S(t), T(t), N(t)), t \geq 0$ of system (2) has a unique ergodic stationary distribution in $\Theta$ for any initial value $(S_0, T_0, N_0) \in \Theta$.*

*Proof.* In order to prove the mentioned property, we need to check conditions of Lemma 2.1.

The diffusion matrix of system (2) is

$$A = \begin{pmatrix} 0 & 0 & 0 \\ 0 & \sigma_1^2(k)\mathcal{G}^2(S)T^2(t) & \sigma_1(k)\sigma_2(k)\mathcal{G}^2(S)T(t)N(t) \\ 0 & \sigma_1(k)\sigma_2(k)\mathcal{G}^2(S)T(t)N(t) & \sigma_2^2(k)\mathcal{G}^2(S)T^2(t) \end{pmatrix}.$$

The assumption $\gamma_{ij} > 0, i \neq j$, from Introduction section, implies that the condition *(C.1)* from Lemma 2.1 is fullfiled. On the other hand, let us consider the following open subset of $\Theta$

$$D_\epsilon = \left\{(S,T,N) \in \Theta \ : \epsilon < S < \frac{\check{a}_1}{\hat{b}\hat{a}_1} - \epsilon,\ \epsilon < T < \frac{1}{\epsilon},\ \epsilon < N < \frac{1}{\epsilon}\right\},$$

where $\epsilon \in (0,1)$. For $(S,T,N) \in \Theta \backslash D_\epsilon$, and, for example $i = 3$, we have

$$a_{33}(S,T,N) = \sigma_2^2(\xi(t))\mathcal{G}^2(S)T^2(t) \geq \frac{\hat{\sigma}_2^2 \epsilon^{n+2}}{c_1 + \left(\frac{\check{a}_1}{\hat{b}\hat{a}_1} - \epsilon\right)^n},$$

which means that the condition *(C.2)* from from Lemma 2.1 is met.

To verify the condition *(C.3)* in Lemma 2.1, let us define

$$V_1(T,N) = -\bar{c}_1 \ln T - \bar{c}_2 \ln N + \bar{c}_3 T + \bar{c}_4 N,$$

where $\bar{c}_1$, $\bar{c}_2$, $\bar{c}_3$ and $\bar{c}_4$ represent positive constants which will be chosen in the sequel.

Note that function $V_1(S,T,N,l)$ is not only continuous, but also tends to $\infty$ as $(S,T,N,l)$ approaches the the boundary of $\Theta \times \mathbb{S}$. Therefore, it must be lower bounded and it achieves this lower bound at a point $(\bar{S},\bar{T},\bar{N},\bar{l})$ in the interior of $\Theta \times \mathbb{S}$. Then, we define a function $\bar{V}_1 \in C^2(\Theta \times \mathbb{S}, \mathbb{R}_+)$ by

$$\bar{V}_1(S,T,N,l) = V_1(S,T,N,l) - V_1(\bar{S},\bar{T},\bar{N},\bar{l}).$$

Application of the Itô formula on $\bar{V}_1$, using the fact that $\mathcal{G}(S) \leq 1$ and omitting some nonpositive therms yield

$$\begin{aligned}
L\bar{V}_1(S,T,N) = & -\frac{\bar{c}_1 b_t(l)}{T} - \bar{c}_1 r(l)\mathcal{G}(S) - \bar{c}_1 e_1(l)\frac{SN}{T} + \bar{c}_1 q(l)S + \frac{1}{2}\bar{c}_1\sigma_1^2(l)\mathcal{G}^2(S) \\
& - \frac{\bar{c}_2 b_n(l)}{N} - \bar{c}_2 k(l)\mathcal{G}(S) + \bar{c}_2 d_{ns}(l)S + \bar{c}_2 d_n(l) + \frac{1}{2}\bar{c}_2\sigma_2^2(l)\mathcal{G}^2(S) \\
& + \bar{c}_3 r(l)\mathcal{G}(S)T + \bar{c}_3 e_1(l)NS - \bar{c}_3 q(l)TS - \bar{c}_3 d_t(l)T + \bar{c}_4 b_n(l) \\
& - \bar{c}_4 d_n(l)N + \bar{c}_4 k(l)\mathcal{G}(S)N + c_1 d_t(l) + \bar{c}_3 b_t(l) - \bar{c}_4 d_{ns}(l)NS \\
\leq & -\frac{\bar{c}_1 b_t(l)}{T} - \frac{\bar{c}_2 b_n(l)}{N} - \bar{c}_3(d_t(l) - r(l))T - \bar{c}_4(d_n(l) - k(l))N \\
& + \bar{c}_3 b_t(l) + \bar{c}_1\left(\frac{\check{a}_1}{\hat{b}\hat{a}_1} q(l) + d_t(l) + \frac{1}{2}\bar{c}_1\sigma_1^2(l)\right) \\
& + \bar{c}_2\left(\frac{\check{a}_1}{\hat{b}\hat{a}_1} d_{ns}(l) + d_n(l) + \frac{1}{2}\bar{c}_1\sigma_2^2(l)\right) + (\bar{c}_3 e_1(l) - \bar{c}_4 d_{ns}(l))NS \\
& + \bar{c}_4 b_n(l).
\end{aligned}$$

By using the well known $AM-GM$ inequality, we obtain

$$\begin{aligned} L\bar{V}_1(S,T,N) \leq & -4\sqrt[4]{b_t(l)b_n(l)(d_t(l)-r(l))(d_n(l)-k(l))\bar{c}_1\bar{c}_2\bar{c}_3\bar{c}_4} \\ & +\bar{c}_1u(l)+\bar{c}_2v(l)+\bar{c}_3b_t(l)+\bar{c}_4b_n(l)+(\bar{c}_3e_1(l)-\bar{c}_4d_{ns}(l))NS \\ = & B_0(l)+(\bar{c}_3e_1(l)-\bar{c}_4d_{ns}(l))NS, \end{aligned}$$

where $B_0(l)=-4\sqrt[4]{b_t(l)b_n(l)(d_t(l)-r(l))(d_n(l)-k(l))\bar{c}_1\bar{c}_2\bar{c}_3\bar{c}_4}+\bar{c}_1u(l)+\bar{c}_2v(l)+\bar{c}_3b_t(l)+\bar{c}_4b_n(l)$. Let $(\omega(1),\omega(2),...,\omega(\bar{M}))^{\mathbf{T}}$ be the solution of the following Poisson system

$$\Gamma\omega=\sum_{l=1}^{\bar{M}}\pi_lB_0(l)\begin{pmatrix}1\\1\\\vdots\\1\end{pmatrix}-B_0,$$

while $B_0=(B_0(1),B_0(2),\ldots,B_0(\bar{M}))^{\mathbf{T}}$. If we choose constants $\bar{c}_1$, $\bar{c}_2$, $\bar{c}_3$ and $\bar{c}_4$ in the following way

$$\bar{c}_1=\frac{\sum_{l=1}^{\bar{M}}\pi_l\Lambda(l)}{\sum_{l=1}^{\bar{M}}\pi_lu(l)},\ \bar{c}_2=\frac{\sum_{l=1}^{\bar{M}}\pi_l\Lambda(l)}{\sum_{l=1}^{\bar{M}}\pi_lv(l)},\ \bar{c}_3=\frac{\sum_{l=1}^{\bar{M}}\pi_l\Lambda(l)}{\sum_{l=1}^{\bar{M}}\pi_lb_t(l)},\ \bar{c}_4=\frac{\sum_{l=1}^{\bar{M}}\pi_l\Lambda(l)}{\sum_{l=1}^{\bar{M}}\pi_lb_n(l)},$$

bearing in mind condition (11), application of differential operator $L$ on $\bar{V}_1+\omega(l)$ gives us

$$\begin{aligned} L(\bar{V}_1+\omega(l)) \leq & B_0(l)+\sum_{j\in\mathbb{S}}\gamma_{lj}\omega(j) \\ = & \sum_{l=1}^{\bar{M}}\pi_lB_0(l) \\ = & -4\sum_{l=1}^{\bar{M}}\pi(l)\Lambda(l)\left(\sqrt[4]{\beta}-1\right). \end{aligned}$$

Define the functions $V_2=S,\ V_3=N,\ V_4=T$. Application of the Itô formula

to defined functions yields

$$\begin{aligned} LV_2 &= a_1(l)S - a_1(l)b(l)S^2 - d_{st}(l)S\mathcal{F}(S,T) - d_{sn}(l)SN - d_1(l)S \\ &\leq (a_1(l) - d_1(l))S - a_1(l)b(l)S^2 - d_{sn}(l)SN \\ &\leq (\check{a}_1 - \hat{d}_1)S - \hat{a}_1\hat{b}S^2 - \hat{d}_{sn}SN, \end{aligned} \tag{12}$$

$$\begin{aligned} LV_3 &= b_n(l) + k(l)\mathcal{G}(S)N - d_{ns}(l)NS - d_n(l)N \\ &\leq b_n(l) - (d_n(l) - k(l))N - d_{ns}(l)NS \\ &\leq \check{b}_n - (\hat{d}_n - \check{k})N - \hat{d}_{ns}NS, \end{aligned} \tag{13}$$

$$\begin{aligned} LV_4 &= b_t(l) + r(l)\mathcal{G}(S)T + e_1(l)NS - q(l)TS - d_t(l)T \\ &\leq b_t(l) + e_1(l)NS - (d_t(l) - r(l))T \\ &\leq \check{b}_t + \check{e}_1 NS - (\hat{d}_t - \check{r})T. \end{aligned} \tag{14}$$

Let $V_5 = V_2 + V_3 + aV_4$ be a positive function, where $a$ is positive constant which will be chosen later. In view of (12), (13) and (14), we get

$$\begin{aligned} LV_5 \leq\ & (\check{a}_1 - \hat{d}_1)S - \hat{a}_1\hat{b}_1S^2 + \check{b}_n - (\hat{d}_n - \check{k})N + a\check{b}_t \\ & - a(\check{d}_t - \hat{r})T - (\hat{d}_{ns} + \hat{d}_{sn} - a\check{e}_1)NS \\ =\ & (\check{a}_1 - \hat{d}_1)S - \hat{a}_1\hat{b}_1S^2 + \check{b}_n - (\hat{d}_n - \check{k})N + a\check{b}_t - a(\check{d}_t - \hat{r})T, \end{aligned}$$

which is obtained by choosing $a = \frac{\hat{d}_{ns} + \hat{d}_{sn}}{\check{e}_1}$. It is obvious that

$$LV_5 \leq H,$$

where $H$ is positive constant.

Finally, let us define nonegative $C^2(\Theta \times \mathbb{S}, \mathbb{R}_+)$ function

$$V(S,T,N,l) = Q\bar{V}_1 + V_5.$$

Application of the Itô formula to finction $V$ yields

$$\begin{aligned} LV &\leq -4Q\sum_{l=1}^{\bar{M}} \pi_l \Lambda(l) \left( \sqrt[4]{\beta} - 1 \right) + H \\ &= -Q\Pi + H, \end{aligned} \tag{15}$$

where

$$\Pi = 4\sum_{l=1}^{\bar{M}} \pi_l \Lambda(l) \left( \sqrt[4]{\beta} - 1 \right) > 0.$$

If we choose constant $Q$ in (15) such that

$$Q \geq \frac{H+1}{\Pi},$$

we conclude that,

$$LV \leq -1,$$

for every $(S,T,N) \in \Theta \backslash D_\epsilon$, which proves the theorem. □

## 5 Extinction of disease

From epidemiological point of view, it is important to determine the conditions for the coefficients of the system (2) which guarantee the extinction of virus particles from human organism.

**Theorem 5.1.** *If the following condition holds*

$$\sum_{l=1}^{\bar{M}} \pi_l \left(a_1(l) - d_1(l)\right) < 0, \tag{16}$$

*then the number of virus particles $S$ of system (2) almost surely exponentially tends to zero.*

*Proof.* By applying the Itô formula on $\ln S(t)$ we get

$$\begin{aligned} & d\ln S(t) \\ & = \Big[a_1(\xi(t)) - a_1(\xi(t))b(\xi(t))S - d_{st}(\xi(t))\mathcal{F}(S,T) - d_{sn}(\xi(t))N - d_1(\xi(t))\Big]dt \\ & \leq \Big[a_1(\xi(t)) - d_1(\xi(t))\Big]dt. \end{aligned} \tag{17}$$

According to the ergodic property of Markov chain $\xi(t)$, it holds that

$$\limsup_{t\to\infty} \frac{1}{t} \int_0^t (a_1(\xi(t)) - d_1(\xi(t)))dt = \sum_{l=1}^{\bar{M}} \pi_l \left(a_1(l) - d_1(l)\right). \tag{18}$$

Integrating $d\ln S$ from 0 to $t$ yields

$$\ln S(t) - \ln S(0) \leq \int_0^t (a_1(\xi(s)) - d_1(\xi(s)))ds. \tag{19}$$

Having in mind condition (16), as well as (17) and (18), we get

$$\limsup_{t\to\infty} \frac{\ln S(t)}{t} \leq \sum_{l=1}^{\bar{M}} \pi_l \left(a_1(l) - d_1(l)\right) < 0. \; a.s.$$

which completes the proof. □

**Remark 2.** Condition (16) suggests that the relation between replication rate of virus particles and their natural death rate is important for extinction of the disease. More precisely, if the natural death rate of virus particles is greater that their replication rate (condition (16)), then the extinction of disease will occur.

**Remark 3.** Let us note that in [6] the authors obtained the basic reproduction number. The basic reproductive number, $\mathcal{R}_0$, is defined as the expected number of secondary infections arising from a single individual during his or her entire infectious period, in a population of susceptible, or as the number of secondary infection due to a single infection in a completely susceptible population. They obtained that

$$\mathcal{R}_0 = \frac{a_1 d_t d_n}{d_1}.$$

Our goal is to try to connect $\mathcal{J}$ from Theorem 4.1 with $\mathcal{R}_0$. From definition of $\mathcal{J}$, we can conclude that

$$\mathcal{J} \leq \frac{\check{b}_t \check{b}_n \check{d}_t \check{d}_n}{\hat{d}_t \hat{d}_n \hat{b}_t \hat{b}_n}.$$

Assume that following condition holds

$$\frac{\check{b}_t \check{b}_n}{\hat{b}_t \hat{b}_n} \leq \frac{\check{a}_1 \hat{d}_t \hat{d}_n}{\hat{d}_1}. \tag{20}$$

In that case we obtain that $\mathcal{J} \leq \frac{\check{a}_1 \check{d}_t \check{d}_n}{\hat{d}_1} := \mathcal{R}_0^S$. It is obvious that $\mathcal{R}_0^S > 1$ if $\mathcal{J} > 1$.

On the other hand, condition (16) is equivalent to

$$\mathcal{I} = \frac{\sum_{l=1}^{\bar{M}} \pi_l a_1(l)}{\sum_{l=1}^{\bar{M}} \pi_l d_1(l)} \leq 1.$$

Since $\frac{\check{a}_1}{\hat{d}_1} \geq \mathcal{R}_0^S$, because $\check{d}_t$ and $\check{d}_n$ represent death rates, we have that $\mathcal{R}_0^S < 1$ holds if $\mathcal{I} < 1$.

Also, let us note that without Markovian switching, $\mathcal{R}_0^S$ becomes $\mathcal{R}_0$, while condition (20) becomes $\mathcal{R}_0 > 1$.

Therefore, conditions $\mathcal{J} > 1$ can also be sufficient condition for persistence of COVID-19 virus particles in deterministic system (1), and condition $\mathcal{I} < 1$ is sufficient condition under which extinction of disease will occur in system (1).

Thus, we can conclude that the dynamical properties of stochastic system (2) are consistent with the corresponding deterministic system (1) when colored noise is not present.

## 6 Numerical simulation

The COVID-19 is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus.

As it was already mentioned in the Introduction section, the first case of infected COVID-19 patient was detected in Wuhan, China in December 2019. Considering that the virus quickly spread to other countries around the world, all because of the fact that a large number of people traveled during the holidays because they did not even know they were infected, the World Health Organization (WHO) characterized the outbreak of this disease as a pandemic on 11 March 2020.

From the first case of COVID-19 in the Europe, over 2 million people have died from the disease. Compared to many other countries, Germany has managed the COVID-19 crisis well. The main reason for that is proper health system [9]. Due to that, there are many laboratories all over the Germany, that can test for the virus, and to investigate its dynamics with the immune system of the infected individuals.

In this example, we turn our attention to the study of Wöffel et al. [25]. Their investigation is based on a detailed virological analysis of nine cases of COVID-19 that provides proof of active virus replication in tissues of the upper respiratory tract. Namely, they have examined the kinetics of viral load and measured the virus replication in tissues of the upper respiratory tract. The infection in the patient was proven, before they have been taken into consideration. The patient were hospitalized in the hospital in Munich that cooperated with laboratories that are equipped with the same technology in PCR-PT and the same standards for virus isolation. All the samples (sputum, throat swab and stool samples) were taken between two and four days after the onset of symptoms.

Depending on the immune system, the dynamics of COVID-19 virus differ from person to person. It is shown that age affects the disease (see [25]), but also seasonal character of the disease is important. More precisely, COVID-19 is more active during the period of summer holidays due to fact that a large number of people travel for their annual vacation, and also in winter, as majority of respiratory illnesses. Therefore, we will take seasonal effect by introducing two different states in our Markov chain, i.e. $\mathbb{S} = \{1, 2\}$ and generator matrix is of the form

$$\Gamma = \begin{bmatrix} -2 & 2 \\ 3 & -3 \end{bmatrix}.$$

The stationary distribution is given by $\pi = (\pi_1, \pi_2) = (0.6, 0.4)$. According to [6] and references cited therein, the values of parameters are given in Table 2.

| Parameter | Unit | Value 1 | Value 2 |
|---|---|---|---|
| $a_1$ | 1/day | 2.86 | 6.87 |
| $b$ | ml/RNA copies | $e^{-9}$ | $e^{-9.9}$ |
| $d_{st}$ | 1/day | 0.0275 | 0.3 |
| $d_{sn}$ | ml/cell (day) | $1.2 \cdot e^{-11}$ | $2 \cdot e^{-10}$ |
| $d_1$ | 1/day | 0.001 | 0.1 |
| $b_t$ | ml/cell (day) | 500 | 1500 |
| $r$ | 1/day | 0.001 | 0.0021 |
| $e_1$ | ml/RNA copies | $2.1 \cdot e^{-5}$ | $1.1 \cdot e^{-5}$ |
| $q$ | ml/RNA copies | $1.1 \cdot e^{-10}$ | $9.5 \cdot e^{-10}$ |
| $d_t$ | ml/cell (day) | 0.03 | 0.8 |
| $b_n$ | cell/ml (day) | 100 | 84 |
| $k$ | cell/ml (day) | 0.002 | 0.017 |
| $d_{ns}$ | ml/RNA copies (day) | $1.02 \cdot e^{-5}$ | $1.02 \cdot e^{-4}$ |
| $d_n$ | 1/day | $4.2 \cdot e^{-2}$ | $4.21 \cdot e^{-2}$ |
| $z$ | / | 0.01 | 0.1 |
| $c_1$ | / | $e^3$ | $e^6$ |
| $\alpha$ | / | 0.95 | 0.98 |
| $\sigma_1^2$ | / | 0.0002 | 0.0000001 |
| $\sigma_2^2$ | / | 0.02 | 0.093 |

Table 2: The values of the model parameters

Finally, let the initial condition be

$$(S(0), T(0), N(0), r(0)) = \left(10^{-2}, 10^4, 10^3, 1\right). \tag{21}$$

The value of $\mathcal{J}$ from Theorem 4.1 is $\mathcal{J} = 1.00138 > 1$. It is not difficult to check out that other conditions of the theorem also hold, and thus, we expect the solution of system (2) to oscillate around endemic equilibrium $E^*$ of system (1), which yields to the *long COVID*, or post COVID-19 syndrome. This phenomenon involves a long-term symptoms of acute COVID-19 disease, which means that disease persists after a normal recovery period, which is presented in Figure 1.

According to [8], the median time from onset to clinical recovery for mild cases is approximately two weeks, and $3-6$ weeks for patients with severe or critical disease symptoms. However, about 1 in 13 people infected with the COVID-19 have experienced long-term symptoms which last longer than 12 weeks. In Figures 2 and 4, we can observe that with time number of T-cells and NK cells will decrease, which is known as *immunity exhaustion* which, in particular, refers to the NK cells exhaustion due to high infections. Hence, in the first days of the disease, it is important to apply antiviral therapy to suppresses the virus activity and, thereby, support the immune system reaction.

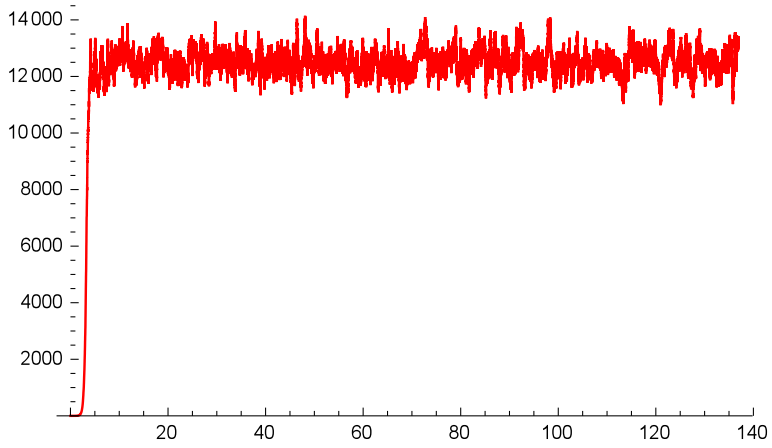


Figure 1: Stochastic trajectory for number of COVID-19 virus particles $S(t)$ of system (2) with model parameters from Table 2, initial value (21) and unit of time $\Delta_t = \frac{1}{365}$.

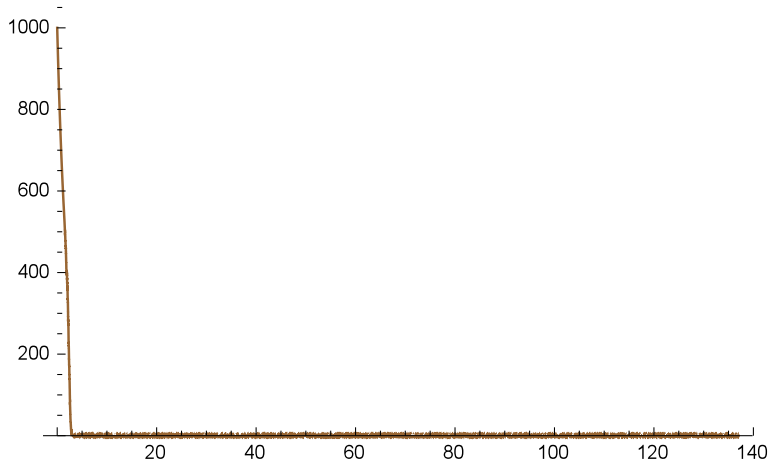


Figure 2: Stochastic trajectories for number of T-cells $T(t)$ of system (2) with model parameters from Table 2, initial value (21) and unit of time $\Delta_t = \frac{1}{365}$.

A computer simulation of the single path of Markov chain with two states $\xi(t)$ with initial value $\xi(0) = 1$ is plotted in Figure 4. We can notice that the state chain takes more time on the first environment than on the second one. Our second environment is the one with higher risk of infection by COVID-19

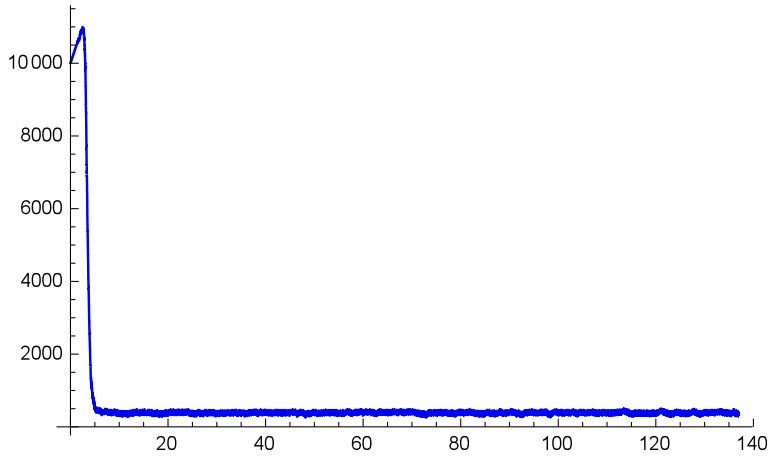


Figure 3: Stochastic trajectories for number of NK cells $N(t)$ of system (2) with model parameters from Table 2, initial value (21) and unit of time $\Delta_t = \frac{1}{365}$.

virus and, as we have already explained, it corresponds to winter and late summer period of the year. Thus, it is reasonable that the state chain spends less time in state two than in state one.

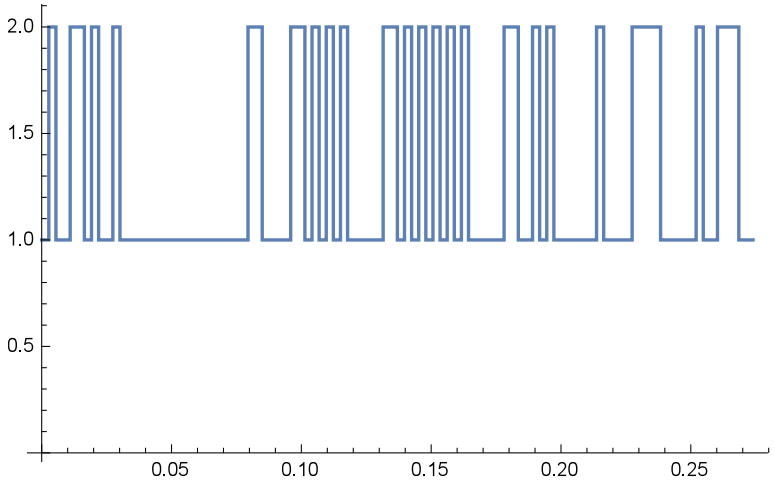


Figure 4: Computer simulation of a single path of Markov chain with two states $\xi(t)$ with initial value $\xi(0) = 1$.

## 7 Conclusions

In this paper we establish and analyze a stochastic competition model between immune cells and COVID-19 particles to examine the effects of the human immune system response to spread of COVID-19 virus. For that purpose, besides the Gaussian white noise, we introduce coloured or telegraphic noise, represented by right-continuous Markov chain, to consider seasonal effects on interaction between immune cells and virus particles. The inclusion of the Markov chain is of particular importance given the facts that, as most human respiratory viral infections, COVID-19 is more frequent during the winter period, as well as in the period of late summer and early autumn due to annual holidays.

We obtained that if natural death rates are greater than activation rates of immune cells, and for $\mathcal{J}$ from Theorem 4.1 it holds that $\mathcal{J} > 1$, the solution of system (2) will oscillate around endemic equilibrium $E^*$ of system (1), which leads to the long COVID phenomenon. Thus, the COVID-19 patients will exhibit symptoms of acute COVID-19 disease even after a normal recovery period. This phenomenon implies the other one known as immunity exhaustion, which, primarily, refers to the NK cells exhaustion due to high infections. We verified the obtained result by real life example in which nine cases of COVID-19 patients were considered. They were admitted in the hospital in Munich for examining the kinetics of viral load and measuring the virus replication in tissues of the upper respiratory tract.

Furthermore, we consider conditions that ensure disease extinction. We obtain that extinction of the disease doesn't depend on the immune system response to the virus directly, but indirectly does, bearing in mind that immune cells influence the replication of virus cells. Namely, if the natural death rate of virus particles is greater that their replication rate then the extinction of disease will occur.

We were able to connect dynamical properties of stochastic system (2) and deterministic system (1). More precisely, we demonstrated that conditions obtained in Theorem 4.1 and Theorem 5.1 can also be sufficient condition for persistence and extinction of COVID-19 virus particles in deterministic system (1), respectively. Thus, we can conclude that the dynamical properties of stochastic system (2) are consistent with the corresponding deterministic system (1) in absence of the coloured noise.

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Marija KRSTIĆ,
Department of Mathematics,
Faculty of Science and Mathematics,
University of Niš,
Višegradska 33, 18000 Niš, Serbia.
Email: marija.krstic@pmf.edu.rs

Vuk VUJOVIĆ,
Department of Mathematics,
Faculty of Science and Mathematics,
University of Niš,
Višegradska 33, 18000 Niš, Serbia.
Email: vukpharm@gmail.com

Milica MARKOVIĆ,
Faculty of Mechanical Engineering,
University of Niš,
Aleksandra Medvedeva 14, 18000 Niš, Serbia.
Email: milica.milunovic@masfak.ni.ac.rs