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Publications

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- Y. Belgaid, M. Helal, A. Lakmeche, and E. Venturino. ***On the stability of periodic solutions of an impulsive system arising in the control of agroecosystems.*** In: Mondaini R.P.(eds) *Trends in Biomathematics*: Chaos and Control in Epidemics. Ecosystems, and Cells. BIOMAT 2020. Springer, Cham. pp. 183-199. 2020.

- Y. Belgaid, M. Helal, and E. Venturino. ***Analysis of a Model for Coronavirus Spread***. *Mathematics*. vol. 8. no 5. 2020.

- Y. Belgaid, M. Helal, A. Lakmeche, and E. Venturino. ***A Mathematical Study of a Coronavirus Model with the Caputo Fractional-Order Derivative***. *Fractal Fract.* vol. 87, no 5. 2021.

Contents

Introduction

The mathematical modeling of a concrete phenomenon has aroused the curiosity of many mathematicians for decades, and it has become an essential tool in the analysis of different dynamic systems including the mention of the dynamics of infectious diseases, such as the transmission of infection which were of considerable importance for understanding the dynamics of epidemics.

The Mathematical models are playing an increasingly important role in the analysis and spread of certain infections. A simple model plays a significant role in better understanding the spread of the epidemic.

In this work, we will deal with some Mathematical Models from biology and we will be interested in the questions of the existence and the stability of solutions. Specifically we are interested in three problems of population dynamics. The first concerns the case of a model of a B-cell chronic lymphocytic leukemia model with immune response, the second relates to a model on agroecosystems, and at the end the third is an epidemiological model of coronavirus, the latter is a compartment model. The epidemiological model consists of two parts: compartments and bases. The compartments divide the population into various possible states related to the disease. The rules or bases specify the proportion of individuals who move from one class to another.

Compared to the characteristics of the infection, there are several types of compartments which can be cited such as the S and I compartments, among others also the latent compartment which exists in the case where the infection takes a long time to make the individual infectious. This compartment is usually denoted E "Exposed". However, in this case, we will focus our study on the SEIAR model which models several types of infection. Among these infections is COV-19,which does not have a immunity and which is avoided worldwide.

The models considered are modeled via ordinary differential equations, fractional differential equations and with impulsive differential equations. The mathematical analysis of these models allows it

possible to identify strategies for controlling the disease in order to reduce or eradicate it completely. We now give an overview of the thesis topical arrangement, the work has four chapters and is organized as follows:

The first chapter, entitled "Preliminary", contains a set of definitions and results necessary for the study of systems of ordinary differential equations from the models obtained, which will be useful later.

The second chapter, is entitled "Mathematical analysis of a B-cell chronic lymphocytic leukemia model with immune response". We consider the rather important theoretical question of the equilibria existence and their setabilities, which are based on the publication[9]. In this chapter we have tried to find a suitable meaningful assumptions all model populations are shown to coexist and stable. Where the model is expressed by the set nonlinear system of ordinary differential equations stated below:

$$\begin{aligned}
\frac{dB}{dt} &= b_B + (r - d_b)B - d_{BN}BN - d_{BT}BT \\
\frac{dN}{dt} &= b_N - d_N N - d_{NB}NB \\
\frac{dT}{dt} &= b_T - d_T T - d_{TB}TB + ka_{TH}\frac{B^L}{s + B^L}T_H \\
\frac{dT_H}{dt} &= b_{T_H} - d_{T_H}T_H + a_{TH}\frac{B^L}{s + B^L}T_H.
\end{aligned}$$

Where B represents the cell population of B-CLL while N, T, T_H indicate the three immune responses in the peripheral blood, namely: N the natural killer cells, T the cytotoxic cells and T_H the helper cells.

The third chapter, is entitled "On the stability of periodic solutions of an impulsive system arising in the control of agroecosystems", was the subject of the work of [10]. We are interested in the existence of periodic solutions of impulsive system arising in the modeling of the use of spiders as biological agents against pest crops, and to study their stability. The abstract functional analytic mathematical framework is suitably set up and used for the scope. It is written by the following

impulsive differential equations:

$$\begin{aligned}
\frac{dx_1}{dt} &= rx_1\left(1-\frac{x_1}{W}\right)-cx_2x_1,\\
\frac{dx_2}{dt} &= x_2\left(-a+\frac{kbx_3}{H+x_3}+kcx_1\right),\\
\frac{dx_3}{dt} &= x_3\left(e-\frac{bx_2}{H+x_3}\right),\\
x_1(t_i^+) &= x_1(t_i)\left(1-\frac{h(1-q)}{\alpha}\right),\\
x_2(t_i^+) &= x_2(t_i)\left(1-\frac{hKq}{\alpha}\right),\\
x_3(t_i^+) &= x_3(t_i)\left(1-\frac{hq}{\alpha}\right),
\end{aligned}$$

where $t_{i+1}-t_i=\tau>0, \forall i\in\mathbb{N}$.

The meaning of the variables is as follows:

x_1 represents the insects population living in the woods.

x_2 represents the spiders populations.

x_3 represents the insects having the vineyards as habitat.

We equally study, the stability of the trivial solution, we gave two main results; one is the existence of periodic solutions under suitable conditions, this result is given by the theorems (3.2), (3.4) and (3.5).

The other result is the stability of the non-trivial equilibrium points.

Finally; **The fourth chapter** is entitled "Study and Analysis of a Model for Coronavirus"; is structured in two section dedicated to mathematical modeling and analysis of Model for Coronavirus. The first section we propose and analyze the following ordinary differential model for Coronavirus Spread.

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda-\beta_I S(I+kA)-d_pS,\\
\frac{dE}{dt} &= \beta_I S(I+kA)-(1-\alpha)\omega_pE-\alpha\omega_p'E-d_pE,\\
\frac{dI}{dt} &= (1-\alpha)\omega_pE-(\gamma_p+d_p+\mu)I+\xi A,\\
\frac{dA}{dt} &= \alpha\omega_p'E-(\gamma_p'+d_p+\nu)A-\xi A,\\
\frac{dR}{dt} &= \gamma_pI+\gamma_p'A-d_pR,
\end{aligned}$$

where we denote respectively by $S(t)$, $E(t)$, $I(t)$, $A(t)$,$R(t)$. The susceptible class, the exposed class, the symptomatic infectious class, the asymptomatic infectious class, the removed class. In this section we will give a theoretical analysis of the proposed system, where we will investigate the existence and stability of the steady states of the model. The trivial steady state, describing disease's free dying out, is proven to be globally asymptotically stable when it is the only equilibrium of the system using the following constructed Lyapunov functional

$$P = \frac{1}{2S_0}(S - S_0)^2 + E + \frac{B_T}{[(1-\alpha)\omega_p H_T + D_T \alpha \omega_p']}(H_T I + D_T A),$$

where

$$B_T = (1-\alpha)\omega_p + \alpha\omega_p' + d_p, \quad C_T = \gamma_p + \mu + d_p, \quad D_T = \xi + k(\gamma_p + \mu + d_p), \quad H_T = \gamma_p' + \nu + \xi + d_p.$$

Furthermore, it is shown that a unique non-trivial steady state can appear through a transcritical bifurcation of the trivial steady state. The asymptotic stability of the positive steady state the most biologically meaningful one, is analyzed using the characteristic equation. This study may be helpful in understanding the uncontrolled proliferation of disease in population, then we will carry out preliminary simulations with realistic parameter values.

The work presented in this section has been published in a peer-reviewed journal [11].

In the second section we propose and analyze a mathematical model describing the dynamics of Coronavirus in which the dynamical system is formulated by means of fractional operators. The model equilibria are analysed. We perform a detailed stability analysis of the following fractional-order epidemiological system

$$\begin{aligned}
D^q S(t) &= \Lambda - \beta_I S(I + kA) - d_p S, \\
D^q E(t) &= \beta_I S(I + kA) - (1-\alpha)\omega_p E - \alpha\omega_p' E - d_p E, \\
D^q I(t) &= (1-\alpha)\omega_p E - (\gamma_p + d_p + \mu) I + \xi A, \\
D^q A(t) &= \alpha\omega_p' E - (\gamma_p' + d_p + \nu) A - \xi A, \\
D^q R(t) &= \gamma_p I + \gamma_p' A - d_p R,
\end{aligned}$$

where D^q is the standard Caputo differentiation with $q \in (0,1)$. We recall the definition of the Caputo fractional derivative of order q [24, 39]

$$D^q x(t) = \frac{1}{\Gamma(n-q)} \int_0^t (t-s)^{n-q-1} x^{(n)}(s)\, ds, \qquad n-1 < q < n, \quad n \in \mathbb{N}.$$

The system is completed by the following initial conditions

$$S(0) \geq 0, \quad E(0) \geq 0, \quad I(0) \geq 0,$$

$$A(0) \geq 0, \quad \text{and} \quad R(0) \geq 0.$$

The existence, uniqueness, non-negativity and boundedness of the solutions of a fractional order epidemiological model are also performed. Afterwords, we consider the following Lyapunov function

$$V_0(S, E, I, A) = \left(S - S_0 - S_0 \ln \frac{S}{S_0}\right) + E + \frac{B_T}{[(1-\alpha)\omega_p H_T + D_T \alpha \omega_p']}(H_T I + D_T A).$$

and use Lemma of [30] we obtain a sufficient condition for the global asymptotic stability of the trivial steady state,

The asymptotic stability of the positive steady state, the most biologically meaningful one, is analyzed using the characteristic equation and Matignon's condition. Moreover, we have confirmed the analytical results by numerical simulations.

The theoretical results indicate that their stability behavior is the same as for the corresponding system formulated via standard derivatives. This suggests that, at least in this case for the model presented, the memory effects contained in the fractional operators apparently do not seem to play a relevant role. The numerical simulations instead reveal that the order of the fractional derivative has a definite influence on both the equilibrium population levels and the speed at which they are attained.

The work presented in this section has been published in a peer-reviewed journal [12].

Then we will give an appendix on the methods used and a conclusion of the work carried out. We end this thesis with a bibliography.

Chapter 1

Preliminaries

In this chapter, we review some analysis results that we will use most often in the rest of the thesis. These results are classical and we will can find the proof of this in most of the books dealing with these questions.

1.1 Generality on the differential equations

First of all, we shall consider the following system of ordinary differential equation:

$$\begin{cases} \dot{x} = f(t,x); & (t,x) \in \Omega = I \times U, \\ x(t_0) = x_0. \end{cases} \tag{1.1}$$

Where $\Omega = I \times U$ be an open set of $\mathbb{R}^+ \times \mathbb{R}^n$ and $f : \Omega = I \times U \to \mathbb{R}^n$ is a given function.

Definition 1.1. ***[Solution]***[60]

The solution of (1.1) on the interval $I \subseteq \mathbb{R}$ is a derivable fonction $x : I \to \mathbb{R}^n$ such that

(i) $\forall t \in I; \quad (t, x(t)) \in \Omega,$

(ii) $\forall t \in I; \quad \dot{x}(t) = f(t, x(t)).$

If the function f does not depend on t, then equation(1.1) is called a **autonomous** differential equation.

Let now $x(t, t_0, x_0)$ denotes a solution $x(t)$ of the system (1.1), such that $x(t_0) = x_0$.

Theorem 1.1. ***Arzela- Péano****[60]*

If f is continuous function, Then for any $(t_0, x_0) \in I \times U$ there is at least one maximal solution $x(t, t_0, x_0)$ of systeme (1.1) defined on $I(x_o) \subseteq I$.

Theorem 1.2. ***Carathéodory****[60]*

Let $f : I \times U \to \mathbb{R}^n$ such that :

(i) for almost all t, $\psi_t : x \in U \mapsto f(t, x)$ is continuous,

(ii) for each $x \in U$, $\varphi_x : t \in I \mapsto f(t, x)$ is mesurable,

(iii) for each compact K of U, ther is a mapping $m_K : I \to \mathbb{R}^+$ integrable on I such that :

$$\forall (t, x) \in I \times K, \qquad |f(t, x)| \leqslant m_K(t).$$

In this case the system:

$$\dot{x} = f(t, x), \quad t \in I,$$

is called system of Carathéodory. Then for all $(t_0, x_0) \in I \times U$ there is at least one solution $x(t, t_0, x_0)$ defined for almost all t.

Definition 1.2. *[68]Let E be an open subset of $\mathbb{R}^n$. A function $f : E \to \mathbb{R}^n$ is said satisfy a Lipschitz condition on E if there is a positive constant C such that for all $x, y \in E$,*

$$|f(x) - f(y)| \leq C|x - y|.$$

the function f is said to be a locally Lipschitz on E if for each point $x_0 \in E$ there is an neighorhood $N_\varepsilon(x_o)$ of x_o and a constantet $C_0 > 0$ such that for all $x, y \in N_\varepsilon(x_o)$,

$$|f(x) - f(y)| \leq C_0|x - y|.$$

Theorem 1.3. ***Cauchy-Lipschitz****[32]*

Let $U \subset \mathbb{R}^n$ be an open set, if $f : I \times U \to \mathbb{R}^n$ is continuous and $f \in Lip_x(I \times U)$,then for each $(t_0; x_0) \in I \times U$, there existe $\delta > 0$ such that the problem (1.1) has a unique solution defined on $[t_0 - \delta, t_0 + \delta] \subset I$.

Remark 1.1. *[68] If $f \in \mathrm{C}^1(\Omega)$, then f is locally Lipschitz on E. moreover, if $f \in C^k(\Omega)$ then the solution of initial value problem "said probleme of Cauchy" is C^{k+1}.*

Definition 1.3. ***[The flow defined by a differential equation]***[68]

Let E be an open subset of $\mathbb{R}^n$ and let $f \in C^1(E)$. For $x_o \in E$, let $\phi(t, x_o)$ be the solution of the initial value problem (1.1) defined on its maximal interval of existence $I(x_o)$. Then for $t \in I(x_o)$, the mapping ϕ_t defined by

$$\phi_t = \phi(t, x_o),$$

is called the flow of differential equation (1.1) or the flow defined by the differential equation (1.1); ϕ_t is also referred to as the flow of the vector field $f(x)$.

Remark 1.2. *[68] The mapping $\phi : J \to \mathbf{R}^m, t \to \phi(t, x_0)$, defines a solution curve or trajectory of the system (1.1) through the point $x_0 \in E$.*

Theorem 1.4. *[68] Let E be an open subset of $\mathbb{R}^n$ and let $f \in C^1(E)$. Then for all $x_0 \in E$, if $t \in I(x_o)$ and $s \in I(\phi_t(x_o))$, it follows that $s + t \in J(x_0)$ and $\phi_{s+t}(x_0) = \phi_s(\phi_t(x_0))$.*

1.2 Generality on dynamic systems

A dynamic system is a mathematical model written by a set of differential equations, which simulates a phenomenon that evolves in over time noted t. It consists of time-dependent variables called dynamic variables of the system, let us note them by $x_i(t)$ with $i = 1, 2, ..., n$. t being the independent variable of the system and n being the number of dynamic variables, also called dimension of the system.

Below we will need the following definitions and notations:

Definition 1.4. *[68]*

Let $x = (x_1, x_2, \cdots, x_n) \in \mathbb{R}^n, A = (a_{ij}) \in \mathcal{M}_n(\mathbb{R})$

- *A vector x, (resp a matrix A) is said strictly positive, and denote $x \gg 0$ (resp $A \gg 0$), if for all $i, 1 \leq i \leq n, x_i > 0$ (resp for all $i, j, 1 \leq i \leq n, 1 \leq j \leq n, a_{ij} > 0$).*
- *A vector x, (respa matrix A) is said positive,and denote $x > 0$ (resp $A > 0$), if for all $i, 1 \leq i \leq n, x_i \geq 0$; and there is at least one i such that $x_i = 0$ (resp for all $i, j, 1 \leq i, j \leq n, a_{ij} \geq 0$ and there is at least one (i, j) such that $a_{ij} = 0$.*

Definition 1.5. *[68][Continuous-time dynamic system]*

A Continuous-time dynamic system on set Ω*, is a family of mappings* $\{\phi_t; t \in \mathbb{R}_+\}$*, set either by the set* $\mathbb{R}_+$*, either by* $\mathbb{R}$*, and satisfies the following properties :*

1. *Aach mapping* ϕ_t *is defined on subset* U_t *of* Ω *with values in* Ω*,*
2. *The mapping* ϕ_0 *defined on* Ω *is the identity map* (id_Ω)*,*
3. *If* $0 \leq t_1 \leq t_2$*, then* $U_{t_2} \subset U_{t_1}$*,*
4. *Let* t *and* s *two elements of* $\mathbb{R}_+$*,(or* $\mathbb{R}$ *). Let* $x \in U_s$*; then* $\phi_s(x)$ *is an elemnt of* U_t *iff,* x *is an elemnt of* U_{s+t} *and, when this is the case, we have*

$$\phi_t\left(\phi_s(x)\right) = \phi_{s+t}(x).$$

The Ω is called phase portrait of the dynamic system.

Autonomous Systems

Let Ω be a subset of $\mathbb{R}^n$. Let us consider the autonomous differential equation defined by

$$\dot{x} = X(x). \tag{1.2}$$

We suppose that $X : \Omega \subset \mathbb{R}^n \to \mathbb{R}^n$ is continuous and satisfied with conditions such as a solution of the system (1.2) exists at all points and unique.

The equilibrium points of the system (1.2) are the points $x_0 \in \Omega$ satisfying $X\left(x_0\right) = 0$. For each $x \in \Omega$, we denote by $X_t(x)$ the solution of (1.2) satisfynig $X_0(x) = x$, and we assume that X satisfies the conditions such that $X_t(x)$ is continuous in (t, x).

Definition 1.6. ***[Trajectory, Orbit]***[68]

– *We call the trajectory of a point* x *of* Ω *the mapping* $X_x : t \longmapsto X_t(x)$*.*

– *We call the orbit of a point* x *of* Ω *the set* $\gamma_x = \{X_t(x), t \in \mathbb{R}\}$ *of phase portrait.*

– *The orbit of a* x *of* Ω *is said to be periodic if* x *is not a equilibrium point and there is a* $T \in \mathbb{R}$*, such that* $X_T(x) = x$*,then we say that* T *is a period of the periodical orbit considered.*

Definition 1.7. *[68] We call the positive orbite $\gamma^+(x_0)$ from x_0 the set*

$$\{x(t, x_0); t \geq 0\}.$$

Definition 1.8. ***[Basin of attraction of a equilibrium point]***[68]

Let $x_0 \in \Omega$ be an equilibrium point of systeme (1.2).

− We call Basin of attraction of a point $x_0 \in \Omega$ the set of the elements $x \in \Omega$ such that for all $t \in \mathbb{R}, X_t(x)$ to be defined and that

$$\lim_{t \to +\infty} X_t(x) = x_0.$$

− We call Basin of replusion of a point $x_0 \in \Omega$the set of the elements $x \in \Omega$ such that for all $t \in \mathbb{R}_-, X_t(x)$ to be defined and that

$$\lim_{t \to -\infty} X_t(x) = x_0.$$

Definition 1.9. ***[Invariant set]***[68]

A set K of Ω is said to be positively (resp. negatively) invariant relative to (1.2) if $x(t, K) \subset K$ for all $t \geq 0$ (resp $t \leq 0$), in addition K is said to be invariant if $x(t, K) = K$ for all t.

Definition 1.10. ***[Monotonous dynamic system]***[68]

Let be a dynamic system whose flow is $\phi_t : x \mapsto \phi_t(x)$ This dynamic system is said to be monotone if it is defined on an ordered metric space and if it has the following property

$$t \geq 0, x \leq y \Rightarrow \phi_t(x) \leq \phi_t(y).$$

It is said to be strongly monotone if

$$t \geq 0, x < y \Rightarrow \phi_t(x) \ll \phi_t(y).$$

1.3 Notion of Stability and Equilibrium Point

1.3.1 Steady State

An equilibrium state of a dynamic system is an invariant state, i.e.such that if at the initial instant the system is in this state then it will remain there as long as it is not perturbed.

Definition 1.11. *[38] [60]*

A point $x^* \in U$ is called an equilibrium point or critical point of (1.1) if

$$\forall t \in I; \quad f(t, x^*) = 0,$$

without loss of generality we will can always consider the equilibrium at 0.

1.3.2 Notion of Stability

Definition 1.12. *[38] [60]*

An equilibrium point x^* of system (1.1) is stable if $x(t, t_0, x_0)$ is defined for $t \geq t_0$ and for all $\epsilon > 0$, and $t_0 \in I$, there is a $\delta(\epsilon, t_0) > 0$ such that :

$$(x_0 \in B_{\delta(\epsilon,t_0)}(x^*)) \Longrightarrow x(t, t_0, x_0) \in B_\epsilon(x^*) \qquad \forall t \geq t_0.$$

Definition 1.13. *[38] [60]**[Unstablity]***

The equilibrium point $x*$ is unstable if it is not stablefor the system (1.1).

Asymptotically Stable

Definition 1.14. *[60]*

*An equilibrium point x^* is **attractif** for the system (1.1) if for all $t_0 \in I$, $x(t, t_0, x_0)$ is defined for $t \geq t_0$ and there is a $\delta(t_0) > 0$ such that :*

$$(x_0 \in B_{\delta(t_0)}(x^*)) \Longrightarrow \lim_{t \to +\infty} d(x(t, t_0, x_0), x^*) = 0.$$

Definition 1.15. *[60]*

The equilibrium point x^* is asymptotically stable for (1.1) if:

1. *x^* is **stable** for (1.1),*
2. *x^* is **attractif** for (1.1).*

Definition 1.16. *[38] [60]*

*We say that the x^* is **globalement asymptotiquement stable** for the system (1.1) if:*

1. *x^* is **stable** for the system (1.1),*
2. *for all $t_0 \in I$, and $x_0 \in U$, $x(t, t_0, x_0)$ is defined for all $t \geq t_0$ and $\lim_{t \to +\infty} d(x(t, t_0, x_0), x^*) = 0$.*

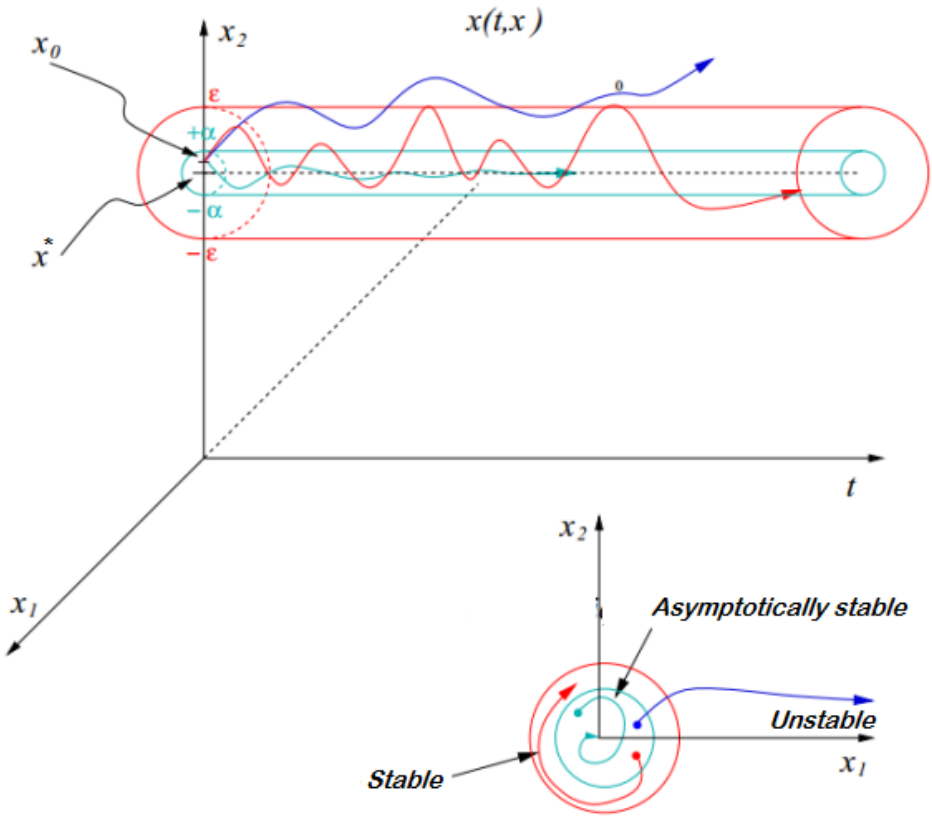

Figure 1.1: Stability of the equilibrium point x^*

1.4 Global and local stability of differential systems

If we compare the possible behaviors in the case of linear and nonlinear systems, we notice that the dynamic behaviors of nonlinear systems are much more complicated, with a much larger range. For example, talking about the stability of equilibrium or the stability of the system amounts to the same thing in the linear case, since we can confuse local stability with global stability. On the other hand, in the case of a nonlinear system the study of the stability of an equilibrium point in the most complete form consists not only in determining the nature of the point of equilibrium or its asymptotic stability but also to determine the domain of attractif, that is to say the set of initial conditions whose solutions converge towards equilibrium. Thus, we speak of local or global stability or instability, local stability signifying the convergence of solutions with close initial conditions, while global instability means divergence of solutions.

1.4.1 Local stability of differential systems

1.4.1.1 The linear case

Let the following linear autonomous differential equation:

$$\dot{x} = f(x) = Ax, \qquad x \in \mathbb{R}^n.\ A \in \mathcal{M}_{n\times n}(\mathbb{R}^n). \tag{1.3}$$

Definition 1.17. *[68][Hyperbolic equilibrium point]*

- *A point $x^* \in R^n$ is called an equilibrium point or critical point of (1.3) if $f(x^*) = 0$.*
- *An equilibrium point x^* is called a hyperbolic equilibrium point of(1.3) if none of the eigenvalues of the matrix $Df(x_0)$ have zero real part.*
- *The linear system (1.3) with the matrix $A = Df(x_0)$ is called the linearization of (1.3) at x_0.*

Remark 1.3. *[68]*
Note that if $x^*$is an equilibrium point of (1.3) and $\phi_t : E \to R^n$ is the flow of the differential equation(1.1), then $\phi_t(x^*) = x^*$ for all $t \in \mathbb{R}$. Thus, x^* is called a fixed point of the flow ϕ_t; it is also called a zero, a critical point, or a singular point of the vector field $\mathrm{f} : \mathbb{R} \to \mathbb{R}^n$.

Definition 1.18. ***[Classification of the equilibrium points]***[68]

- *An equilibrium point $x^*$of (1.3) is called a sink if all of the eigenvalues of the matrix $Df(x^*)$ have negative real part.*
- *it is called a source if all of the eigenvalues of $Df(x^*)$ have positive real part.*
- *it is called a saddle if it is a hyperbolic equilibrium point and $Df(x^*)$ has at least one eigenvalue with a positive real part and one with a negative real part.*

Remark 1.4. *[32]*
– The origin is always an equilibrium of (1.3), but there may be others: all of $KerA$ is an equilibrium.
– The stability of any equilibrium point of (1.3) is determined by the signs of the real parts of the eigenvalues λ of the mattix A. We recall that the solution of the system is $x(t) = e^{tA}x(0)$.

Theorem 1.5. *[32]*

- *The origin is asymptotically stable of* (1.3) *iff all the eigenvalues of A have strictly negative real part.*
- *If A has at least a strictly positive real part eigenvalue, then the origin is unstable.*

The affine case

We consider an affine vector field $f(x) = Ax + b$ on $\mathbb{R}^n$, where $A \in \mathcal{M}_{n\times n}(\mathbb{R}^n)$ to be a matrix and $b \in \mathbb{R}^n$ to be a vector.
An equilibrium of equation

$$\dot{x}(t) = Ax(t) + b,$$

is a point x^* wich satisfies $Ax^* + b = 0$ (note that the point only exists if $b \in ImA$). By replacing b with$-Ax^*$, we rewrite the differential equation in the form

$$\frac{d}{dt}(x(t) - x^*) = A(x(t) - x^*).$$

Thus the stability and asymptotically stability of an equilibrium of the affine equation $\dot{x} = Ax(t) + b$ are equivalent respectively to those of the origin for the linear equation $\dot{y}(t) = Ay(t)$. such that $y(t) = x(t) - x^*$

1.4.1.2 The nonlinear case

Let x^* be a equilibrium of $\dot{x}(t) = f(x(t))$. The next two theorems proved that the study of the eigenvalues of the matrix $Df(x^*)$ generally allows to characterize the stability of the equilibrium.

Theorem 1.6. *[32]*
If all the eigenvalues of $Df(x^*)$ are the strictly negative real part, then x^* is an asymptotically stable equilibrium.

Remark 1.5. *[32] Unlike the case of linear equations, the condition given in this theorem is sufficient but not necessary.*

Theorem 1.7. *[32]*
If $Df(x^*)$ has at least one strictly positive real part eigenvalue, then the equilibrium x^* is unstable.

1.4.2 Globale stability

To see the stability of the origin, a method consists is to calculate the solution of the system and then to check if the stability properties given previously are assured, in this case we notice that the use of the definition of stability represents certain disadvantages such as:
-The calculation of the explicit solution: that can present great difficulties depending on the complexity of the model considered and the dimension of the system.
-Direct application of definition: where it is difficult to determine.
In this case the method of **Lyapunov**allows to study the global stability of the systems without having recourse to the computation of the explicit solution of the nonlinear differential equations. The procedure consists in finding a function called Lyapunov function and examining its time derivative of the function evaluated along any trajectory of the system considered. we presented in the following the main results related to this method which are essentially inspired by [60],[26],[32],[38],[34],[35].

1.4.2.1 Lyapunov's methods

Lyapunov's functions play a big role in the study of the stability of dynamic systems. This section is devoted to some results Lyapunov's methods.
Let $V : \Omega \subset \mathrm{R}^n \to \mathrm{R}$ be a continuous function.

Definition 1.19. *[50]*

- *The function V is said to be positive-definite if $V(x_0) = 0$ and $V(x) > 0$ in a neighborhood Ω_0 of x_0 for each $x \neq x_0$ in this neighborhood.*
- *The function V is said to be negative-definite if $-V$ is positive-definite.*
- *The function V is said to be semi-positive if $V(x_0) = 0$ and $V(x) \geq 0$ in a neighborhood Ω_0 of x_0.*

Definition 1.20. ***[Lyapunov's functions]****[50]*
A function $V : \Omega \to \mathbb{R}^+$ is said to be Lyapunov's function Lyapunov of system (1.2) if it decreases along the trajectories of the system.
If $V \in C^1$,that is to say that its derivative $\dot{V}$ along the system (1.2) is negative Ω, i.e, $\dot{V}(x) \leq 0$ for each $x \in \Omega$

Theorem 1.8. ***[Lyapunov's theorem 1892]***[50]

1. *If the function V is positive-definite and the time derivative $\dot{V}$ such that*

$$\dot{V}(x) = \frac{\partial V(x)}{\partial x} f(x) = \sum_{i=1}^{n} \frac{\partial V(x)}{\partial x_i} \cdot f_i(x)$$

is semi negative-definite on Ω, then the equlibrium point x_0 is stable for the system (1.2).

2. *If the function V is positive- definite and the time derivative $\dot{V}$ is negative-definite Ω, then x_0 is asymptotically stable of(1.2).*

This theorem prove that to show that an equilibrium point x_0 is stable, it suffices to find a Lyapunov function at this point. Furthermore, to use Lyapunov's theorem to show the asymptotic stability of a given system, we must determine a positive definite V function whose the derivative $\dot{V}$ is defined negative. In the general case, this is not obvious. The condition on the derivative $\dot{V}$ can be alleviated using the LaSalle principle which will be given in the following.

1.4.2.2 LaSalle's Invariance principe

Theorem 1.9. ***[Invariance principe]***[49],[50],[48]

Let Ω be any subset of $\mathbb{R}^n$; assume that Ω be an open positively invariant of (1.2) at x_0.

Let $V : \Omega \to \mathbb{R}$ be a function in C^1 for the system (1.2) at x_0 such that:

1- $\dot{V} \leq 0$ on Ω,

2- Let $E = \{x \in \Omega | \dot{V}(x) = 0\}$ and M the largest invariant set and contained in the set E. Then, any bounded solution starting in Ω tends to the set M when time tends to infinity.

This theorem is a very important tool for systems analysis, Unlike Lyapunov's theorems, LaSalle's principle does not require the function $V(x)$ to be positive definite. If the largest invariant set M, contained in the set E of points where $\dot{V}$ vanishes, is reduced to the equilibrium point, i.e. if $M = \{x_0\}$, the LaSalle's principle allows to conlude that the equilibrium is attractive. But a drawback of LaSalle's principle, when significant, is that it proves only the attractivity of the equilibrium point. It is well known that in the nonlinear case attractivity does not imply stability. But when the function

V is not positive definite, Lyapunov stability must be proven. This is why LaSalle's principle is often misquoted. Some additional condition enables, with LaSalle's principle, to ascertain asymptotic stability. When we want to establish the asymptotic stability of an equilibrium point x_0 of Ω, we use the following corollary which is a consequence of the LaSalle invariance principle.

Corollary 1.1. *[49] Let Ω be any subset of $\mathbb{R}^n$; assume that Ω be an open positively invariant of autonomous system of (1.1) at x_0.*
Let $V : \Omega \to \mathbb{R}$ be a positive definite function and in class C^1 for the autonomous system of (1.1) at x_0 such that

- *$\dot{V} \leq 0$ on Ω,*
- *Let $E = \{x \in \Omega | \dot{V}(x) = 0\}$,*
- *Suppose that the largest positively invariant set contained in E is reduced to the point x_0.*

Then x_0 is an asymptotically stable equilibrium point for the system (1.2).

Corollary 1.2. *Under the hypotheses of the previous theorem, if the set M is reduced to the point $x_0 \in \Omega$, then x_0 is a globally asymptotically stable equilibrium point for the system (1.2) defined on Ω.*

1.4.3 Routh-Hurwitz Criterion and Descartes Rule of Signs

In many cases, the determination of eigenvalues is not obvious. Thus, we will give some methods and criterion which do not require the exact knowledge of the eigenvalues. This is the Routh-Hurwitz criterion for local stability, and finally, we will give the Descartes's Rule of Signs, which allows to know the sign of the roots of the characteristic polynomial without specifying them.

1.4.3.1 Routh-Hurwitz Criterion

The Routh-Hurwitz criterion [37], [73] allows to determine a necessary and sufficient condition for that a polynomial admits all its roots in the open left half-plane.

Definition 1.21. *[37] We call Hurwitz-polynomial, a real polynomial which has all its roots in the left half-plane*

Let us consider the characteristic polynomial $P(\lambda)$ of $Df(x^*)$

$$P(\lambda) = a_n\lambda^n + a_{n-1}\lambda^{n-1} + \cdots + a_0.$$

λ^n	a_n	a_{n-2}	a_{n-4}	$\dots$	a_2	a_0		$\dots$	a_3	a_1
λ^{n-1}	a_{n-1}	a_{n-3}	a_{n-5}	$\dots$	a_1			$\dots$	a_2	a_0
λ^{n-2}	b_{n-2}	b_{n-4}	b_{n-6}	$\dots$	n	even			n	odd
λ^{n-3}	c_{n-3}	$\dots$	$\dots$	$\dots$				$\dots$		
$\vdots$	$\vdots$	$\vdots$						$\vdots$		
λ^1	$\dots$	$\dots$		$\dots$				$\dots$		
λ^0	$\dots$	$\dots$		$\dots$				$\dots$		

The first line of the table is called the pivot-line. It contains the coefficients of the terms in p^{n-2k} in order of decreasing powers..

The second line contains the coefficients of the terms in $p^{n-1-2k}$and ends according to parity of n.

The remaining lines are filled using the following formulations:

$$b_{n-2} = \frac{-1}{a_{n-1}}\begin{vmatrix} a_n & a_{n-2} \\ a_{n-1} & a_{n-3} \end{vmatrix}, \quad b_{n-i} = \frac{-1}{a_{n-1}}\begin{vmatrix} a_n & a_{n-i} \\ a_{n-1} & a_{n-i-1} \end{vmatrix}$$

$$c_{n-3} = \frac{-1}{b_{n-2}}\begin{vmatrix} a_{n-1} & a_{n-3} \\ b_{n-2} & b_{n-4} \end{vmatrix}, \quad c_{n-i} = \frac{-1}{b_{n-2}}\begin{vmatrix} a_{n-1} & a_{n-i} \\ b_{n-2} & b_{n-i-1} \end{vmatrix}$$

If necessary an empty box is taken equal to zero.

The row calculation continues until the first column is completed.

Criterion 1.1. *[37], [73]**[Routh-Hurwitz]***

The system is stable if and only if all the terms of first column L *are strictly positive.*

Remark 1.6. *[37], [73]*

1. *There are as many roots with positive real part as sign changes in the first column.*

2. *the appearance of lines of zeros indicates the existence of pure imaginary roots. In this case, corresponding to an oscillating system, an continues the table by replacing the null line by the coefficients obtained by deriving the polynomial reconstructed from the upper line, the pure imaginary roots being the imaginary roots of this reconstituted polynomial .*

1.4.3.2 Descartes' Rule of Signs

Descartes' Rule of Signs provides information about the number and location of the real zeros of a polynomial function written in standard form.

Theorem 1.10. ***[Number of Real Zeros]***[27]
A polynomial function cannot have more real zeros than its degree.

Let us consider a polynomial of degree n with real coefficients:

$$P(x) = a_0 + a_1x + a_2x^2 + \ldots + a_nx^n, a_n \neq 0 \tag{1.4}$$

The Descartes' Rule applies when the polynomial $P(x)$ is ordered by increasing or decreasing powers as in (1.4). Two successive non-zero coefficients a_k form a permanence if they are of the same sign, and a variation if they are of opposite signs. Descartes' criterion then specifies:

Theorem 1.11. ***[Descartes' Rule of Signs]***[27]
Let P denote a polynomial function written in standard form (descending powers of x).

1. *The number n_rp of positive real zeros of P either equals the number of variations in the sign of the nonzero coefficients of $P(x)$ or else equals that number less an even integer.*

2. *The number of negative real zeros of P either equals the number of variations in the sign of the nonzero coefficients of $P(-x)$ or else equals that number less an even integer.*

So for
$P_1(x) = -x^5 - x^3 - 2x^2 + 1$, we have $V = 1$, then $n_p = 1$.
$P_2(x) = x^5 - x^3 + 7x^2 - 2x - 3$ donne $V = 3$, then $n_p = 1$ or 3.
Of course the same criterion can apply to <the equation to opposites> for which $y = -x$ and thus give indications on the number n_{rn} of the negative real roots of the equation (1.4) from the number V_n of the variations of the corresponding polynomial $Q(y)$

$$P(-x) = Q(y) = a_0 - a_1y + a_2y^2 - a_3y^3 + \ldots. + (-1)^n a_n y^n.$$

Which leads to $V_n = 2$ and so $n_{rn} = 2$ or 0 for the polynomial $P_1(x)$, and to $V_n = 2$, so $n_{rn} = 0$ or 2 for the polynomial $P_2(x)$. We will notice that $V + V_n = n$ in the general case where the coefficients a_k are all non-zero Since there are in total n roots for an equation of degree n, Descartes' criterion then gives no indication on complex roots.

Proposition 1.1. *[27] If all the coefficients of P are strictly positive then P does not have a positive root.*

Criterion 1.2. *[27]If all the coefficients of P are non-zero and of alternating sign then P does not admit a negative root.*

Proposition 1.2. *If there is a variation of the coefficients of P then P has at least one positive root.*

1.4.3.3 Used of the second additive compound matrix

This method is very useful when the equilibrium point x^* is not known explicitly. And like the Routh-Hurwitz criterion, it does not require an exact knowledge of the eigenvalues of the Jacobian to conclude on stability.

Lemma 1.1. *[51] A matrix A of order n is stable if and only if:*

1.) The second additive compound matrix $A^{[2]}$ is stable

2.) $(-1)^n \det(A) > 0$

Generally, to avoid the eigenvalue calculations of $A^{[2]}$, this result is combined with the theorem of **Gershgorin**, which we recalled in the Appendix with an application.

Chapter 2

Mathematical analysis of a B-cell chronic lymphocytic leukemia model with immune response

2.1 Introduction

In [64] a thorough study of B-cell chronic lymphocytic leukemia (B-CLL) has been undertaken by means of a highly nonlinear mathematical model based on ordinary differential equations. The relevance of this investigation is apparent from the realistic situations that have been scrutinized via numerical simulations, based on published data of B-CLL patients.

While there is nothing to add to this comprehensive study from the applicative point of view, in this short chapter we would reconsider the model to tackle one issue that is still missing in the analysis of [64]. Specifically, we consider a rather important theoretical question, namely the issue of the equilibria existence of the mentioned model. This point has not been addressed in [64] and although the simulations show the validity of the statement, from the mathematical point of view, something is still lacking.

In this chapter we fill the gap, by providing a proof showing that all the model populations can always coexist, under suitable and meaningful assumptions.

The chapter is organized as follows. The mathematical model is briefly summarized in Section 2.2. In the following Section 2.3, its coexistence equilibrium is analytically found with an explicit form

for almost all its components, while one of the populations appears to be the root of an algebraic equation. Section 2.4 further characterizes this coexistence equilibrium, by providing its local stability analysis.

2.2 Mathematical model

For the benefit of the reader, we summarize here the basic model presented in [64].

The cell population of B-CLL is denoted by B while N, T, T_H indicate the three immune responses in the peripheral blood, namely:
The natural killer cells N that are not B-CLL-specific, which are present in the body at all times.
The cytotoxic T cells, e.g., $CD8^+T$, which respond specifically to the B-CLL.
The helper cells T_H which are part of the specific immune response. The latter assume an essential role in
the recruitment, proliferation and
activation of cytotoxic T cells.

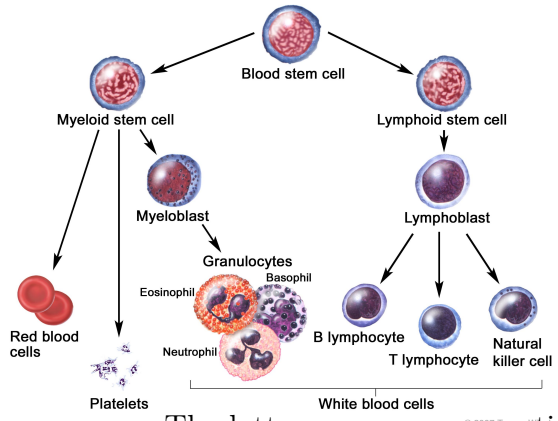

Figure 2.1: Blood cancer camily Tree [93]

These different populations are all measured by their concentrations expressed in units of cells per microliter (μl). Time is denoted by t and measured in days. The model is fully described in [64]. We just outline here the basic relationships between the various compartments and refer the reader to the above paper for a fuller description.
Basically, the first equation models the B-CLL dynamics originating the disease. These cells are mainly produced by bone marrow, can replicate, die naturally and, when detected, are killed by the immune response of the organism, which is performed by the N and T cells. The second equation translates the fact that the natural killer cells are produced in the body continuously at a constant rate, die naturally and become deactivated once they attack the B-CLL cells. The citotoxic T cells, described in the third equation, are the specific response of the organism to the B-CLL cells: they also are constantly produced, die and are deactived upon killing the B cells, but are also produced

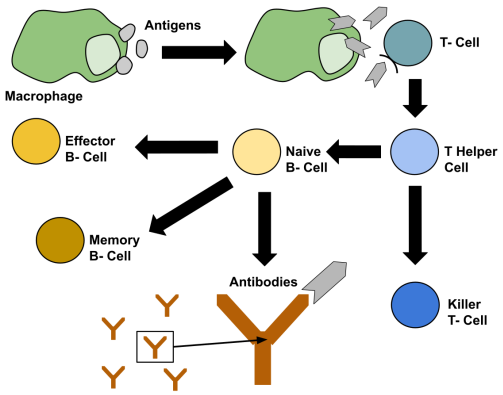

Figure 2.2: B-cell activation lymphocytic [93]

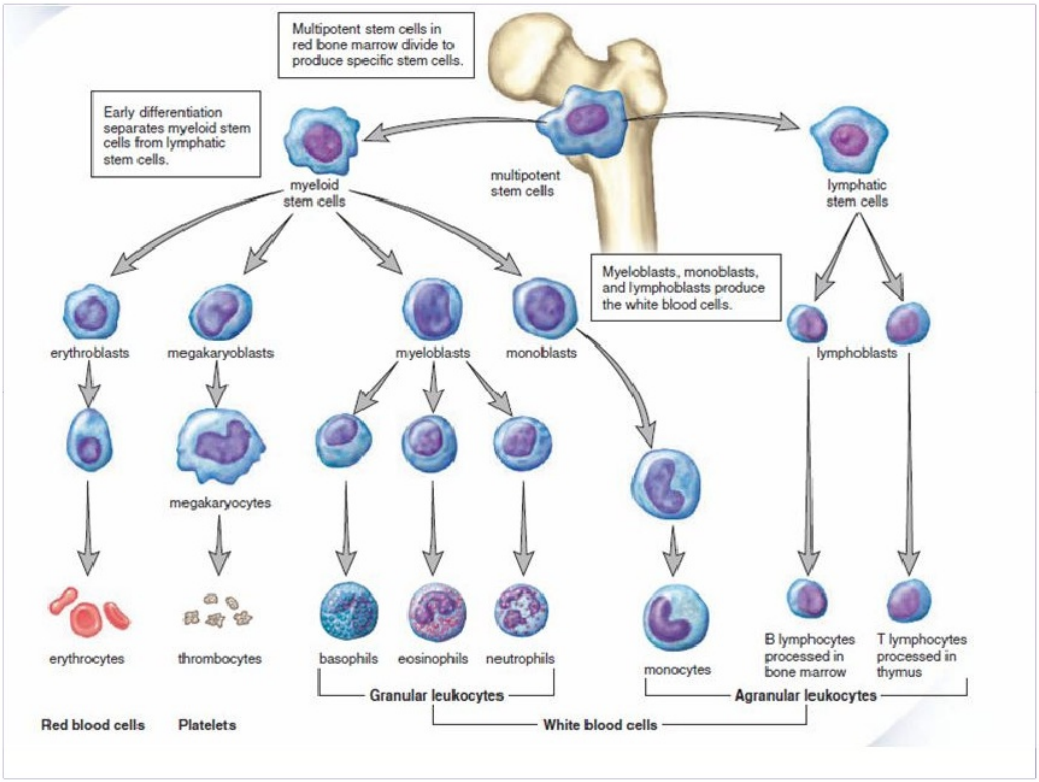

Figure 2.3: Blood Cells. Red Blood Cells. White Blood Cells[94]

by the activated helper cells. This mechanism is modeled via a saturating sigmoid function, whose shape is described by the integer parameter $L \in \mathbf{Z}_+$. This response of the T_H cells is triggered when they encounter the B-CLL cells. A fraction k of this production rate results also in new T cells. The T_H helper cells dynamics is written in the fourth equation. Beside the above triggering boosting,

they are also continuously produced at a constant rate and experience natural mortality. Based on the above assumptions, the mathematical translation of the system dynamics just described thus is expressed by the set nonlinear system of ordinary differential equations stated below:

$$\frac{dB}{dt} = b_B + (r - d_b)B - d_{BN}BN - d_{BT}BT \tag{2.1}$$

$$\frac{dN}{dt} = b_N - d_N N - d_{NB}NB \tag{2.2}$$

$$\frac{dT}{dt} = b_T - d_T T - d_{TB}TB + ka_{TH}\frac{B^L}{s + B^L}T_H \tag{2.3}$$

$$\frac{dT_H}{dt} = b_{T_H} - d_{T_H}T_H + a_{TH}\frac{B^L}{s + B^L}T_H. \tag{2.4}$$

The parameters are all assumed to be positive and their meaning is defined in Table 2.1. Specific assumptions on some of the parameters are

$$d_{BT} \ll 1, \quad r > d_B. \tag{2.5}$$

2.3 Coexisting Equilibrium

In view of the fact that there are constant source terms in (2.1)-(2.4), no equilibrium with any vanishing compartment can exist. Therefore the model can possibly have only the equilibrium point at which all populations have a constant nonvanishing value. The study of this equilibrium, $E^*(B^*, N^*, T^*, T_H^*)$, is indeed our main goal in this chapter.

To evaluate it, we need to satisfy the equilibrium equations, which are obtained from (2.1)-(2.4) by setting the derivatives to zero. The resulting algebraic equations give three of the variables in terms of the fourth one, which here is taken to be the B-CLL cells concentration B. Namely, solving the equations (2.2), (2.3), (2.4) we find:

$$N^* = \frac{b_N}{d_N + d_{NB}B^*}, \quad T_H^* = \frac{(b_{T_H})(s + B^{*L})}{B^{*L}(d_{T_H} - a_{T_H}) + sd_{T_H}},$$

$$T^* = \frac{B^{*L}[b_T(d_{T_H} - a_{T_H}) + ka_{T_H}b_{T_H}] + sb_T d_{T_H}}{(d_T + d_{TB}B^*)[B^{*L}(d_{TH} - a_{T_H}) + sd_{T_H}]}. \tag{2.6}$$

Table 2.1: Model parameters and their meaning

b_B	constant source rate of B-CLL produced by bone marrow
r	replication rate of the leukemic B cells
d_B	natural mortality rate of the leukemic B cells
d_{BN}	killing rate of B-CLL cells by N cells
d_{BT}	killing rate of B-CLL cells by T cells
b_N	constant source rate of N cells
d_N	mortality rate of N cells
d_{NB}	deactivation rate of N cells by contact with B-CLL cells
b_T	constant production rate of T cells
d_T	natural mortality rate of T cells
d_{TB}	T cells activity suppression rate by contact with B-CLL cells
k	fraction of T_H cell activation that results in T cells recruitment
a_{TH}	maximal T_H cells activation rate by contact with B-CLL cells
b_{T_H}	constant production rate of T_H cells
d_{T_H}	natural mortality rate of T_H cells
s	half saturation constant
L	parameter shaping the saturating sigmoid response

Now, substituting these values of N^*, T^*, T_H^* into the first equation of the system (2.1) and simplifying we obtain the following equation:

$$\alpha_{L+3}B^{*L+3} + \alpha_{L+2}B^{*L+2} + \alpha_{L+1}B^{*L+1} + \alpha_L B^{*L} + \alpha_3 B^{*3} + \alpha_2 B^{*2} + \alpha_1(B^*) + \alpha_0 = 0 \qquad (2.7)$$

where the coefficients are explicitly known:

$$
\begin{aligned}
\alpha_{L+3} &= (r-d_B)d_{NB}d_{TB}(d_{T_H}-a_{T_H}),\\
\alpha_{L+2} &= (d_{T_H}-a_{T_H})[b_B d_{NB}d_{TB}+(r-d_B)(d_N d_{TB}+d_{NB}d_T)],\\
\alpha_{L+1} &= (d_{T_H}-a_{T_H})[b_B(d_N d_{TB}+d_{NB}d_T)+(r-d_B)d_N d_T+d_{BN}d_{TB}b_N-d_{BT}d_{NB}b_T]-kd_{NB}d_{TB}b_{T_H}a_{T_H},\\
\alpha_L &= (d_{T_H}-a_{T_H})b_B d_N d_{TB}+(d_{T_H}-a_{T_H})[b_N d_{BN}d_T-d_{BT}d_N b_T]-kd_{BT}d_N b_{T_H}a_{T_H},\\
\alpha_3 &= (r-d_B)sd_{NB}d_{T_H}d_{TB},\\
\alpha_1 &= b_B sd_{T_H}(d_N d_{TB}+d_{NB}d_T)+sd_{T_H}[(r-d_B)d_N d_T+d_{BN}b_N d_{TB}-d_{BT}b_{NB}d_T],\\
\alpha_2 &= b_B sd_{NB}d_{T_H}d_{TB}+(r-d_B)sd_{T_H}(d_N d_{TB}+d_{NB}d_T),\\
\alpha_0 &= sd_{T_H}d_T[d_{BN}b_N+(1-d_{BT})d_N].
\end{aligned}
\tag{2.8}
$$

2.3.1 The case $L = 2$

In [64], the value of the parameter L is taken to be $L = 2$. It thus follows:

$$
a_5 B^{*5}+a_4 B^{*4}+a_3 B^{*3}+a_2 B^{*2}+a_1(B^*)+a_0 = 0. \tag{2.9}
$$

The new coefficients are in part the same of those in (2.8), in part need to be recalculated. We find:

$$
\begin{aligned}
a_5 &= \alpha_{L+3},\\
a_4 &= \alpha_{L+2},\\
a_3 &= (d_{T_H}-a_{T_H})[b_B(d_N d_{TB}+d_{NB}d_T)+(r-d_B)d_N d_T+d_{BN}d_{TB}b_N-d_{BT}d_{NB}b_T]\\
&-kd_{NB}d_{TB}b_{T_H}a_{T_H}+(r-d_B)sd_{NB}d_{T_H}d_{TB},\\
a_2 &= (d_{T_H}-a_{T_H})[b_B d_N d_{TB}+b_N d_{BN}d_T-d_{BT}d_N b_T]\\
&-kd_{BT}d_N b_{T_H}a_{T_H}+b_B sd_{NB}d_{T_H}d_{TB}+(r-d_B)sd_{T_H}(d_N d_{TB}+d_{NB}d_T).\\
a_1 &= \alpha_1,\\
a_0 &= \alpha_0,
\end{aligned}
$$

By the model assumptions (2.5), a_0 turns out to be always positive. Note that using the actually estimated parameter values of [64], it turns out that according to the parameter ranges given, there might be situations in which $d_{T_H} > a_{T_H}$ holds.

This inequality may also not be satisfied, giving the following condition

$$d_{T_H} - a_{T_H} < 0. \tag{2.10}$$

From the latter, the negativity of two more coefficients follows, namely $a_5 < 0$, $a_4 < 0$. We proceed now by applying Descartes rule of signs to equation (2.9).

Our aim is to find at least a positive root of the quintic algebraic equation. There are several cases that need to be discussed, based on the possible signs of the remaining coefficients:

(i) if $a_3 < 0$, $a_2 < 0$, $a_1 < 0$, then there is just one change of sign, so there exists one positive roots of Eq.(2.9);

(ii) if $a_3 < 0$, $a_2 < 0$, $a_1 > 0$, there is one positive roots of Eq.(2.9);

(iii) if $a_3 < 0$, $a_2 > 0$, $a_1 > 0$, there is one positive roots of Eq.(2.9);

(iv) if $a_3 < 0$, $a_2 > 0$, $a_1 < 0$, there exist three or one positive roots of Eq.(2.9);

(v) if $a_3 > 0$, $a_2 > 0$, $a_1 > 0$, there exist one positive roots of Eq.(2.9);

(vi) if $a_3 > 0$, $a_2 > 0$, $a_1 < 0$, there exist three or one positive roots of Eq.(2.9);

(vii) if $a_3 > 0$, $a_2 < 0$, $a_1 > 0$, there exist three or one positive roots of Eq.(2.9);

(viii) if $a_3 > 0$, $a_2 < 0$, $a_1 < 0$, there exist three or one positive roots of Eq.(2.9);

Therefore, since in all these cases there is at least one sign change, the existence of a positive root B^* of equation (2.9) is unconditionally ensured.

The extra two roots that arise in cases **(iv)**, **(vi)**, **(vii)** and **(viii)** may or may not be real. The occurrence of these multiple roots is related to the sigmoid function used in (2.3) and (2.4). This also entails the possible appearance or disappearance of these equilibria, through saddle node bifurcations. This issue will not be further investigated here.

Feasibility of the coexistence equilibrium further hinges on the nonnegativity of the remaining populations, namely we need to require $T_H^* \geq 0$ and $T^* \geq 0$. If condition (2.10) is not satisfied, it ensures the positivity only of T_H^*, but not the one of T^*. In view of this fact, in general we therefore need to impose both the above further nonnegativity conditions, that give the requirements:

$$d_{T_H} B^{*L} + s d_{T_H} > a_{T_H} B^{*L}, \quad B^{*L}[b_T d_{T_H} + k a_{T_H} b_{T_H}] + s b_T d_{T_H} \geq a_{T_H} B^{*L}. \tag{2.11}$$

In summary, we have the following result.

Theorem 2.1. *The coexistence equilibrium* $E^*(B^*, N^*, T^*, T_H^*)$ *of the system (2.1)-(2.4) with* $L = 2$ *exists unconditionally and it is feasible if conditions (2.11) are satisfied.*

2.3.2 The case $L = 3$

In this case, we have the equation

$$a_6 B^{*6} + a_5 B^{*5} + a_4 B^{*4} + a_3 B^{*3} + a_2 B^{*2} + a_1(B^*) + a_0 = 0. \tag{2.12}$$

It is easy to see that $a_k = \alpha_k$ for $k = 0, 1, 2, 4, \ldots, 6$. For a_3 we find instead

$$a_3 = (d_{T_H} - a_{T_H}) b_B d_N d_{TB} + (d_{T_H} - a_{T_H})[b_N d_{BN} d_T - d_{BT} d_N b_T] - k d_{BT} d_N b_{T_H} a_{T_H} + (r - d_B) s d_{NB} d_{T_H} d_{TB},$$

which is of uncertain sign. For the remaining coefficients we find

$$a_0 > 0, \quad a_2 > 0, \quad a_5 < 0, \quad a_6 < 0.$$

On using (2.5) and (2.10). Combining all the possible cases, we have the situations described in Table 2.2. We have thus proven the following result.

Table 2.2: Signs of the coefficients of equation (2.12) for the case $L = 3$

a_6	a_5	a_4	a_3	a_2	a_1	a_0	sign variations	positive roots
-	-	+	+	+	+	+	1	1
-	-	+	+	+	-	+	3	1 or 3
-	-	+	-	+	+	+	3	1 or 3
-	-	+	-	+	-	+	5	1 or 3 or 5
-	-	-	+	+	+	+	1	1
-	-	-	+	+	-	+	3	1 or 3
-	-	-	-	+	+	+	1	1
-	-	-	-	+	-	+	3	1 or 3

Theorem 2.2. *The coexistence equilibrium $E^*(B^*, N^*, T^*, T_H^*)$ of the system (2.1)-(2.4) in the case $L = 3$ exists unconditionally. Once again, for it to be feasible, conditions (2.11) need to be satisfied. Multiple roots are possible, arising possibly through saddle-node bifurcations, in the cases listed in Table 2.2.*

2.3.3 The general case $L \geq 4$

In this situation, the equation is in general of order L. Therefore we need to study direcly the characteristic equation (2.7) whose coefficients are then $a_k = \alpha_k$, $k = 0, \ldots, 3$, $k = L, \ldots, L+3$, the only 8 ones that do not vanish. Furthermore, from (2.5) and (2.10) we once again find

$$a_0 > 0, \quad a_2 > 0, \quad a_3 > 0, \quad a_{L+2} < 0, \quad a_{L+3} < 0.$$

The vanishing ones do not influence Descartes' rule, for which now the situations described in Table 2.3 arise. Again, the multiple equilibria seen to arise in some cases of Table 2.3 would be originated

Table 2.3: Signs of the coefficients of equation (2.7) for a general value of L

a_{L+3}	a_{L+2}	a_{L+1}	a_L	a_{L-1}	$\ldots$	a_4	a_3	a_2	a_1	a_0	sign variations	positive roots
-	-	+	+	0	0	0	+	+	+	+	1	1
-	-	+	+	0	0	0	+	+	-	+	3	1 or 3
-	-	+	-	0	0	0	+	+	+	+	3	1 or 3
-	-	+	-	0	0	0	+	+	-	+	5	1 or 3 or 5
-	-	-	+	0	0	0	+	+	+	+	1	1
-	-	-	+	0	0	0	+	+	-	+	3	1 or 3
-	-	-	-	0	0	0	+	+	+	+	1	1
-	-	-	-	0	0	0	+	+	-	+	3	1 or 3

by saddle-node bifurcations.

In summary we can state the following claim.

Theorem 2.3. *The coexistence equilibrium $E^*(B^*, N^*, T^*, T_H^*)$ of the system (2.1)-(2.4) in the general case $L \geq 4$ exists unconditionally. Once again, for it to be feasible, conditions (2.11) need to be*

satisfied.

2.4 Stability Analysis

In this section we investigate the local stability of the coexistence equilibrium, in the particular case $L = 2$ and in the general one $L \geq 3$.

2.4.1 The case $L = 2$

The Jacobian matrix of system at the coexisting equilibrium E^* is given by

$$J_2(E^*) = \begin{pmatrix} (r - d_B) - d_{BN}N^* - d_{BT}T^* & -d_{BN}B^* & -d_{BT}B^* & 0 \\ -d_{NB}N^* & -d_N - d_{NB}B^* & 0 & 0 \\ -d_{TB}T^* + ka_{T_H}\dfrac{2B^*s}{(s+B^{*2})^2}T_H^* & 0 & -d_T - d_{TB}B^* & ka_{T_H}\dfrac{B^{*2}}{s+B^{*2}} \\ a_{T_H}\dfrac{2B^*s}{(s+B^{*2})^2}T_H^* & 0 & 0 & -d_{T_H} + a_{T_H}\dfrac{B^{*2}}{s+B^{*2}} \end{pmatrix} \tag{2.13}$$

We have the following result:

Theorem 2.4. *For $L = 2$, The coexistence equilibrium $E^*(B^*, N^*, T^*, T_H^*)$ of the system (2.1)-(2.4) is locally asymptotically stable if $b_i > 0$, $i = 0...3$, et $b_3b_2b_1 > b_1^2 + b_3^2b_0$, where these coefficients are defined in the proof.*

Proof. We use the linearization method [68], followed by another application of Descartes' rule of signs. From (5.1), the eigenvalues of the characteristic equation of $J(E^*)$ are the solution of the following equation:

$$P(\lambda) = \lambda^4 + b_3\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0 = 0 \tag{2.14}$$

whose coefficients are

$$
\begin{aligned}
b_3 &= d_N + d_{NB}B^* + d_{BN}N^* + d_{BT}T^* - r + d_B + d_T + d_{TB}B^* - a_{T_H}\frac{B^{*2}}{s+B^{*2}} + d_{T_H},\\
b_2 &= \left[d_T + d_{BT}B^* - a_{T_H}\frac{B^{*2}}{s+B^{*2}} + d_{T_H} + d_{BN}N^* + d_{BT}T^* - r + d_B)\right](d_N + d_{NB}B^*)\\
&-d_{NB}d_{BN}N^*B^* + \left[d_T + d_{TB}B^* - a_{T_H}\frac{B^{*2}}{s+B^{*2}} + d_{T_H}\right][d_{BN}N^* + d_{BT}T^* - r + d_B]\\
&-(d_T + d_{TB}B^*)\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right) + d_{BT}B^*\left(ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* - d_{TB}\right),\\
b_1 &= -d_{NB}d_{BN}N^*B^*\left[d_N + d_{TB}B^* - a_{T_H}\frac{B^{*2}}{s+B^{*2}} + d_{T_H}\right]\\
&-(d_N + d_{NB}B^*)\left[(d_T + d_{TB}B^*)\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right) - (d_T + d_{TB}B^*)\right.\\
&\left.-\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right)[d_{BN}N^* + d_{BT}T^* - r + d_B] - d_{BT}B^*\left(ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* - d_{TB}\right)\right]\\
&-[d_{BN}N^* + d_{BT}T^* - r + d_B](d_T + d_{BT}B^*)\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right)\\
&-d_{BT}B^*\left[\left(ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* - d_{TB}\right)\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right) + \left(a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^*\right)ka_{T_H}\frac{B^{*2}}{s+B^{*2}}\right],\\
b_0 &= d_{NB}d_{BN}N^*B^*(d_T + d_{BT}B^*)\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right)\\
&-(d_N + d_{NB}B^*)\left[[d_{BN}N^* + d_{BT}T^* - r + d_B](d_T + d_{BT}B^*)\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right)\right]\\
&+d_{BT}B^*\left[\left(ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* - d_{TB}\right)\left(a_{T_H}\frac{B^{*2}}{s+B^{*2}} - d_{T_H}\right) - \left(a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^*\right)ka_{T_H}\frac{B^{*2}}{s+B^{*2}}\right].
\end{aligned}
$$

Now, the necessary condition for the characteristic equation to have roots with negative real parts is $b_0 > 0$.

Therefore, by using Descartes rule of signs, and Routh-Hurwitz criterium, all the roots of equation (2.14) are real negative if $b_1 > 0$, $b_2 > 0$, $b_3 > 0$ and $b_3b_2b_1 > b_1^2 + b_3^2b_0$. □

2.4.2 The case $L \geq 3$

The Jacobian in this case is slightly modified from the expression (5.1), in that it becomes, using also the first three equilibrium equations to simplify some of the diagonal entries:

$$J_L(E^*) = \begin{pmatrix} -\frac{b_B}{B^*} & -d_{BN}B^* & -d_{BT}B^* & 0 \\ -d_{NB}N^* & -\frac{b_N}{N^*} & 0 & 0 \\ -d_{TB}T^* + ka_{T_H}T_H^*\frac{sLB^{*L-1}}{(s+B^{*L})^2} & 0 & -d_T - d_{TB}B^* & ka_{T_H}\frac{B^{*L}}{s+B^{*L}} \\ ka_{T_H}T_H^*\frac{sLB^{*L-1}}{(s+B^{*L})^2} & 0 & 0 & -\frac{b_{T_H}}{T_H^*} \end{pmatrix} \tag{2.15}$$

We now show that $-J_L(E^*)$ is positive definite, under suitable conditions. This will ensure the stability of the coexistence point E^*. We consider in turn the signs of the principal minors of all possible order, Δ_j, $j = 1, \ldots, 4$, imposing that they are all positive. We thus find

$$\Delta_1 = \frac{b_B}{B^*} > 0, \quad \Delta_2 = \frac{b_N}{N^*}\frac{b_B}{B^*} - d_{NB}N^*d_{BN}B^*,$$

and

$$\Delta_3 = (d_T + d_{TB}B^*)\Delta_2 - b_N d_{BT}\frac{B^*}{N^*}\left[d_{TB}T^* - ka_{T_H}T_H^*\frac{sLB^{*L-1}}{(s+B^{*L})^2}\right].$$

For the determinant Δ_4, we finally have

$$\Delta_4 = -\det J_L(E^*) = \frac{b_{T_H}}{T_H^*}\Delta_3 + k^2a_{T_H}^2\frac{T_H^*}{N^*}b_N d_{BT}\frac{sLB^{*L^2}}{(s+B^{*L})^3} > 0.$$

Thus the conditions ensuring positivity of the remaining above minors Δ_j, $j = 1, \ldots, 3$, are:

$$b_B b_N > d_{BN}d_{NB}B^{*2}N^{*2}, \quad (d_T + d_{TB}B^*)\Delta_2 + b_N d_{BT}ka_{T_H}\frac{T_H^*}{N^*}\frac{sLB^{*L}}{(s+B^{*L})^2} > b_N d_{BT}\frac{B^*}{N^*}d_{TB}T^*. \tag{2.16}$$

In summary we have the desired stability result:

Theorem 2.5. *For $L \geq 3$, the coexistence equilibrium $E^*(B^*, N^*, T^*, T_H^*)$ of the system (2.3)-(2.4) is locally asymptotically stable if conditions (2.16) hold.*

2.5 Glossary

Angiogenesis: The formation of new blood vessels, a process controlled by chemicals produced in the body that stimulate blood vessels or form new ones. Angiogenesis plays an important role in the growth and spread of cancer. Angiogenesis also occurs in the healthy body for healing of wounds and restoring blood flow to tissues after injury.

Antigenic: Having the properties of an antigen.

Antigen: Any substance capable of inducing a specific immune response and of reacting with the products of that response, i.e., with specific antibody or specifically sensitized T lymphocytes, or both.

Apoptosis: A model of cell death affecting individual cells, marked by cell shrinkage, chromatin condensation and cell fragmentation in bound bodies to the membrane which are eliminated by phagocytosis. Often used as a synonym for programmed cell death.

Cancer: Any disorder of cell growth that results in invasion and destruction of surrounding healthy tissue by abnormal cells. Cancer cells arise from normal cells whose nature is permanently changed. They multiply more rapidly than healthy body cells and do not seem subject to normal control by nerves and hormones. They may spread via the bloodstream or lymphatic system to other parts of the body, where they produce further tissue damage(metastases).

Carcinogenesis: The origin, production, or development of cancer, including carcinomas and other malignant neoplasms.

CD4+T cell: An immunologically important white cell that is responsible for cell-mediated immunity. It is the cell invaded by the human immunodeficiency virus and in which the virus replicates itself.

CD8: A type I transmembrane protein found on suppressor (cytotoxic) T cells, some natural killer cells, and most thymocytes that is involved in T-cell antigen recognition; expressed in some T-cell lymphomas and large granular lymphocyte leukemias.

Chemotherapy: treatment of disease by means of chemical substances or drugs; usually used in reference to neoplastic disease.

Chronic lymphocytic leukemia CLL:Is a cancer of the blood which is characterized by an excessive accumulation of certain white blood cells, B lymphocytes which have become abnormal, in

the bone marrow, the blood, the lymph nodes and the missed.

Cytotoxic: Detrimental or destructive to cells.

Hematopoiesis: The normal formation and development of blood cells in the bone marrow.

Immune response: The reaction of the body to foreign or potentially dangerous substances (antigens), particularly disease-producing microorganisms.

Immunotherapy: Treatment of disease by inducing, enhancing, or suppressing an immune response.

Leukopoiesis: The production of white blood cells. Monocytes, neutrophils, basophils, and eosinophils are produced from bone marrow myeloblasts. Lymphocytes develop from lymphoblastic precursors in peripheral lymphoid tissue.

Lymphocyte: A family of mononuclear, nonphagocytic white blood cells that circulate in blood, lymph, and peripheral lymphatic tissues. Lymphocytes are categorized as B and T lymphocytes and natural killer cells and are responsible for humoral and cellular immunity and tumor surveillance.

Myelogenous: Pertaining to the cells produced in bone marrow or the tissue from which such cells originate.

Natural killer cell: A lymphocyte that is activated by double-stranded RNA or lymphokines and fights off viral infections and tumors without evident antigenic specificity

Stem cell: A cell that is not differentiated itself but can undergo unlimited division to form other cells, which either remain as stem cells or differentiate to form specialized cells.

T cell: A lymphocyte that participates in cellular immunity, including cellto-cell communication. The major T cell categories are T-helper and T-suppressor cytotoxic cell.

Tumor: A new growth of tissue in which cell multiplication is uncontrolled and progressive. Tumors are also called neoplasms, which means that they are composed of new and actively growing tissue. Their growth is faster than that of normal tissue, continuing after cessation of the stimuli that evoked the growth, and serving no useful physiologic purpose.

Chapter 3

On the stability of periodic solutions of an impulsive system arising in the control of agroecosystems

3.1 Introduction

Natural resources are being depleted nowadays at a fast rate. In agriculture, the use of synthetic fertilizers in the past several decades has brought two different types of problems. On one side, the poisoning of the environment, for which for instance DDT has been banned as a pest control since many years, but in any case after causing several problems in the environment. On the other hand, the insects in time tend to develop resistance to the pesticides used, by suitable mutations, which in turn generate the need of devising new poisons for their combat. An alternative to the widespread use of pesticides is to try to control pests via organic means, using for instance specific predators or parasitoids of the involved crop pests. in the terrestrial ecosystems.

Wise and all ([85], [86], [87]) proposed the spider as a model terrestrial predator and specified that some spider families differ so much in how they forage and utilize their surroundings . From a point of view it can be assessed that the spiders frequently face a shortage of prey in nature. Confronted with prey shortages, the wanderers spiders search for more productive microhabitats. Many wandering spiders, in fact, select microhabitat on the basis of prey abundance ([72], [22], [61], [41]).

Most agroecosystems provide no permanent habitats for many species. Hence, for the thriving of the

latter, the presence of refuge areas, such as woods, is fundamental ([28], [80]).

A model for the biological control of agroecosystems has been proposed in [81], where the use of spiders is suggested, by preserving suitable habitats for these species around the fields where the crops grow.

The model has been analysed, and finally coupled with the use of insecticides, because in particular environments the latter are heavily used anyway. Spraying insecticides from flying planes or helicopters on large fiels will interfere also with the species that are helpful in controlling the pests and needs to be suitably taken in consideration. Spraying is usually administered at regular time intervals, a fact that in the corresponding dynamical system is modeled via impulsive functions.

The impulsive models arise, generally, in the description of phenomena subjected to abrupt external changes, where the time of the change can be neglected, and the change can be modelled as jump in the phenomena under study. A rich literature on the theory of impulsive diferential equations can be found in ([6], [7], [46]). This new branch of diferential equations developed quickly for the past 50 years (see [58]). In particular, important contributions have been made by Bainov and Simeonov ([6], [7]), Lakshmikantham et al. [46], and their colleagues.

In [81] simulations have been carried out, but a theoretical analysis of the system behavior is lacking. The main objective is to study the stability of the periodic solutions that have been empirically found in [81]. For the ease of the reader we restate here the model introduced in [81], whose oscillating solutions are the aim of this chapter:

$$\frac{dx_1}{dt} = rx_1\left(1 - \frac{x_1}{W}\right) - cx_2x_1 \tag{3.1}$$

$$\frac{dx_2}{dt} = x_2\left(-a + \frac{kbx_3}{H + x_3} + kcx_1\right) \tag{3.2}$$

$$\frac{dx_3}{dt} = x_3\left(e - \frac{bx_2}{H + x_3}\right) \tag{3.3}$$

$$x_1(t_i^+) = x_1(t_i)\left(1 - \frac{h(1-q)}{\alpha}\right) \tag{3.4}$$

$$x_2(t_i^+) = x_2(t_i)\left(1 - \frac{hKq}{\alpha}\right) \tag{3.5}$$

$$x_3(t_i^+) = x_3(t_i)\left(1 - \frac{hq}{\alpha}\right) \tag{3.6}$$

where $t_{i+1} - t_i = \tau > 0, \forall i \in \mathbb{N}$.

The meaning of the variables is as follows:

x_1 represents the insects population living in the woods.

x_2 represents the spiders populations.

x_3 represents the insects having the vineyards as habitat.

And the positive parameters are defined in table 3.1 as follows: The rest of the chapter contains the

Table 3.1: Model parameters and their meaning

r	logistic growth
c	spider's hunting rate on insects
W	woods and green patches carrying capacity
e	insect growth rate in open fields
b	spider's hunting rate on field insects
a	spider's mortality rate
H	half saturation constant
$k < 1$	conversion factor of prey into new spiders
q	portion of insecticide sprayed on vineyards
$1 - q$	portion of insecticide accidentally sprayed on the woods
h	insecticide effectiveness against the parasites
$0 < K < 1$	smaller insecticide effect on the spiders

theoretical analysis, organized in just one section. In it, the various subsections address in turn the basic definitions, the stability of the unique non-trivial, positive, well-defined, and stable periodic solution of the wood insects only. Then, the stability of the other solution is studied, namely the τ-periodic pest-only solution and the τ-periodic spider-free solution. The Appendices contain the most techical mathematical details.

3.2 Analysis of the model

In the following, we proceed to analyze our model. To this purpose, we shall use a fixed point approach.

Let $\Phi(t; X_0)$ be the solution of the system (3.1)-(3.6) for the initial condition X_0.

We define the mappings $F_1, F_2, F_3 : \mathbb{R}^3 \longrightarrow \mathbb{R}$ by

$$F_1(x_1, x_2, x_3) = rx_1\left(1 - \frac{x_1}{W}\right) - cx_2x_1.$$
$$F_2(x_1, x_2, x_3) = x_2\left(-a + \frac{kbx_3}{H + x_3} + kcx_1\right).$$
$$F_3(x_1, x_2, x_3) = x_3\left(e - \frac{bx_2}{H + x_3}\right).$$

and $\Theta_1, \Theta_2, \Theta_3 : \mathbb{R}^3 \longrightarrow \mathbb{R}$ by

$$\Theta_1(x_1(t_i), x_2(t_t), x_3(t_i)) = x_1(t_i)\left(1 - \frac{h(1-q)}{\alpha}\right),$$
$$\Theta_2(x_1(t_i), x_2(t_t), x_3(t_i)) = x_2(t_i)\left(1 - \frac{hKq}{\alpha}\right),$$
$$\Theta_3(x_1(t_i), x_2(t_t), x_3(t_i)) = x_3(t_i)\left(1 - \frac{hq}{\alpha}\right).$$

3.2.1 Definitions and assumptions

Definition 3.1. *A solution $\zeta = (x_1; x_2; x_3)$ of the problem (3.1)-(3.6) is a function defined in $\mathbb{R}^+$, with nonnegative components, continuously differentiable in $\mathbb{R}^+ - \{t_i\}$ with $t_0 = 0$, and satisfying all relations (3.1) through (3.6).*

Definition 3.2. *ζ is called a wood insect-only solution of problem (3.1)-(3.6) if and only if its second and third components are zeros.*

Definition 3.3. *Also, ζ is called a τ-periodic wood insect-only solution if it is a wood insect-only solution satisfying $\zeta(n\tau) = \zeta((n+1)\tau)$, for all $n \geq 0$.*

In our study, we further assume that $F = (F_1; F_2; F_3)$ and Θ are smooth enough, $\Theta = (\Theta_1; \Theta_2; \Theta_3)$

is positive and $F_i(x_1, x_2, x_3) = 0$ for $x_i = 0, i = 1; 2; 3$.

Letting Φ be the flow associated with (3.1)-(3.6), we have

$$\zeta(t) = \Phi(t, X_0), 0 < t \leq \tau,$$

where $\zeta(0) = X_0$. We assume that the flow Φ applies up to time τ. So $\zeta(\tau) = \Phi(\tau, X_0)$. Then, within a very small time interval starting at time τ, we assume that the treatment is administered and instantaneously kills a fraction of the population.

The term $\zeta(\tau^+)$ denotes the state of the population after the treatment, $\zeta(\tau^+)$ is determined in terms of $\zeta(\tau)$ according to equations (3.4)-(3.6). We have $\zeta(\tau^+) = \Theta(\zeta(\tau)) = \Theta(\Phi(\tau, X_0))$.

Let Ψ be the operator defined by

$$\begin{aligned} \Psi(\tau, .) : \ \mathbb{R}^3_+ &\longrightarrow \mathbb{R}^3_+ \\ X_0 &\longmapsto \Psi(\tau, X_0) = \Theta(\Phi(\tau, X_0)). \end{aligned}$$

and denote by $D_X\Psi$ the derivative of Ψ with respect to X.

Theorem 3.1. *The model (3.1)-(3.6) has a unique global positive solution for all positive initial conditions*

Proof.

Because $F_i, (i = 1, 2, 3)$ are smooth functions, from the Cauchy-Lipschitz theorem we obtain the local existence and uniqueness of the solutions of (3.1)-(3.3). Since the solutions are bounded then the solution is global in $[0, t_1]$.

The system (3.1)-(3.3) is quasi-positive because for all $x_i \in \mathbb{R}^+$ we have $F_i(x_1, x_2, x_3) \geq 0$ for $x_i = 0$, $i = 1; 2; 3$. Thus a unique positive global solution exists in $[0, t_1]$.

By recurrence we can prove that $\forall k \in \mathbb{N}^*$, we have a unique positive global solution in the interval $[t_k; t_{k+1}]$.

Hence, the existence of a unique positive global solution of (3.1)-(3.6) follows. □

We now recall the following result, [45].

Lemma 3.1. *$\zeta = \Phi(., X_0)$ is a τ -periodic solution of (3.1)-(3.6) if and only if $\Psi(\tau, X_0) = X_0$*

Remark 3.1. *This lemma states that X_0 is a fixed point of $\Psi(\tau,.)$. A fixed point X_0 of $\Psi(\tau,.)$ is given by the initial ζ verifying $\zeta(0) = X_0$. Consequently, for each fixed point X_0 of $\Psi(\tau,.)$ there is an associated τ -periodic solution ζ.*

Definition 3.4. *[31] We say that a fixed point is trivial if it is associated to a trivial periodic solution.*

Remark 3.2. *The fixed point of $\Psi(\tau,.)$ can be determined using a fixed point method.*

Definition 3.5. *[31] The solution ζ is exponentially stable if and only if the spectral radius $\rho(D_X\Psi(\tau,.))$ is strictly less than 1.*

Remark 3.3. *If $x_2 = x_3 = 0$ the problem (3.1), (3.4), has a τ_0-periodic solution denoted by $x_1(t) = x(t,\widehat{x}_1)$, where*

$$x_1(t) = \frac{W\widehat{x}_1 e^{rt}}{W - \widehat{x}_1(1-e^{rt})}, \tag{3.7}$$

and $\widehat{x}_1$ is determined by

$$\widehat{x}_1 = \frac{W}{\alpha}\frac{\alpha(e^{r\tau_0}-1) - h(1-q)e^{r\tau_0}}{e^{r\tau_0}-1}, \tag{3.8}$$

which is positive if

$$h(1-q) < \alpha, \quad \tau_0 > \frac{1}{r}\ln\frac{\alpha}{\alpha - h(1-q)}. \tag{3.9}$$

Conditions that ensure the following result.

Theorem 3.2. *If (3.9) are satisfied, then the problem (3.1), (3.4), has a τ_0-periodic solution $x_1(t) = x(t,\widehat{x}_1)$ determined by (3.7) where $\widehat{x}_1$ given by (3.8).*

Proof. Calcul the $x_1(t)$

We have

$$\frac{dx_1}{x_1\left(1-\frac{x_1}{W}\right)} = rdt.$$

After separating the variables the equation is

$$\frac{dx_1}{x_1} + \frac{\frac{1}{W}dx_1}{\left(1-\frac{x_1}{W}\right)} = rdt,$$

and so integrating both sides we have

$$\ln\left(\frac{x_1(t)}{1-\frac{x_1(t)}{W}}\right)-\ln\left(\frac{x_1(0)}{1-\frac{x_1(0)}{W}}\right)=rt.$$

Exponentiating we have

$$\left(\frac{x_1(t)(1-\frac{x_1(0)}{W})}{x_1(0)(1-\frac{x_1(t)}{W})}\right)=e^{rt},$$

which is

$$\left(\frac{x_1(t)}{(W-x_1(t))}\right)=\left(\frac{x_1(0)}{(W-x_1(0))}\right)e^{rt},$$

it follows that

$$x_1(t)=\frac{Wx_1(0)e^{rt}}{W-x_1(0)(1-e^{rt})}.$$

For the initial condition $x_1(0)$ we used the equation (3.4) where $x_1(\tau_0^+)=x_1(0)$ and $x_1(\tau_0^+)=\left(1-\frac{h(1-q)}{\alpha}\right)x_1(\tau_0)$, then

$$x_1(\tau_0^+)=x_1(0)=\left(1-\frac{h(1-q)}{\alpha}\right)\frac{Wx_1(0)e^{r\tau_0}}{W-x_1(0)(1-e^{r\tau_0})},$$

and finally after a rearrangement we can obtain

$$x_1(0)=\frac{W}{\alpha}\frac{\alpha(e^{r\tau_0}-1)-h(1-q)e^{r\tau_0}}{e^{r\tau_0}-1}.$$

□

Remark 3.4. *By extension it follows that the function $\zeta(t)=(x(t),0,0)$ is a τ_0-periodic solution of (3.1)-(3.6) in the three dimensional space.*

3.2.2 Stability of ζ

In the case $x_2=x_3=0$, then the system (3.1)-(3.6) reduces to the particular case (3.1)-(3.4). The latter has a unique non-trivial positive periodic solution x_s given by (3.7) well-defined and stable for $h(1-q)<\alpha, \quad \tau_0>\frac{1}{r}\ln\frac{\alpha}{\alpha-h(1-q)}$.

To determine the stability of the wood insect-only solution $\zeta=(x_s;0;0)$ in the three dimensional

space, we must evaluate $D_X\Psi(\tau_0; X_0)$. Specifically, we find

$$D_X\Psi(\tau_0; X_0) = D_X\Theta(\Phi(\tau_0; X_0))\frac{\partial\Phi}{\partial X}(\tau_0; X_0) \tag{3.10}$$
$$= \begin{pmatrix} \frac{\partial\Theta_1}{\partial x_1} & \frac{\partial\Theta_1}{\partial x_2} & \frac{\partial\Theta_1}{\partial x_3} \\ \frac{\partial\Theta_2}{\partial x_1} & \frac{\partial\Theta_2}{\partial x_2} & \frac{\partial\Theta_2}{\partial x_3} \\ \frac{\partial\Theta_3}{\partial x_1} & \frac{\partial\Theta_3}{\partial x_2} & \frac{\partial\Theta_3}{\partial x_3} \end{pmatrix} \begin{pmatrix} \frac{\partial\Phi_1}{\partial x_1} & \frac{\partial\Phi_1}{\partial x_2} & \frac{\partial\Phi_1}{\partial x_3} \\ 0 & \frac{\partial\Phi_2}{\partial x_2} & 0 \\ 0 & 0 & \frac{\partial\Phi_3}{\partial x_3} \end{pmatrix} (\tau_0; X_0).$$

The solution ζ is exponentially stable if and only if the spectral radius is less than one, namely for $i = 1, 2, 3$,

$$\left|\frac{\partial\Theta_i}{\partial x_i}(\Phi(\tau_0; X_0))\frac{\partial\Phi_i}{\partial x_i}(\tau_0; X_0)\right| < 1.$$

Following [45] and [18], we now consider the variational equation associated to the system (3.1)-(3.6):

$$\frac{d}{dt}(D_X\Phi(t; X_0)) = D_X F(\Phi(t; X_0))(D_X\Phi(t; X_0)), \tag{3.11}$$

together with the initial condition $D_X\Phi(0; X_0) = Id_{\mathbb{R}^3}$. Following [45], integrating and deferring the details to the Appendix **A1**, we obtain:

$$\frac{\partial\Phi_1(t; X_0)}{\partial x_1} = e^{\int_0^t \frac{\partial F_1(\zeta(r))}{\partial x_1}dr}, \quad \frac{\partial\Phi_2(t; X_0)}{\partial x_2} = e^{\int_0^t \frac{\partial F_2(\zeta(r))}{\partial x_2}dr}, \tag{3.12}$$
$$\frac{\partial\Phi_3(t; X_0)}{\partial x_3} = e^{\int_0^t \frac{\partial F_3(\zeta(r))}{\partial x_3}dr}.$$

We have the following stability result:

Theorem 3.3. *The trivial solution $\zeta = (x_s; 0; 0)$ is exponentially stable if and only if*

$$\frac{1}{r}\ln\frac{\alpha}{\alpha - h(1-q)} < \tau_0 \tag{3.13}$$
$$< \min\left\{\frac{1}{kcW - a}\ln\frac{\alpha^{\frac{kcW}{r}+1}}{(\alpha - hKq)(\alpha - h(1-q))^{\frac{kcW}{r}}}; \quad \frac{1}{e}\ln\frac{\alpha}{\alpha - hq}\right\}.$$

Proof. Observe that

$$\left|\frac{\partial\Theta_1}{\partial x_1}(\Phi(\tau_0; X_0))\frac{\partial\Phi_1}{\partial x_1}(\tau_0; X_0)\right| = \frac{\alpha e^{-r\tau_0}}{\alpha - h(1-q)},$$
$$\left|\frac{\partial\Theta_2}{\partial x_2}(\Phi(\tau_0; X_0))\frac{\partial\Phi_2}{\partial x_2}(\tau_0; X_0)\right| = \frac{(\alpha - hKq)(\alpha - h(1-q))^{\frac{kcW}{r}}e^{(kcW-a)\tau_0}}{\alpha^{\frac{kcW}{r}+1}}$$

and

$$\left|\frac{\partial\Theta_3}{\partial x_3}(\Phi(\tau_0;X_0))\frac{\partial\Phi_3}{\partial x_3}(\tau_0;X_0)\right| = \left(1-\frac{hq}{\alpha}\right)e^{e\tau_0}.$$

□

3.2.3 Stability of the remaining τ-periodic solution

The system (3.1)-(3.6) has two more τ-periodic solution, namely the τ-periodic pest-only solution and τ-periodic spider-free solution:

$$\zeta(t) := \zeta_f = (0;0;x_3(t))\,, \quad \zeta(t) := \zeta_v = (x_1(t);0;x_3(t))\,.$$

The existence conditions of the τ-periodic solutions ζ_f and ζ_v are discussed in what follows.

Existence of the τ-periodic pest-only solution

If $x_1 = x_2 = 0$; the problem (3.3), (3.6), has a τ_0-periodic solution denoted by $x_3(t) = x(t,\widehat{x}_3)$, where

$$x_3(t) = \widehat{x}_3 e^{et}, \tag{3.14}$$

with $\widehat{x}_3 \in \mathbb{R}^{*+}$. It is defined and positive if

$$hq < \alpha, \quad \tau_0 = \frac{1}{e}\ln\frac{\alpha}{\alpha - hq}, \tag{3.15}$$

conditions that ensure the following result.

Theorem 3.4. *If (3.15) are satisfied, then the problem (3.3), (3.6), has a stable τ_0-periodic solution $x_3(t) = x(t,\widehat{x}_3)$ determined by (3.14).*

Proof. For $x_1 = x_2 = 0$, we have

$$\frac{dx_3}{dt} = ex_3,$$

then

$$\frac{dx_3}{x_3} = edt,$$

after integrating we find

$$\ln\frac{x_3(t)}{x_3(0)} = et,$$

this gives

$$x_3(t) = x_3(0)e^{et}.$$

For the initial condition $x_3(0)$ we use the equation (3.6) where $x_3(\tau_0^+) = x_3(0)$ and $x_3(\tau_0^+) = \left(1 - \frac{hq}{\alpha}\right) x_3(\tau_0)$ then

$$x_3(\tau_0^+) = x_3(0) = \left(1 - \frac{hq}{\alpha}\right) x_3(0)e^{e\tau},$$

finaly we have $x_3(0) \in \mathbb{R}^+$, and

$$\tau = \frac{1}{e} \ln(\frac{\alpha}{\alpha - hq}).$$

□

Remark 3.5. *By extension it follows that the function $\zeta(t) = \zeta_f = (0, 0, x_3(t))$ is a τ_0-periodic solution of (3.1)-(3.6) in the three dimensional space with τ_0 given in (3.15).*

Existence of the τ-periodic spider-free solution

If $x_2 = 0$, the problem (3.1), (3.3), (3.4), (3.6), has a τ_0-periodic solution denoted by $(x_1(t), x_3(t)) = (x_f(t, \widehat{x}_1), x_v(t, \widehat{x}_3))$, where

$$(x_1(t), x_3(t)) = \left(\frac{W\widehat{x}_1 e^{rt}}{W - \widehat{x}_1(1 - e^{rt})}, \widehat{x}_3 e^{et}\right), \tag{3.16}$$

with $\widehat{x}_3 \in \mathbb{R}^{*+}$, $\widehat{x}_1$ is determined by

$$\widehat{x}_1 = \frac{W}{\alpha} \frac{\alpha(e^{r\tau_0} - 1) - h(1 - q)e^{r\tau_0}}{e^{r\tau_0} - 1}, \tag{3.17}$$

and it is defined and positive if

$$\frac{1}{e} \ln(1 - \frac{hq}{\alpha}) < \frac{1}{r} \ln(1 - \frac{h(1 - q)}{\alpha}), \quad \tau_0 = \frac{1}{e} \ln \frac{\alpha}{\alpha - hq}, \tag{3.18}$$

conditions that ensure the following result.

Theorem 3.5. *If (3.18) are satisfied, then the problem (3.1), (3.3), (3.4), (3.6),has a τ_0-periodic solution $(x_1(t), x_3(t)) = (x_f(t, \widehat{x}_1), x_v(t, \widehat{x}_3))$ determined by (3.16), where $\widehat{x}_3 \in \mathbb{R}^{*+}$ and $\widehat{x}_1$ given by (3.17).*

To prove it, it suffices to combine the two results of theorems (3.2) and (3.4).

Remark 3.6. *By extension it follows that the function* $\zeta(t) = \zeta_v = (x_1(t), 0, x_3(t))$ *is a* τ_0*-periodic solution of (3.1)-(3.6) in the three dimensional space with*

$$\tau_0 = \frac{1}{e}\ln\frac{\alpha}{\alpha - hq}, \quad \frac{1}{e}\ln(1-\frac{hq}{\alpha}) < \frac{1}{r}\ln(1-\frac{h(1-q)}{\alpha}).$$

To study the stability of ζ_f ,ζ_v we use a the same fixed point approach.

Since solutions of (3.1)-(3.3) exist globally in $\mathbb{R}^+$ and are nonnegative we have

$$X(t) = \Phi(t, X_0), \tag{3.19}$$

where $X(t) = (x_1, x_2, x_3)(t)$, $X(0) = X_0$ and Φ is the flow associated to (3.1)-(3.6).

The state of the population after the spraying is denoted by

$$X(\tau^+) = \Theta(X(\tau)) = \Theta(\Phi(\tau, X_0)).$$

To have a periodic solution we must have $X(\tau^+) = X_0$ that is $X_0 = \Theta(\Phi(\tau, X_0))$. Now, for $X_0 = \zeta_j$, $j = f$ or $j = v$ and $\tau = \tau_0$ we have

$$D_X\Psi(\tau_0; X_0) = D_X\Theta(\Phi(\tau_0; X_0))\frac{\partial\Phi}{\partial X}(\tau_0; X_0)$$

$$= \begin{pmatrix} 1-\frac{h(1-q)}{\alpha} & 0 & 0 \\ 0 & 1-\frac{hKq}{\alpha} & 0 \\ 0 & 0 & 1-\frac{hq}{\alpha} \end{pmatrix} \begin{pmatrix} \frac{\partial\Phi_1}{\partial x_1} & \frac{\partial\Phi_1}{\partial x_2} & \frac{\partial\Phi_1}{\partial x_3} \\ \frac{\partial\Phi_2}{\partial x_1} & \frac{\partial\Phi_2}{\partial x_2} & \frac{\partial\Phi_2}{\partial x_3} \\ \frac{\partial\Phi_3}{\partial x_1} & \frac{\partial\Phi_3}{\partial x_2} & \frac{\partial\Phi_3}{\partial x_3} \end{pmatrix}(\tau_0; X_0)$$

$$= \begin{pmatrix} \left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_1} & \left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_2} & \left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_3} \\ (1-\frac{hKq}{\alpha})\frac{\partial\Phi_2}{\partial x_1} & (1-\frac{hKq}{\alpha})\frac{\partial\Phi_2}{\partial x_2} & (1-\frac{hKq}{\alpha})\frac{\partial\Phi_2}{\partial x_3} \\ (1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_1} & (1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_2} & (1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_3} \end{pmatrix}(\tau_0; X_0).$$

Further,

$$D_X\Psi(\tau_0; \zeta_f) = \begin{pmatrix} \left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_1} & 0 & 0 \\ 0 & (1-\frac{hKq}{\alpha})\frac{\partial\Phi_2}{\partial x_2} & 0 \\ 0 & (1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_2} & (1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_3} \end{pmatrix}(\tau_0; \zeta_f),$$

and

$$D_X\Psi(\tau_0;\zeta_v) = \begin{pmatrix} \left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_1} & \left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_2} & 0 \\ 0 & (1-\frac{hKq}{\alpha})\frac{\partial\Phi_2}{\partial x_2} & 0 \\ 0 & (1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_2} & (1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_3} \end{pmatrix}(\tau_0;\zeta_v).$$

To calculate $\dfrac{\partial\Phi_i}{\partial x_j}$ we used the variational equation (3.11) associated to the system (3.1)-(3.6), whose details are contained in **Appendix A1**.

For each τ-periodic solution, now we assess stability, recalling that exponential stability is equivalent to imposing that the spectral radius is less than one. We examine each solution separately in what follows.

3.2.3.1 Stability of ζ_f

For the solution ζ_f we need to solve $\det(D_X\Psi(\tau_0;\zeta_f)-\mu I)=0$, with

$$\det(D_X\Psi(\tau_0;\zeta_f)-\mu I) = \begin{vmatrix} D_{X,11}-\mu & 0 & 0 \\ 0 & D_{X,22}-\mu & 0 \\ 0 & D_{X,32} & D_{X,33}(\tau_0;\zeta_f)-\mu \end{vmatrix} \tag{3.20}$$

where

$$\begin{aligned} D_{X,11} &= \left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_1}(\tau_0;\zeta_f), \\ D_{X,22} &= \left(1-\frac{hKq}{\alpha}\right)\frac{\partial\Phi_2}{\partial x_2}(\tau_0;\zeta_f), \\ D_{X,32} &= \left(1-\frac{hq}{\alpha}\right)\frac{\partial\Phi_3}{\partial x_2}(\tau_0;\zeta_f), \\ D_{X,33} &= \left(1-\frac{hq}{\alpha}\right)\frac{\partial\Phi_3}{\partial x_3}(\tau_0;\zeta_f). \end{aligned}$$

From (3.20), it follows that the solution ζ_f is exponentially stable if and only if

$$\left|\left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_1}(\tau_0;\zeta_f)\right|<1; \qquad \left|\left(1-\frac{hKq}{\alpha}\right)\frac{\partial\Phi_2}{\partial x_2}(\tau_0;\zeta_f)\right|<1$$

and $\left|\left(1-\frac{hq}{\alpha}\right)\frac{\partial\Phi_3}{\partial x_3}(\tau_0;\zeta_f)\right|<1$. From the variational equation, for all $0<t\leq\tau_0$ we have

$$\begin{cases}\dfrac{\partial\Phi_1(t;X_0)}{x_1} &= e^{rt}\\ \dfrac{\partial\Phi_2(t;X_0)}{\partial x_2} &= e^{-at}\left[\dfrac{H+\widehat{x}_3e^{et}}{H+\widehat{x}_3}\right]^{\frac{kb}{e}}\\ \dfrac{\partial\Phi_3(t;X_0)}{\partial x_3} &= e^{et}\end{cases}.$$

The details being contained in the Appendix **A2**. Therefore the following result holds

Theorem 3.6. *The equilibrium ζ_f is unconditionally unstable.*

Proof.

From the conditions (3.15) of existence of the τ-periodic spider-free solution, we have $\tau_0=\frac{1}{e}\ln\frac{\alpha}{\alpha-hq}$, we apply in the condition of stability $\left|\left(1-\frac{hq}{\alpha}\right)\frac{\partial\Phi_3}{\partial x_3}(\tau_0;\zeta_f)\right|<1$ we obtain:

$$\left|\left(1-\frac{hq}{\alpha}\right)e^{e\frac{1}{e}\ln\frac{\alpha}{\alpha-hq}}\right|=1\not<1$$

□

3.2.3.2 Stability of ζ_v

For the solution ζ_v we need to solve $\det(D_X\Psi(\tau_0;\zeta_v)-\mu I)=0$ which amounts to the equation:

$$\left(\left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1(\tau_0;\zeta_v)}{\partial x_1}-\mu\right)\left((1-\frac{hKq}{\alpha})\frac{\partial\Phi_2(\tau_0;\zeta_v)}{\partial x_2}-\mu\right)\times\left((1-\frac{hq}{\alpha})\frac{\partial\Phi_3(\tau_0;\zeta_v)}{\partial x_3}-\mu\right)=0. \tag{3.21}$$

From (3.21), the solution ζ_v is exponentially stable whenever

$$\left|\left(1-\frac{h(1-q)}{\alpha}\right)\frac{\partial\Phi_1}{\partial x_1}(\tau_0;\zeta_v)\right|<1;\qquad\left|(1-\frac{hKq}{\alpha})\frac{\partial\Phi_2}{\partial x_2}(\tau_0;\zeta_v)\right|<1;$$

$$\left|(1-\frac{hq}{\alpha})\frac{\partial\Phi_3}{\partial x_3}(\tau_0;\zeta_v)\right|<1.$$

From the variational equation, we have for all $0<t\leq\tau_0$

$$\begin{cases}\dfrac{\partial\Phi_1(t;X_0)}{\partial x_1} &= \dfrac{W^2e^{rt}}{[W-\widehat{x}_1(1-e^{rt})]^2},\\ \dfrac{\partial\Phi_2(t;X_0)}{\partial x_2} &= e^{-at}\left[\dfrac{H+\widehat{x}_3e^{et}}{H+\widehat{x}_3}\right]^{\frac{kb}{e}}\left[\dfrac{W-\widehat{x}_1(1-e^{rt})}{W}\right]^{\frac{kcW}{r}},\\ \dfrac{\partial\Phi_3(t;X_0)}{x_3} &= e^{et},\end{cases}$$

for which the details are contained in **Appendix A3**. From (3.18) we find

$$\left|\left(1-\frac{hq}{\alpha}\right)\frac{\partial\Phi_3}{\partial x_3}(\tau_0;\zeta_v)\right| = \left|\left(1-\frac{hq}{\alpha}\right)e^{e\frac{1}{e}\ln\frac{\alpha}{\alpha-hq}}\right| = 1 \not< 1.$$

Then the following result follows:

Theorem 3.7. *The equilibrium ζ_v is unconditionally unstable.*

Appendix

We begin by giving some general computational results, in what follows, and then specialize them for each solution in the four following subsections.

For all $t \in (0, \tau]$ we have

$$\frac{d}{dt}(D_X\Phi(t;X_0)) = \frac{\partial F}{\partial X}(\Phi(t;X_0))\frac{\partial\Phi}{\partial X}(t;X_0))$$

with the initial condition $D_X\Phi(0;X_0) = Id_{\mathbb{R}^3}$. Here

$$\frac{d}{dt}D_X\Phi(t;X_0) = \frac{d}{dt}\begin{pmatrix} \frac{\partial\Phi_1}{\partial x_1} & \frac{\partial\Phi_1}{\partial x_2} & \frac{\partial\Phi_1}{\partial x_3} \\ \frac{\partial\Phi_2}{\partial x_1} & \frac{\partial\Phi_2}{\partial x_2} & \frac{\partial\Phi_2}{\partial x_3} \\ \frac{\partial\Phi_3}{\partial x_1} & \frac{\partial\Phi_3}{\partial x_2} & \frac{\partial\Phi_3}{\partial x_3} \end{pmatrix}(t;X_0),$$

and

$$\frac{\partial F}{\partial X}(\Phi(t;X_0)) = \begin{pmatrix} \frac{\partial F_1}{\partial x_1} & \frac{\partial F_1}{\partial x_2} & \frac{\partial F_1}{\partial x_3} \\ \frac{\partial F_2}{\partial x_1} & \frac{\partial F_2}{\partial x_2} & \frac{\partial F_2}{\partial x_3} \\ \frac{\partial F_3}{\partial x_1} & \frac{\partial F_3}{\partial x_2} & \frac{\partial F_3}{\partial x_3} \end{pmatrix}(t;X_0)$$

$$= \begin{pmatrix} r(1-2\frac{x_1}{W}) - cx_2 & -cx_1 & 0 \\ kcx_2 & \left(-a + \frac{kbx_3}{H+x_3} + kcx_1\right) & \frac{kbHx_2}{(H+x_3)^2} \\ 0 & \frac{bx_3}{H+x_3} & e - \frac{bHx_2}{(H+x_3)^2} \end{pmatrix}(t;X_0),$$

and

$$\frac{\partial\Phi}{\partial X}(\Phi(t;X_0)) = \begin{pmatrix} \frac{\partial\Phi_1}{\partial x_1} & \frac{\partial\Phi_1}{\partial x_2} & \frac{\partial\Phi_1}{\partial x_3} \\ \frac{\partial\Phi_2}{\partial x_1} & \frac{\partial\Phi_2}{\partial x_2} & \frac{\partial\Phi_2}{\partial x_3} \\ \frac{\partial\Phi_3}{\partial x_1} & \frac{\partial\Phi_3}{\partial x_2} & \frac{\partial\Phi_3}{\partial x_3} \end{pmatrix}(t;X_0).$$

Moreover, we have

$$\frac{d}{dt}\left(\frac{\partial\Phi_1(t;X_0)}{\partial x_1}\right)=\frac{\partial F_1(t;X_0)}{\partial x_1}\frac{\partial\Phi_1(t;X_0)}{\partial x_1}+\frac{\partial F_1(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_1}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_1(t;X_0)}{\partial x_2}\right)=\frac{\partial F_1(t;X_0)}{\partial x_1}\frac{\partial\Phi_1(t;X_0)}{\partial x_2}+\frac{\partial F_1(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_2}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_1(t;X_0)}{\partial x_3}\right)=\frac{\partial F_1(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_3}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_2(t;X_0)}{\partial x_1}\right)=\frac{\partial F_2(t;X_0)}{\partial x_1}\frac{\partial\Phi_1(t;X_0)}{\partial x_1}+\frac{\partial F_2(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_1}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_2(t;X_0)}{\partial x_2}\right)=\frac{\partial F_2(t;X_0)}{\partial x_1}\frac{\partial\Phi_1(t;X_0)}{\partial x_2}$$
$$+\frac{\partial F_2(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_2}+\frac{\partial F_2(t;X_0)}{\partial x_3}\frac{\partial\Phi_3(t;X_0)}{\partial x_2}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_2(t;X_0)}{\partial x_3}\right)=\frac{\partial F_2(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_3}+\frac{\partial F_2(t;X_0)}{\partial x_3}\frac{\partial\Phi_3(t;X_0)}{\partial x_3}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_3(t;X_0)}{\partial x_1}\right)=\frac{\partial F_3(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_1}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_3(t;X_0)}{\partial x_2}\right)=\frac{\partial F_3(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_2}+\frac{\partial F_3(t;X_0)}{\partial x_3}\frac{\partial\Phi_3(t;X_0)}{\partial x_2}.$$
$$\frac{d}{dt}\left(\frac{\partial\Phi_3(t;X_0)}{\partial x_3}\right)=\frac{\partial F_3(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_3}+\frac{\partial F_3(t;X_0)}{\partial x_3}\frac{\partial\Phi_3(t;X_0)}{\partial x_3}.$$

We next specialize these computations to each individual equilibrium.

Appendix A1

For the equilibrium $X_0=\zeta$ we have

$$\frac{\partial\Phi_1(t;X_0)}{\partial x_3}=\frac{\partial\Phi_2(t;X_0)}{\partial x_1}=\frac{\partial\Phi_2(t;X_0)}{\partial x_3}=\frac{\partial\Phi_3(t;X_0)}{\partial x_1}=\frac{\partial\Phi_3(t;X_0)}{\partial x_2}=0.$$

Further,

$$\frac{d}{dt}\left(\frac{\partial\Phi_1(t;X_0)}{\partial x_1}\right)=\frac{\partial F_1(t;X_0)}{\partial x_1}\frac{\partial\Phi_1(t;X_0)}{\partial x_1} \tag{3.22}$$

$$\frac{d}{dt}\left(\frac{\partial\Phi_1(t;X_0)}{\partial x_2}\right)=\frac{\partial F_1(t;X_0)}{\partial x_1}\frac{\partial\Phi_1(t;X_0)}{\partial x_2}+\frac{\partial F_1(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_2} \tag{3.23}$$

$$\frac{d}{dt}\left(\frac{\partial\Phi_2(t;X_0)}{\partial x_2}\right)=\frac{\partial F_2(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_2} \tag{3.24}$$

$$\frac{d}{dt}\left(\frac{\partial\Phi_3(t;X_0)}{\partial x_3}\right)=\frac{\partial F_3(t;X_0)}{\partial x_3}\frac{\partial\Phi_3(t;X_0)}{\partial x_3}. \tag{3.25}$$

From (3.22), (3.24) and (3.25) it follows

$$\frac{\partial\Phi_1(t;X_0)}{\partial x_1}=e^{\int_0^t\frac{\partial F_1(\zeta(r))}{\partial x_1}dr}=e^{\frac{r}{W}\int_0^t(W-2x_s(\rho))d\rho}=\frac{W^2e^{rt}}{[W-\widehat{x}_1(1-e^{rt})]^2}.$$

$$\frac{\partial\Phi_2(t;X_0)}{\partial x_2}=e^{\int_0^t\frac{\partial F_2(\zeta(r))}{\partial x_2}dr}=e^{\int_0^t(kcx_s(\rho)-a)d\rho}=\frac{[W-\widehat{x}_1(1-e^{rt})]^{\frac{kcW}{r}}}{W^{\frac{kcW}{r}}e^{at}}.$$

$$\frac{\partial\Phi_3(t;X_0)}{\partial x_3}=e^{\int_0^t\frac{\partial F_3(\zeta(r))}{\partial x_3}dr}=e^{et}.$$

Appendix A2

For the equilibrium $X_0=\zeta_f$ we have

$$\frac{\partial\Phi_1(t;X_0)}{\partial x_2}=\frac{\partial\Phi_1(t;X_0)}{\partial x_3}=\frac{\partial\Phi_2(t;X_0)}{\partial x_1}=\frac{\partial\Phi_2(t;X_0)}{\partial x_3}=\frac{\partial\Phi_3(t;X_0)}{\partial x_1}=0.$$

Further,

$$\frac{d}{dt}\left(\frac{\partial\Phi_1(t;X_0)}{\partial x_1}\right)=\frac{\partial F_1(t;X_0)}{\partial x_1}\frac{\partial\Phi_1(t;X_0)}{\partial x_1} \tag{3.26}$$

$$\frac{d}{dt}\left(\frac{\partial\Phi_2(t;X_0)}{\partial x_2}\right)=\frac{\partial F_2(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_2} \tag{3.27}$$

$$\frac{d}{dt}\left(\frac{\partial\Phi_3(t;X_0)}{\partial x_2}\right)=\frac{\partial F_3(t;X_0)}{\partial x_2}\frac{\partial\Phi_2(t;X_0)}{\partial x_2}+\frac{\partial F_3(t;X_0)}{\partial x_3}\frac{\partial\Phi_3(t;X_0)}{\partial x_2} \tag{3.28}$$

$$\frac{d}{dt}\left(\frac{\partial\Phi_3(t;X_0)}{\partial x_3}\right)=\frac{\partial F_3(t;X_0)}{x_3}\frac{\partial\Phi_3(t;X_0)}{\partial x_3}. \tag{3.29}$$

From (3.26) it follows

$$\frac{\partial\Phi_1(t;X_0)}{\partial x_1}=e^{\int_0^t\frac{\partial F_1(\zeta_f(r))}{\partial x_1}dr}=e^{rt}.$$

Moreover, from (3.27) and(3.29) we have instead

$$\frac{\partial\Phi_2(t;X_0)}{\partial x_2}=e^{\int_0^t\frac{\partial F_2(\zeta_f(r))}{\partial x_2}dr}=e^{\int_0^t(-a+\frac{kbx_3(r)}{H+x_3(r)})dr}=e^{-at}\left[\frac{H+\widehat{x}_3e^{et}}{H+\widehat{x}_3}\right]^{\frac{kb}{e}}.$$

and

$$\frac{\partial \Phi_3(t;X_0)}{\partial x_3} = e^{\int_0^t \frac{\partial F_3(\zeta_f(r))}{\partial x_3} dr} = e^{et}.$$

Appendix A3

For the point $X_0 = \zeta_v$ we have

$$\frac{\partial \Phi_1(t;X_0)}{\partial x_3} = \frac{\partial \Phi_2(t;X_0)}{\partial x_3} = \frac{\partial \Phi_3(t;X_0)}{\partial x_1} = \frac{\partial \Phi_2(t;X_0)}{\partial x_1} = 0$$

together with

$$\frac{d}{dt}\left(\frac{\partial \Phi_1(t;X_0)}{\partial x_1}\right) = \frac{\partial F_1(t;X_0)}{\partial x_1}\frac{\partial \Phi_1(t;X_0)}{\partial x_1} \tag{3.30}$$

$$\frac{d}{dt}\left(\frac{\partial \Phi_1(t;X_0)}{\partial x_2}\right) = \frac{\partial F_1(t;X_0)}{\partial x_1}\frac{\partial \Phi_1(t;X_0)}{\partial x_2} + \frac{\partial F_1(t;X_0)}{\partial x_2}\frac{\partial \Phi_2(t;X_0)}{\partial x_2} \tag{3.31}$$

$$\frac{d}{dt}\left(\frac{\partial \Phi_2(t;X_0)}{\partial x_2}\right) = \frac{\partial F_2(t;X_0)}{\partial x_2}\frac{\partial \Phi_2(t;X_0)}{\partial x_2} \tag{3.32}$$

$$\frac{d}{dt}\left(\frac{\partial \Phi_3(t;X_0)}{\partial x_2}\right) = \frac{\partial F_3(t;X_0)}{\partial x_2}\frac{\partial \Phi_2(t;X_0)}{\partial x_2} + \frac{\partial F_3(t;X_0)}{\partial x_3}\frac{\partial \Phi_3(t;X_0)}{\partial x_2} \tag{3.33}$$

$$\frac{d}{dt}\left(\frac{\partial \Phi_3(t;X_0)}{x_3}\right) = \frac{\partial F_3(t;X_0)}{x_3}\frac{\partial \Phi_3(t;X_0)}{x_3}. \tag{3.34}$$

From (3.34) it follows

$$\frac{\partial \Phi_3(t;X_0)}{x_3} = e^{\int_0^t \frac{\partial F_3(\zeta_v(r))}{\partial x_3} dr} = e^{et}.$$

From (3.30) it follows

$$\frac{\partial \Phi_1(t;X_0)}{\partial x_1} = e^{\int_0^t \frac{\partial F_1(\zeta_v(r))}{\partial x_1} dr} = e^{\frac{r}{W}\int_0^t (W - 2x_1(\rho))d\rho} = \frac{W^2 e^{rt}}{[W - \widehat{x}_1(1-e^{rt})]^2}.$$

and finnaly, from (3.32) it follows

$$\begin{aligned}\frac{\partial \Phi_2(t;X_0)}{\partial x_2} = e^{\int_0^t \frac{\partial F_2(\zeta_v(r))}{\partial x_2} dr} &= e^{\int_0^t \left(-a + \frac{kbx_3(r)}{H + x_3(r)} + kcx_1(r)\right) dr} \\ &= e^{-at}\left[\frac{H + \widehat{x}_3 e^{et}}{H + \widehat{x}_3}\right]^{\frac{kb}{e}} \left[\frac{W - \widehat{x}_1(1-e^{rt})}{W}\right]^{\frac{kcW}{r}}.\end{aligned}$$

Chapter 4

Study and Analysis of a Model for Coronavirus

4.1 Analysis of a Model for Coronavirus Spread

4.1.1 Introduction

The coronavirus infection has been spreading for a few months. Authorities in several countries have relied on scientific tools for fighting the epidemics. With the lack of a vaccine, distancing methods have been forced on populations to avoid the transmission by direct contact. In laboratories, possible vaccines are being developed, but at the moment they are still at the experimental stage [17]. Meanwhile several models, mathematical, statistical and computer-science-based, are being developed to study the disease and contribute to fighting it.

Models for the spread of epidemics are classic, and an excellent presentation is [29]. In general, the total population is partitioned into at least two classes, susceptibles and infectives, with migrations from the former to the latter by disease propagation through direct or indirect contact, if the disease is transmissible. Additionally, if it can be overcome but causes relapses, the infected can become susceptible again, after maybe going through an intermediate class of being recovered. More sophisticated versions include quarantined and exposed individuals. Some of these classes will be considered also in the present study and illustrated in detail before the model formulation process.

In [56] the disease evolution forecast in several of the most affected countries is attempted, using for that purpose, parameter estimation techniques to calibrate the model. The involved compartments are susceptibles, asymptomatic individuals and symptomatic ones, which in turn are partitioned into reported and unreported cases.

In [**?**] a simple SIRI model is considered, in which the recovered could still contribute to the disease spreading. The model is then extended to account for a possible vaccine, which, unfortunately, at present is not yet available, although several laboratories worldwide are trying to develop and test it, as mentioned above.

In [19] a dynamic model for the diffusion of Covid-19 has been proposed. The transmission network is made by the bats–hosts–reservoir–people compartments; compare also [17]. As it amounts to about 14 differential equations and 25 parameters, it is rather complex. From it, the authors have obtained a simplified version, consisting of six compartments and 13 parameters. Then, the disease basic reproduction number has been calculated.

Our aim here is the mathematical analysis of a slightly modified version of the simpler model in [19]. The most important change accounts for the fact that asymptomatic people may indeed turn into fully symptomatic and infectious individuals. This feature also distinguishes the system introduced here from the one studied in [33], which, however, contains more compartments. The main aim of that study is the forecast of the epidemic spread in various cities in China, considering, additionally, weather data, which finally indicate that higher humidity favors the containment of a coronavirus epidemic. Our focus in the first part of this investigation is the theoretical analysis of the proposed system, and then we perform some preliminary simulations with realistic parameter values. More extended simulations will be devoted to a subsequent study.

The analysis of dynamical systems usually considers the possible equilibria that can be attained, assessing their feasibility and stability, and possible connections between them. For more details on these issues we refer the reader to classical texts, such as [63, 68, 75].

The section is organized as follows. The main findings are outlined in the next subsection, which also discusses the results of numerical simulations. subSection 4.1.4 contains an evaluation of their implications under various distancing policies. We formulate the model in subSection 4.1.2, where we also analyze it mathematically, showing boundedness of the trajectories, establishing an expression for the disease basic reproduction number, finding its equilibria and assessing their local stability,

and global stability is established just for the disease-free equilibrium. The subsection ends with the details on the numerical simulations.

4.1.2 Materials and Methods

Here we develop a mathematical model of coronavirus, which is a zoonotic disease. Its biological characteristics indicate that the virus transmission occurred first from infected animals to humans [19], and then spread among populations worldwide by contact with infected individuals, to make it a pandemic. Let $N(t)$ denote the total population. It is partitioned into the following five disjoint classes of individuals:

$S(t)$: The susceptible class, the individuals who have not yet been exposed to the virus.

$E(t)$: The exposed class, describing people who have become in contact with the virus, but are in incubation period and not yet able to spread the disease; possible presymptomatic individuals that can transmit the infection [8, 40, 83] are assumed to have already moved to the asymptomatic class defined below.

$I(t)$: The symptomatic infectious class, individuals that manifest symptoms and can spread the disease.

$A(t)$: The asymptomatic infectious class; those persons that can spread the disease even without having explicit symptoms.

$R(t)$: The removed class, that includes the people that recovered from the disease.

Thus, $N(t) = S(t) + E(t) + I(t) + A(t) + R(t)$. The basic mechanisms underlying the model are shown in Figure 4.1. The model is formulated taking into account all the possible interactions among the compartments that were described above. Under the quasi-steady-state assumption of the total human population, we impose that susceptible individuals are recruited at the constant rate Λ, become infected by direct contact with an infectious individual at rate β_I, which is scaled by a factor k to account for the possibility that the latter is asymptomatic. Finally, all human individuals are subject to natural mortality d_p. These considerations are incorporated in the first equation of the system (4.16).

Individuals that contract the disease are accounted for in the second equation of (4.16). They become exposed, i.e., they cannot yet spread the virus, which needs an incubation period within the body of its hosts. In this class enter the susceptibles that were contaminated in the two ways described

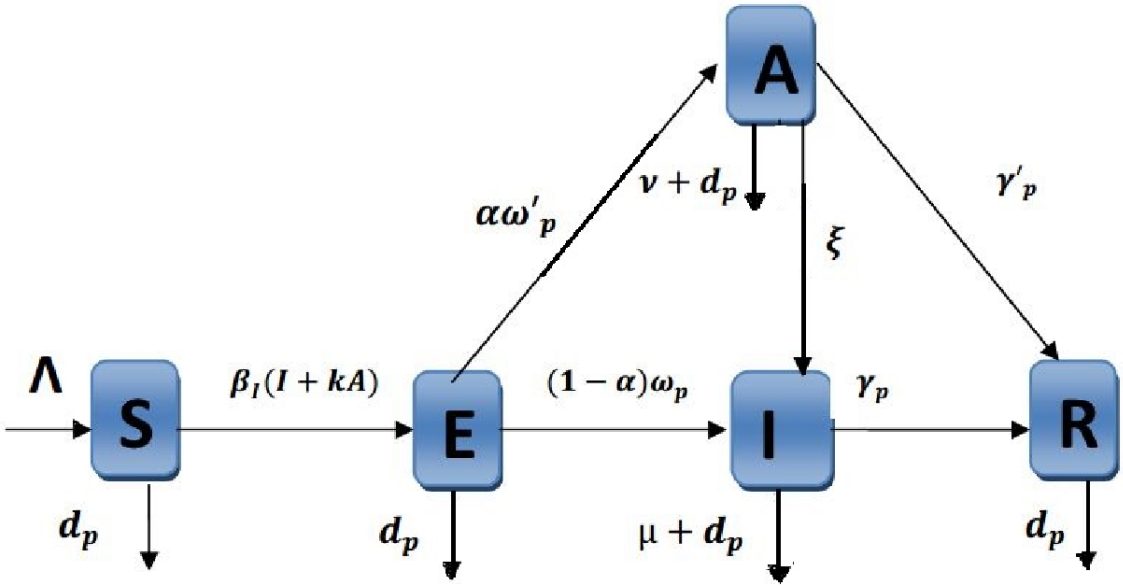

Figure 4.1: The basic interactions among the compartments.

earlier. People leave it by becoming infectious, and either showing symptoms, thereby migrating into class I, or not, therefore, finding themselves in class A. The progression rates into these two classes are ω_p and ω'_p. Furthermore, we assume that a fraction α becomes asymptomatic and $1-\alpha$ instead will manifest symptoms.

The third equation models the symptomatic infectious, recruited from the exposed class at rate $(1-\alpha)\omega$ as described above. Furthermore, there could be asymptomatic individuals that become symptomatic at rate ξ. They leave this class by either progressing to the recovered class at rate γ_p, or dying, naturally or by causes related to the disease at rate μ.

The asymptomatic individuals modeled in the fourth equation appear from the exposed ones, and leave the class by overcoming the disease at rate γ'_p, dying naturally or by disease-related causes at rate ν, or eventually showing the symptoms, for which they migrate into class I.

Recovered individuals are those that have healed from the disease. They are subject only to natural mortality. We assume that they have also become immune so that they are unaffected if become in contact with the infectious.

Note that in the simulations also the cumulative class of disease-related deceased people is shown, although the dead are not explicitly accounted for in the model. They indeed represent a sink, and thus

do not contribute to the disease propagation. Incidentally, instead, in cultures where the deceased are kept for a while before burial and become in contact with the relatives, it may be necessary to introduce this class in the model, as another potential source of infection.

Taking into account the above considerations, the model dynamics is regulated by the following system of nonlinear ordinary differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta_I S(I + kA) - d_p S, \\
\frac{dE}{dt} &= \beta_I S(I + kA) - (1-\alpha)\omega_p E - \alpha\omega_p' E - d_p E, \\
\frac{dI}{dt} &= (1-\alpha)\omega_p E - (\gamma_p + d_p + \mu) I + \xi A, \\
\frac{dA}{dt} &= \alpha\omega_p' E - (\gamma_p' + d_p + \nu) A - \xi A, \\
\frac{dR}{dt} &= \gamma_p I + \gamma_p' A - d_p R,
\end{aligned} \tag{4.1}$$

or alternatively, excluding completely the demographic features, by setting $\Lambda = 0$ and $d_p = 0$ in (4.16). All the parameters are nonnegative and their meaning is summarized in Table 4.1. Note that in view of the definitions, $\frac{1}{\omega_p}$, $\frac{1}{\omega_p'}$ $\frac{1}{\gamma_p}$, $\frac{1}{\gamma_p'}$, represent respectively the incubation period before manifesting symptoms, the latent period before becoming asymptomatic infectious, the infectious period for symptomatic infection and the infectious period for asymptomatic infection.

Theorem 4.1. *The system trajectories are bounded. Letting*

$$M = \max\left\{N(0), \frac{\Lambda}{d_p}\right\}.$$

The set

$$\Gamma = \{(S, E, I, A, R) : S + E + I + A + R \leq M, \quad S > 0,\ E \geq 0,\ I \geq 0,\ A \geq 0,\ R \geq 0\}. \tag{4.2}$$

represents their ultimate attractor. In particular, if $N(0) < \Lambda d_p^{-1}$, $M = \Lambda d_p^{-1}$.

Proof. From the system (4.16) it follows that the total population evolves as follows:

$$\frac{dN}{dt} + d_p N = \Lambda - \nu A - \mu I \leq \Lambda.$$

Solving the differential inequality easily gives

$$N(t) \leq N(0)\exp(-d_p t) + \frac{\Lambda}{d_p}[1 - \exp(-d_p t)] \leq M,$$

so that all subpopulations, being nonnegative, are bounded as well. □

Table 4.1: Model parameters and their meaning.

Λ	susceptibles recruitment rate
d_p	natural mortality
β_I	disease transmission rate
k	transmissibility ratio between asymptomatics and symptomatics
μ	disease-related mortality for infected
ν	disease-related mortality for asymptomatics
ω_p	progression rate from exposed to symptomatic
ω_p'	progression rate from exposed to asymptomatic
α	fraction of exposed that turn asymptomatic
ξ	progression rate from asymptomatic to symptomatic
γ_p	recovery rate from symptomatic infection
γ_p'	recovery rate from asymptomatic infection

Note that Γ is positively invariant since all solutions of system (4.16) originating in Γ remain there for all $t > 0$, in view of the existence and uniqueness of its solutions.

4.1.2.1 System's Equilibria Assessment

The equilibrium points of the model are obtained by equating the right hand side of system (4.16) to zero. The solution of the so-obtained algebraic system gives three equilibrium points: the coronavirus-free equilibrium $C_0 = (S_0, 0, 0, 0, 0,)$, the coronavirus-symptomatic-infected-free equilibrium $C_I = (S_I, E_I, 0, A_I, R_I)$ with conditions $\alpha = 1$ and $\xi = 0$, and the fully coronavirus endemic equilibrium $C^* = (S^*, E^*, I^*, A^*, R^*)$ when either $\alpha \neq 1$ or Specifically, for the former two we have:

$$S_0 = \frac{\Lambda}{d_p}, \quad E_I = \frac{1}{B_T}\left(\Lambda - \frac{d_p B_T C_T H_T}{\beta_I \omega_p' D_T}\right), \quad S_I = \frac{\Lambda - B_T E^*}{d_p}, \quad A_I = \left(\frac{\omega_p'}{H_T}\right) E_I, \quad R_I = \left(\frac{\gamma_p'}{d_p}\frac{\omega_p'}{H_T}\right) E_I,$$

where

$$B_T = (1-\alpha)\omega_p + \alpha\omega_p' + d_p, \quad C_T = \gamma_p + \mu + d_p, \quad D_T = \xi + k(\gamma_p + \mu + d_p), \quad H_T = \gamma_p' + \nu + \xi + d_p. \quad (4.3)$$

The feasibility conditions for C_I are

$$\Lambda > \frac{d_p B_T C_T H_T}{\beta_I \omega_p' D_T}, \quad \alpha = 1 \quad \text{et} \quad \xi = 0. \tag{4.4}$$

For the fully endemic equilibrium we find

$$E^* = \frac{1}{B_T}\left(\Lambda - \frac{d_p B_T C_T H_T}{\beta_I\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}\right), \qquad S^* = \frac{\Lambda - B_T E^*}{d_p},$$

$$I^* = \left(\frac{(1-\alpha)\omega_p H_T + \alpha\omega_p'\xi}{C_T H_T}\right) E^*, \qquad A^* = \left(\frac{\alpha\omega_p'}{H_T}\right) E^*$$

$$\text{and } R^* = \left(\frac{\gamma_p}{d_p}\left(\frac{(1-\alpha)\omega_p H_T + \alpha\omega_p'\xi}{C_T H_T}\right) + \frac{\gamma_p'}{d_p}\left(\frac{\alpha\omega_p'}{H_T}\right)\right) E^*,$$

with feasibility condition

$$\Lambda > \frac{d_p B_T C_T H_T}{\beta_I\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}, \qquad \text{et de plus} \qquad \alpha \neq 1 \qquad \text{or} \qquad \xi \neq 0. \tag{4.5}$$

4.1.2.2 The Basic Reproduction Number

The basic reproduction number R_0 for system (4.16) is found using the next generation matrix method, [78]. The reduced system of (4.16) may be written in compact form as: $X' = F(X) - V(X)$ where $X = (E, I, A)$

$$F(E,I,A) = \begin{pmatrix} \beta_I S(I + kA) \\ 0 \\ 0 \end{pmatrix}, \quad -V(E,I,A) = \begin{pmatrix} -(1-\alpha)\omega_p E - \alpha\omega_p' E - d_p E \\ (1-\alpha)\omega_p E - (\gamma_p + d_p + \mu)I + \xi A \\ \alpha\omega_p' E - (\gamma_p' + d_p + \nu)A - \xi A \end{pmatrix}.$$

The Jacobian matrices of $F(X)$ and $V(X)$ at the disease-free equilibrium point C_0 are

$$J_F(C_0) = \begin{pmatrix} 0 & \beta_I S_0 & \beta_I S_0 k \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$J_V(C_0) = \begin{pmatrix} -B_T & 0 & 0 \\ (1-\alpha)\omega_p & -C_T & \xi \\ \alpha\omega_p' & 0 & -H_T \end{pmatrix}.$$

We find that

$$J_V^{-1}(C_0) = \begin{pmatrix} \frac{-1}{B_T} & 0 & 0 \\ \frac{-[(1-\alpha)\omega_p H_T + \alpha\omega_p'\xi]}{C_T B_T H_T} & \frac{-1}{C_T} & \frac{-\xi}{C_T H_T} \\ \frac{-\alpha\omega_p'}{B_T H_T} & 0 & \frac{-1}{H_T} \end{pmatrix}.$$

The next generation matrix is

$$-J_F(C_0)J_V^{-1}(C_0) = \begin{pmatrix} \beta_I S_0 \frac{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T}{C_T B_T H_T} & \frac{\beta_I S_0}{C_T} & \frac{\beta_I S_0 D_T}{C_T H_T} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

Thus

$$R_0 = \rho(-J_F(C_0)J_V^{-1}(C_0)) = \beta_I S_0 \frac{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T}{C_T B_T H_T}. \tag{4.6}$$

The conditions (4.20) (resp. (4.22)) are equivalent to $R_0 > 1$ for $\alpha = 1$ and $\xi = 0$ (resp.$R_0 > 1$ for either $\alpha \neq 1$ or $\xi \neq 0$).

We have the following theorem

Theorem 4.2. *System (4.16) has the following equilibria:*

1. *The coronavirus-free equilibrium* $C_0 = (S_0, 0, 0, 0, 0) = \left(\frac{\Lambda}{d_p}, 0, 0, 0, 0\right)$ *which exists always.*
2. *In addition, if* $R_0 > 0$ *then system (4.16) admits another nontrivial equilibrium, in fact:*

When $\alpha = 1$ *and* $\xi = 0$*, it is the coronavirus-symptomatic-infected-free equilibrium* $C_I = (S_I, E_I, I_I, A_I, R_I)$*. When either* $\alpha \neq 1$ *or* $\xi \neq 0$*, it is the fully coronavirus endemic equilibrium* $C^* = (S^*, E^*, I^*, A^*, R^*)$*.*

4.1.2.3 System's Equilibria Stability

4.1.2.4 Local Stability

In this subsection we investigate the local stability of the system's equilibria.

Theorem 4.3.

1. *The coronavirus-free equilibrium* $C_0 = (S_0, 0, 0, 0, 0)$ *of the system (4.16) is locally asymptotically stable if*

$$\Lambda < \frac{d_p}{\beta_I} \frac{B_T C_T H_T}{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T}, \ (\textit{ resp. } R_0 < 1). \tag{4.7}$$

2. *If* $\Lambda > \dfrac{d_p}{\beta_I}\dfrac{B_T C_T H_T}{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T}$, *(resp.* $R_0 > 1$*), then the coronavirus-free equilibrium* C_0 *of the system (4.16) is unstable.*

Proof. The Jacobian matrix of system (4.16) at the coronavirus-free equilibrium C_0 is:

$$J(C_0) = \begin{pmatrix} -d_p & 0 & -\dfrac{\beta_I\Lambda}{d_p} & -\dfrac{k\beta_I\Lambda}{d_p} & 0 \\ 0 & -B_T & \dfrac{\beta_I\Lambda}{d_p} & \dfrac{k\beta_I\Lambda}{d_p} & 0 \\ 0 & (1-\alpha)\omega_p & -C_T & \xi & 0 \\ 0 & \alpha\omega_p' & 0 & -H_T & 0 \\ 0 & 0 & \gamma_p & \gamma_p' & -d_p \end{pmatrix}.$$

At point C_0, the eigenvalues of J are $-d_p$ of multiplicity order two and the roots of the following characteristic polynomial of a three by three submatrix of J whose coefficients a_i, $i = 0, \ldots, 2$ are given in (4.9):

$$\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0. \tag{4.8}$$

Where

$$\begin{aligned} a_2 &= B_T + C_T + H_T, \\ a_1 &= H_T[B_T + C_T] + B_T C_T - \beta_I S_0((1-\alpha)\omega_p + k\alpha\omega_p') \\ a_0 &= B_T C_T H_T - \beta_I S_0\left((1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right). \end{aligned} \tag{4.9}$$

It is evident that $a_2 > 0$. From condition (4.27) the following inequalities are also satisfied

$$\begin{aligned} a_0 &= B_T C_T H_T - \beta_I S_0\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right] \\ &= \frac{\beta_I}{d_p}\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]\left(\frac{d_p}{\beta_I}\frac{B_T C_T H_T}{\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]} - \Lambda\right) > 0, \end{aligned}$$

$$\begin{aligned} \left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right] a_1 &= [H_T(B_T + C_T) + B_T C_T]\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right] \\ &\quad -\beta_I S_0\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right][(1-\alpha)\omega_p + k\alpha\omega_p'] \\ &= [H_T(B_T + C_T) + B_T C_T]\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right] \\ &\quad +[a_0 - B_T C_T H_T][(1-\alpha)\omega_p + k\alpha\omega_p'] \\ &= H_T(B_T + C_T)(1-\alpha)\omega_p H_T + (H_T C_T + B_T C_T)\alpha\omega_p'\xi \\ &\quad +a_0[(1-\alpha)\omega_p + k\alpha\omega_p'] > 0 \end{aligned}$$

and

$$\begin{aligned}
\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right] a_1 a_2 &= H_T(B_T+C_T)(1-\alpha)\omega_p H_T a_2 + (H_T C_T + B_T C_T)\alpha\omega_p'\xi\ a_2 \\
&\quad + a_0[(1-\alpha)\omega_p + k\alpha\omega_p']a_2 \\
&= H_T(B_T+C_T)(1-\alpha)\omega_p H_T a_2 + (H_T C_T + B_T C_T)\alpha\omega_p'\xi\ a_2 \\
&\quad + a_0(1-\alpha)\omega_p(B_T+C_T+H_T) + a_0 k\alpha\omega_p'(B_T+C_T+H_T) \\
&> B_T C_T \alpha\omega_p'\xi a_2 + a_0(1-\alpha)\omega_p H_T + a_0\alpha\omega_p'(kC_T+\xi) - a_0\alpha\omega_p'\xi \\
&> B_T C_T H_T \alpha\omega_p'\xi + a_0[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T] - B_T C_T H_T \alpha\omega_p'\xi \\
&= a_0[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T].
\end{aligned}$$

Thus, $a_i > 0$, $i = 0, \ldots, 2$ and $a_2 a_1 > a_0$.

Then, according to the Routh–Hurwitz criterion, all the roots of the characteristic Equation (4.29) have negative real parts. Therefore, the coronavirus-free equilibrium point C_0 is locally asymptotically stable under condition (4.27). □

Since we can deduce the stability of the coronavirus symptomatic infected-free equilibrium C_I from the stability of the coronavirus endemic equilibrium C^* simply by taking $\alpha = 1$ and $\xi = 0$ in the latter, we now just analyze the coronavirus endemic equilibrium C^*.

Theorem 4.4. *The coronavirus endemic equilibrium C^* is locally asymptotically stable if*

$$\Lambda > \frac{d_p}{\beta_I}\frac{B_T C_T H_T}{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T},\ (\ resp.\ R_0 > 1). \tag{4.10}$$

Proof. The Jacobian matrix of system (4.16)) at the coronavirus endemic equilibrium C^* is:

$$J(C^*) = \begin{pmatrix}
-\beta_I(I^*+kA^*) - d_p & 0 & -\beta_I S^* & -\beta_I S^* k & 0 \\
\beta_I(I^*+kA^*) & -B_T & \beta_I S^* & \beta_I S^* k & 0 \\
0 & (1-\alpha)\omega_p & -C_T & \xi & 0 \\
0 & \alpha\omega_p' & 0 & -H_T & 0 \\
0 & 0 & \gamma_p & \gamma_p' & -d_p
\end{pmatrix}.$$

At point C^*, the eigenvalues of J are $-d_p$ and the roots of the characteristic polynomial of a three by three submatrix of J. The characteristic equation, in which the coefficients c_i, $i = 0, \ldots, 3$ are

given in (4.12), is:

$$\lambda^4 + c_3\lambda^3 + c_2\lambda^2 + c_1\lambda + c_0 = 0. \tag{4.11}$$

Where

$$\begin{cases} c_3 &= \beta_I(I^* + kA^*) + d_p + H_T + B_T + C_T > 0, \\ c_2 &= [\beta_I(I^* + kA^*) + d_p](H_T + B_T + C_T) + B_TC_T + H_T(B_T + C_T) \\ & \quad -[\alpha\omega_p'k + (1-\alpha)\omega_p]\beta_I S^*, \\ c_1 &= [\beta_I(I^* + kA^*) + d_p][B_TC_T + H_T(B_T + C_T)] + H_TB_TC_T \\ & \quad -[\alpha\omega_p'(kd_p + D_T) + (1-\alpha)\omega_p(d_p + H_T)]\beta_I S^*, \\ c_0 &= [\beta_I(I^* + kA^*) + d_p]H_TB_TC_T - d_p[\alpha\omega_p'D_T + (1-\alpha)\omega_pH_T]\beta_I S^*. \end{cases} \tag{4.12}$$

It is evident that $c_3 > 0$. From condition (4.30) the following inequalities are also satisfied.

$$\begin{aligned} c_0 &= [\beta_I(I^* + kA^*) + d_p]H_TB_TC_T - \beta_I[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T]d_pS^* \\ &= \beta_I\left[(1-\alpha)\omega_pH_T + \alpha\omega_p'(\xi + kC_T)\right]B_TE^* + d_pH_TC_TB_T \\ &\quad -\beta_I[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T](\Lambda - B_TE^*) \\ &= \beta_I\left[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T\right]\left(2B_TE^* + \frac{d_pH_TC_TB_T}{\beta_I[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T]} - \Lambda\right) \\ &= \beta_I\left[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T\right]B_TE^* > 0, \end{aligned}$$

$$\begin{aligned} c_1 &= [\beta_I(I^* + kA^*) + d_p][B_TC_T + H_T(B_T + C_T)] + H_TB_TC_T \\ &\quad -[(1-\alpha)\omega_p(d_p + H_T) + \alpha\omega_p'(kd_p + D_T)]\beta_I S^* \\ &= \left[\beta_I\left(\frac{(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T}{C_TH_T}\right)E^* + d_p\right][B_TC_T + H_T(B_T + C_T)] \\ &\quad -\beta_I[(1-\alpha)\omega_p + \alpha\omega_p'k](\Lambda - B_TE^*) \\ &= \beta_I\left(\frac{(1-\alpha)\omega_pH_T(B_T + C_T)}{C_T} + \frac{\alpha\omega_p'\xi B_T}{C_T} + \frac{\alpha\omega_p'D_T(B_T + H_T)}{H_T}\right)E^* \\ &\quad +d_p[B_TC_T + H_T(B_T + C_T)] - \beta_I[(1-\alpha)\omega_p + \alpha\omega_p'k](\Lambda - 2B_TE^*) \\ &= \beta_I\left(\frac{(1-\alpha)\omega_pH_T(B_T + C_T)}{C_T} + \frac{\alpha\omega_p'\xi B_T}{C_T} + \frac{\alpha\omega_p'D_T(B_T + H_T)}{H_T}\right)E^* \\ &\quad +d_p[B_TC_T + H_T(B_T + C_T)] - \beta_I[(1-\alpha)\omega_p + \alpha\omega_p'k]\left(\frac{2d_pB_TC_TH_T}{\beta_I\left[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T\right]} - \Lambda\right) \\ &= \beta_I[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T]\left(\frac{C_TH_T + B_T(C_T + H_T)}{C_TH_T}\right)E^* \\ &\quad +d_p\left(\frac{(B_T + C_T)H_T^2(1-\alpha)\omega_p + H_TB_T\alpha\omega_p'\xi + C_T(B_T + H_T)\alpha\omega_p'D_T}{\left[(1-\alpha)\omega_pH_T + \alpha\omega_p'D_T\right]}\right) > 0, \end{aligned}$$

$$
\begin{aligned}
c_2 &= [\beta_I(I^*+kA^*)+d_p](H_T+B_T+C_T)+B_TC_T+H_T(B_T+C_T)\\
&\quad -[\alpha\omega_p'k+(1-\alpha)\omega_p]\beta_I S^*\\
&= \left[\beta_I\left(\frac{(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T}{C_TH_T}\right)E^*+d_p\right](H_T+B_T+C_T)+B_TC_T+H_T(B_T+C_T)\\
&\quad -[\alpha\omega_p'k+(1-\alpha)\omega_p]\beta_I\frac{\Lambda-B_TE^*}{d_p}\\
&= \beta_I\left(\frac{(1-\alpha)\omega_p(H_T+B_T)}{C_T}+\frac{\alpha\omega_p'\xi(H_T+B_T+C_T)}{C_TH_T}+\frac{\alpha\omega_p'k(B_T+C_T)}{H_T}\right)E^*\\
&\quad +d_p(H_T+B_T+C_T)+B_TC_T+H_T(B_T+C_T)\\
&\quad +\beta_I[(1-\alpha)\omega_p+\alpha\omega_p'k]\left(\frac{(d_p+B_T)E^*-\Lambda}{d_p}\right)\\
&= \beta_I\left(\frac{(1-\alpha)\omega_p(H_T+B_T)}{C_T}+\frac{\alpha\omega_p'\xi(H_T+B_T+C_T)}{C_TH_T}+\frac{\alpha\omega_p'k(B_T+C_T)}{H_T}\right)E^*\\
&\quad +d_p(H_T+B_T+C_T)+B_TC_T+H_T(B_T+C_T)\\
&\quad +\frac{\beta_I[(1-\alpha)\omega_p+\alpha\omega_p'k]}{B_T}\left(\Lambda-\frac{(d_p+B_T)B_TC_TH_T}{\beta_I\left[(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T\right]}\right)\\
&= \beta_I(B_T+C_T+H_T)\left(\frac{(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T}{C_TH_T}\right)E^*\\
&\quad +d_p(H_T+B_T+C_T)+C_TH_T+B_T\left(\frac{(1-\alpha)\omega_pH_T^2+H_T\alpha\omega_p'\xi+\alpha\omega_p'C_TD_T}{\left[(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T\right]}\right)>0
\end{aligned}
$$

and

$$
\begin{aligned}
c_1(c_3c_2-c_1) &= \beta_I\left(\frac{(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T}{C_TH_T}\right)E^*c_1c_2\\
&\quad +\beta_I\left[(H_T+C_T+d_p)H_T+C_T(C_T+d_p)\right]\left(\frac{\left[(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T\right]}{C_TH_T}\right)E^*c_1\\
&\quad +\beta_I(H_T+B_T+C_T+d_p)B_T\left(\frac{(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T}{C_TH_T}\right)E^*c_1\\
&\quad +(H_T+B_T+C_T)(H_T+B_T+C_T+d_p)d_pc_1+C_TH_T(C_T+H_T+B_T)c_1\\
&\quad +B_T(B_T+C_T+H_T)\left(\frac{[(1-\alpha)\omega_pH_T^2+\alpha\omega_p'C_TD_T]+\alpha\omega_p'\xi H_T}{\left[(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T\right]}\right)c_1\\
&> \beta_I^2B_TE^{*2}\left\{\beta_I\left[(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T\right]\left(\frac{(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T}{C_TH_T}\right)^2E^*\right.\\
&\quad \left.+2(d_p+H_T+B_T+C_T)\left[(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T\right]\left(\frac{(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T}{C_TH_T}\right)\right\}\\
&\quad +\beta_IB_T(d_p+H_T+B_T+C_T)^2\left[(1-\alpha)\omega_pH_T+\alpha\omega_p'D_T\right]E^*\\
&= c_0c_3^2.
\end{aligned}
$$

Thus, $c_i > 0$, $i = 0, \ldots, 3$ and $c_1(c_3c_2 - c_1) > c_0c_3^2$. Then, according to the Routh–Hurwitz criterion, all the roots of the characteristic Equation (4.31) have negative real parts. Therefore, the coronavirus endemic equilibrium point C^* is locally asymptotically stable under condition (4.30). □

From Theorem 4.4 the following result is reached.

Theorem 4.5. *The coronavirus symptomatic-infected-free equilibrium C_I of the system (4.16) is locally asymptotically stable if*

$$\Lambda > \frac{d_p}{\beta_I}\frac{B_TC_TH_T}{\omega_p'D_T}, \ (\ resp.\ R_0 > 1). \tag{4.13}$$

Proof. The result can easily obtained from Theorem 4.4 by taking $\alpha = 1$ and $\xi = 0$. □

Additionally, from the previous discussion, we can claim the following result:

Theorem 4.6. *There is a transcritical bifurcation between C_0 and C^*.*

4.1.2.5 Global Stability

Next, we address the issue of global stability of the coronavirus–free equilibrium, employing as a tool a suitably constructed Lyapunov function and La Salle's Invariance Principle.

Theorem 4.7. *The coronavirus-free equilibrium C_0 of model (4.16) is globally asymptotically stable if*

$$\Lambda < \frac{d_pB_TC_TH_T}{\beta_I[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']}, \ (\ resp.\ R_0 < 1). \tag{4.14}$$

Proof. First, the four equations of (4.16) are independent of R, therefore, the last equation of (4.16) can be omitted without loss of generality. Hence, let us consider the following function:

$$P = \frac{1}{2S_0}(S - S_0)^2 + E + \frac{B_T}{[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']}(H_TI + D_TA) \tag{4.15}$$

It is easily seen that the above function is nonnegative and also $P = 0$ if and only if $S = S_0$, $E = 0$, $I = 0$ and $A = 0$. Further, calculating the time derivative of P along the positive solutions of (4.16),

we find:

$$\begin{aligned}
\frac{dP}{dt} &= \frac{1}{S_0}(S-S_0)(-\beta_I S(I+kA)-d_p(S-S_0))+\beta_I S(I+kA)-B_T E \\
&\quad +\frac{B_T H_T((1-\alpha)\omega_p E-C_T I+\xi A)}{[(1-\alpha)\omega_p H_T+D_T\alpha\omega'_p]}+\frac{B_T D_T(\alpha\omega'_p E-H_T A)}{[(1-\alpha)\omega_p H_T+D_T\alpha\omega'_p]} \\
&= -\frac{d_p}{S_0}(S-S_0)^2+\beta_I[2S-\frac{S^2}{S_0}-S_0](I+kA)+\beta_I S_0(I+kA) \\
&\quad -\frac{B_T C_T H_T I}{[(1-\alpha)\omega_p H_T+D_T\alpha\omega'_p]}-\frac{B_T(-\xi+D_T)H_T A}{[(1-\alpha)\omega_p H_T+D_T\alpha\omega'_p]} \\
&= -\frac{d_p}{S_0}(S-S_0)^2+\beta_I[2S-\frac{S^2}{S_0}-S_0](I+kA) \\
&\quad +\left(\beta_I S_0-\frac{B_T C_T H_T}{[(1-\alpha)\omega_p H_T+D_T\alpha\omega'_p]}\right)(I+kA) \\
&= -\frac{d_p}{S_0}(S-S_0)^2+\beta_I[2S-\frac{S^2}{S_0}-S_0](I+kA) \\
&\quad +\frac{\beta_I}{d_p}\left(\Lambda-\frac{d_p B_T C_T H_T}{\beta_I[(1-\alpha)\omega_p H_T+D_T\alpha\omega'_p]}\right)(I+kA).
\end{aligned}$$

From condition (4.33) we can show that the coefficients of the term $I+kA$ in the last equality are negative. Further, we have $2S-\frac{S^2}{S_0}-S_0=-\frac{S^2-2SS_0+S_0^2}{S_0}=-\frac{(S-S_0)^2}{S_0}\leq 0$ for all $S\geq 0$. Thus, we have $\frac{dP}{dt}\leq 0$ for all $(S,E,I,A)\in\mathbb{R}^4_+$ and $\frac{dP}{dt}=0$ if and only if $(S,E,I,A)=(S_0,0,0,0)$. Thus, the only invariant set contained in $\mathbb{R}^4_+$ is $\{(S_0,0,0,0)\}$. Hence, La Salle's theorem implies convergence of the solutions (S,E,I,A) to $(S_0,0,0,0)$. From the last equation if (4.16) we can show obviously that R converge also to 0.

Therefore C_0 is globally asymptotically stable if $R_0<1$. □

4.1.3 Results

4.1.3.1 Theoretical Findings

The main analytical findings of this investigation are summarized in Tables 4.2 and 4.3. The expressions of B_T, C_T,H_T, D_T and R_0 are given by Equations (4.21) and (4.6).

The model (4.16) allows only three possible equilibria; the disease-free state C_0, where only susceptibles thrive; an equilibrium without symptomatic infected, which occurs only for a very particular case, when the exposed individuals become all asymptomatic infected; and finally, the endemic equilibrium C^*. All these equilibria are locally asymptotically stable, if suitable, rather complicated conditions, hold. Among the endemic and the disease-free equilibrium bistability is impossible, since they are related via a transcritical bifurcation.

Table 4.2: Equilibria of the model (4.16) and their feasibility conditions.

Equilibrium	**Populations**	**Feasibility**
C_0	$S_0 = \dfrac{\Lambda}{d_p}$	–
$= (S_0, 0, 0, 0, 0, 0)$		
C_I	$S_I = \dfrac{\Lambda - B_T E_I}{d_p}$	
$= (S_I, E_I, 0, A_I, R_I)$	$E_I = \dfrac{1}{B_T}\left(\Lambda - \dfrac{d_p B_T C_T H_T}{\beta_I \omega_p' D_T}\right)$	$\Lambda > \dfrac{d_p B_T C_T H_T}{\beta_I \omega_p' D_T}$
	$A_I = \left(\dfrac{\omega_p'}{H_T}\right) E_I$	(resp. $R_0 > 1$)
	$R_I = \dfrac{\gamma_p'}{d_p}\left(\dfrac{\omega_p'}{H_T}\right) E_I$	$\alpha = 1$ and $\xi = 0$
C^*	$S^* = \dfrac{\Lambda - B_T E^*}{d_p}$	$\Lambda >$
$= (S^*, E^*, I^*, A^*, R^*)$	$E^* = \dfrac{1}{B_T}\left(\Lambda - \dfrac{d_p B_T C_T H_T}{\beta_I \left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}\right)$	$\dfrac{d_p B_T C_T H_T}{\beta_I \left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}$
	$I^* = \left(\dfrac{(1-\alpha)\omega_p H_T + \alpha\omega_p'\xi}{C_T H_T}\right) E^*$	(resp. $R_0 > 1$)
	$A^* = \left(\dfrac{\alpha\omega_p'}{H_T}\right) E^*$	$\alpha \neq 1$ or $\xi \neq 0$
	$R^* = \left[\dfrac{\gamma_p}{d_p}\left(\dfrac{(1-\alpha)\omega_p H_T + \alpha\omega_p'\xi}{C_T H_T}\right) + \dfrac{\gamma_p'}{d_p}\left(\dfrac{\alpha\omega_p'}{H_T}\right)\right] E^*$	

Table 4.3: Stability conditions of the equilibria of the model (4.16).

Point	Coefficients	Stability
C_0	$a_2 = B_T + C_T + H_T$	
	$a_1 = H_T[B_T + C_T] + B_T C_T - \beta_I S_0((1-\alpha)\omega_p + k\alpha\omega_p')$	$\Lambda < \dfrac{d_p B_T C_T H_T}{\beta_I\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}$
	$a_0 = B_T C_T H_T - \beta_I S_0\left((1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right)$	(resp. $R_0 < 1$)
C_I	$b_3 = \beta_I k A_I + d_p + H_T + B_T + C_T,$	
	$b_2 = [\beta_I k A_I + d_p](H_T + B_T + C_T)$	$\Lambda > \dfrac{d_p B_T C_T H_T}{\beta_I \omega_p' D_T}$
	$+B_T C_T + H_T(B_T + C_T) - \omega_p' k \beta_I S_I$	
	$b_1 = [\beta_I k A_I + d_p][B_T C_T + H_T(B_T + C_T)]$	(resp. $R_0 > 1$)
	$+H_T B_T C_T - \omega_p'(k d_p + D_T)\beta_I S_I$	
	$b_0 = [\beta_I k A_I + d_p] H_T B_T C_T - d_p \omega_p' D_T \beta_I S^*$	$\alpha = 1$ and $\xi = 0$
C^*	$c_3 = \beta_I(I^* + kA^*) + d_p + H_T + B_T + C_T,$	
	$c_2 = [\beta_I(I^* + kA^*) + d_p](H_T + B_T + C_T)$	$\Lambda > \dfrac{d_p B_T C_T H_T}{\beta_I\left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}$
	$+B_T C_T + H_T(B_T + C_T) - [\alpha\omega_p' k + (1-\alpha)\omega_p]\beta_I S^*$	(resp. $R_0 > 1$)
	$c_1 = [\beta_I(I^* + kA^*) + d_p][B_T C_T + H_T(B_T + C_T)] + H_T B_T C_T$	$\alpha \neq 1$ or $\xi \neq 0$
	$-[\alpha\omega_p'(k d_p + D_T) + (1-\alpha)\omega_p(d_p + H_T)]\beta_I S^*$	
	$c_0 = [\beta_I(I^* + kA^*) + d_p] H_T B_T C_T$	
	$-d_p[\alpha\omega_p' D_T + (1-\alpha)\omega_p H_T]\beta_I S^*$	

4.1.3.2 Simulations Results

We have performed some simulations with the parameter values listed in Table 4.4, to simulate various implementations of the distancing policy, which actually is in current use in several countries. The simulations may not be fully realistic, but our point is to investigate their qualitative behavior, not to give quantitative forecasts.

We look at the influence that the time of starting the restrictive measures has on the disease spread, while keeping fixed the time of their lifting. We next investigate the effect of the time at which the restricting measures are lifted.

Table 4.4: Parameters values.

Parameter	**Value**	**Parameter**	**Value**
Λ	500	d_p	8.2×10^{-6}
γ_p	1.764	γ'_p	0.6024
ξ	0.1	k	$0.1 \in [0{:}005;\ 0{:}2]$
μ	0.001	α	$0.15 \in [0.01, 0.3]$
ω_p	0.1	ω'_p	0.1
ν	0		

Now comparing the results for the start of implementation at $t_1 = 1$ and $t_1 = 10$, and ending them at the same time, it is seen that the earlier the measures are taken, the better it is, because the epidemic's outbreak is kept in check. In Figure 4.2 the epidemic outbreak starts around time 30, immediately after lifting the restrictions, while in Figure 4.3 the initial surge before the measures are implemented is damped by their implementation, and after their lifting the outbreak occurs. Both figures use $t_2 = 30$. The same result is seen using $t_2 = 90$ as the time for removing the restrictions; compare Figures 4.4 and 4.5. In Figure 4.4 nothing apparently happens until time 100 because of the restrictions. When they are lifted, the epidemic spreads. In Figure 4.5 there is a small peak at the onset of the contagion, immediately curbed by the containment measures, lasting as long as they are in use. In spite of their longer implementation, the outbreak occurs nevertheless with the peak at the same time as in Figure 4.4.

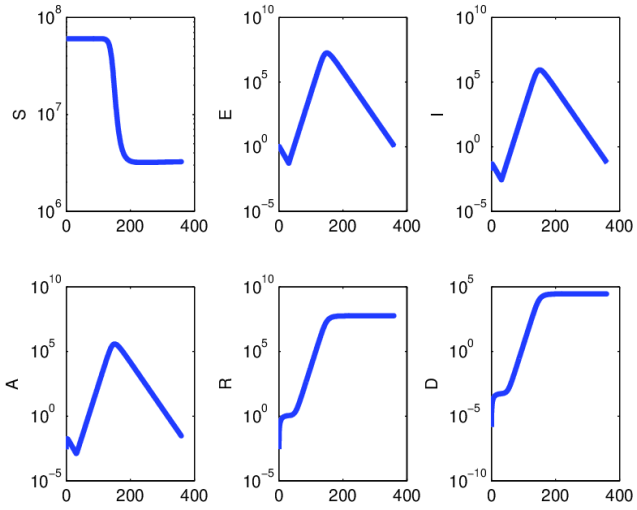

Figure 4.2: Using a semilogarithmic scale for the vertical axis, we show the results of starting the restrictions at time $t_1 = 1$, using $\beta_I = 10^{-10}$ and lifting them at time $t_2 = 30$, returning to $\beta_I = 10^{-7}$ one month later, over a one year timespan for the model with demographics (4.16). Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

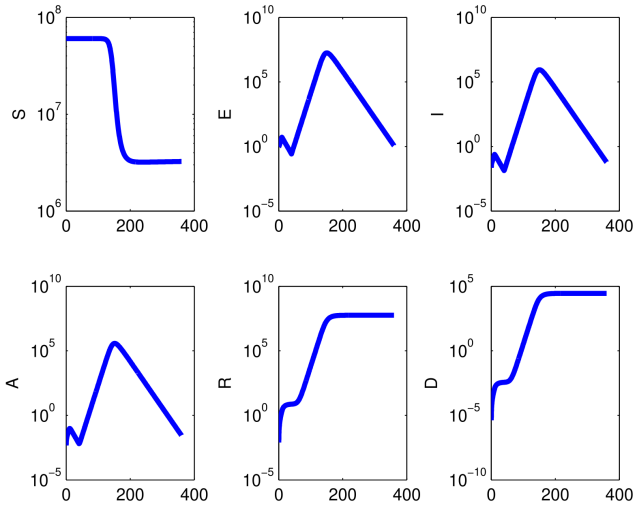

Figure 4.3: Using a semilogarithmic scale for the vertical axis, we show the results of starting the restrictions at time $t_1 = 10$, using $\beta_I = 10^{-10}$ and lifting them at time $t_2 = 30$, returning to $\beta_I = 10^{-7}$ one month later, over a one year timespan for the model with demographics (4.16). Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

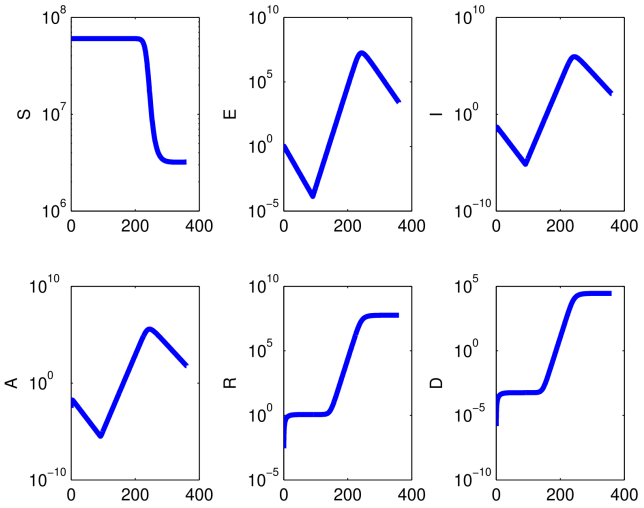

Figure 4.4: Using a semilogarithmic scale for the vertical axis, we show the results of starting the restrictions at time $t_1 = 1$, using $\beta_I = 10^{-10}$ and lifting them at time $t_2 = 90$, returning to $\beta_I = 10^{-7}$ three months later, over a one year timespan for the model with demographics (4.16). Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

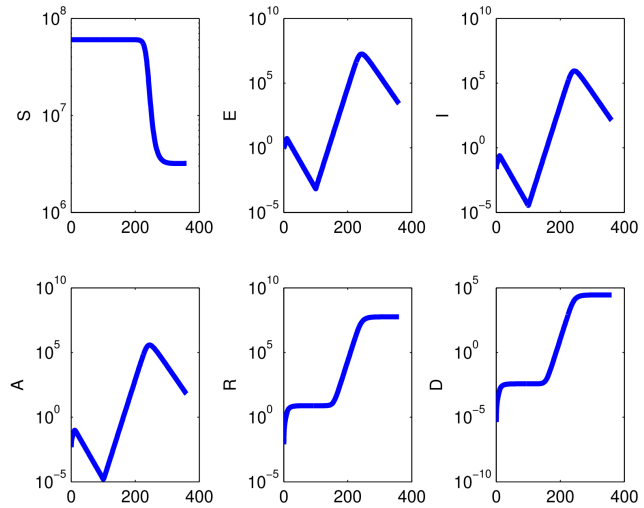

Figure 4.5: Using a semilogarithmic scale for the vertical axis, we show the results of starting the restrictions at time $t_1 = 10$, using $\beta_I = 10^{-10}$ and lifting them at time $t_2 = 90$, returning to $\beta_I = 10^{-7}$ three months later, over a one year timespan for the model with demographics (4.16). Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

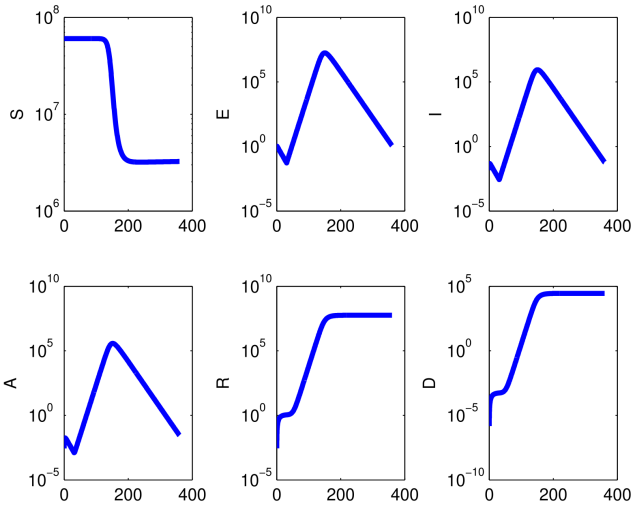

Figure 4.6: Using a semilogarithmic scale for the vertical axis, we show the results of absolute isolation, starting at time $t_1 = 1$ setting $\beta_I = 0$ and lifting it at time $t_2 = 30$, returning to $\beta_I = 10^{-7}$ one month later, over a one year timespan for the model with demographics (4.16). Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

The investigation of different timings for introducing and relaxing the distancing measures shows that a late implementation has no effect, as the peak of the epidemic occurs and then these measures are ineffective, independently of how long they are implemented. An earlier implementation followed by their subsequent lifting leads to a secondary peak at some time later, the occurrence of which seems to be related to the time for which the measures are implemented; the longer the latter, the longer the delay in the secondary outbreak. However, the number of affected people remains the same.
Unfortunately, the result of the simulations indicates that essentially the whole population gets affected by the disease. Only the timings differ, if distancing measures are taken.
Thus, if the measures are implemented too late, independently of the time at which they are removed, the outbreak occurs and their subsequent application becomes, therefore, irrelevant, as it cannot be kept in check any longer; compare Figures 4.3 and 4.5. On the other hand, by implementing them at the early stages of the contagion process, the outbreak can be delayed, as long as these measures are implemented, as can be seen from Figures 4.2 and 4.4. If they are lifted, the final results of the epidemic's outbreak are essentially the same as if they were not at all implemented, in terms of

the number of people being affected by the disease and with possible ultimate fatal consequences; compare the peaks of all the infected classes in Figures 4.2–4.6 also with the results in Figure 4.7 where no measures are taken to prevent the epidemic from spreading.

An intermittent lock-down policy, simulated as an alternative way of coping with the outbreak, might be important to render the burden on hospitalizations smaller, as it tends to spread the epidemic over a longer timespan.

For the particular situation in Italy, note that patient number 1 was diagnosed on 21 February, and the distancing measures in the area were in place starting the following days up to about two weeks later, and then extended to the whole country. Incidentally, patient number 0, the initial carrier of the disease, has never been identified, although there are some speculations. However, in the current news, it is reported that the virus was already circulating yet not known of in Northern Italy in January, which means that additional time had elapsed before the restrictions were applied.

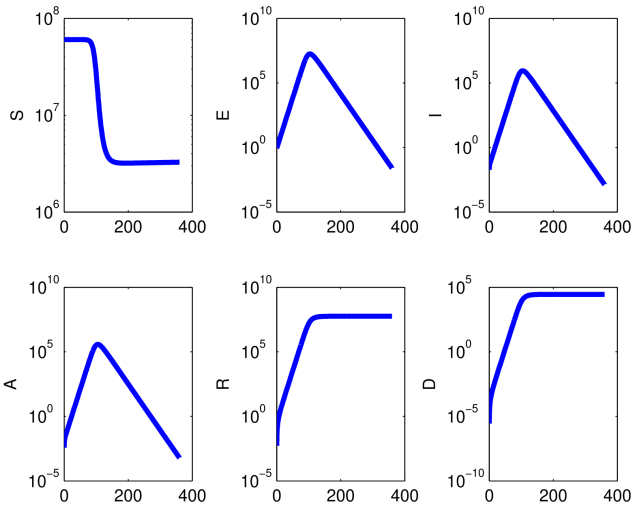

Figure 4.7: The epidemic's effect on the population in the absence of measures for $\beta_I = 10^{-7}$, on a semilogarithmic scale, over a period of one year. Left to right and top to bottom: S, E, I, A, R and D, the disease-related deceased class.

Thus, apparently, these results are negative as for the possibility of containing the spread in the long run, in line with what is hinted in [1], with the exception of the intermittent distancing measures policy, which may spread the epidemic's effects over longer timespans. However, there are some assumptions in the model that make it too crude, so that we plan a deeper subsequent study. In par-

ticular, here the results depend on homogeneous mixing, which for a large country is hardly the case. Secondly, this is a continuous model, for which the compartments are depleted only asymptotically. Thus it is not possible to prevent the class of infectives from vanishing in finite time, so that even a small residual in it would start the epidemic's outbreak again. Therefore the somewhat negative results obtained might hopefully be better off in practice. Suitable modifications of the model along these lines will be the subject of a further investigation.

4.1.4 Discussion

We have investigated a simple model for the coronavirus pandemic. The steady states, apart from a symptomatic-infected-free point, which is unlikely to exist, are the disease-free equilibrium and the endemic state. The model differs from other current models that are being studied for a few features. From the simplified model that appears in [19], because our formulation contains less equations, it does not consider the viruses compartment, and above all, we allow disease-related mortality, which apparently is missing in the cited paper. Furthermore, we allow the progression of asymptomatic individuals to the class of fully symptomatic. This feature certainly distinguishes it also from [33], where asymptomatics recover or become diagnosed with the disease, but do not spread it any longer. In the present situation in Italy our assumption is very realistic.

There is no possibility of bistability in our situation, as the two fully meaningful equilibria are related to each other via a transcritical bifurcation. The disease-free equilibrium is also globally asymptotically stable, if it is locally asymptotically stable. An expression for the basic reproduction number is established, with a possibly realistic numerical value [54, 89].

The simulations show that containment measures could be effective in delaying the epidemic's outbreaks if taken at a very early stage, but when lifted the outbreaks would occur anyway and affect almost the whole population. However, this last statement should be mitigated by the drawbacks inherent in the model's assumptions, as mentioned in the previous section, thereby leaving hope that in practice it will not occur, if the measures are properly implemented.

We next discuss in detail the various different restriction policies that we have simulated.

4.1.4.1 Epidemic with a Lock-Down

In this case, in particular, assuming for the disease transmission coefficient the reference value $\beta_I = 10^{-7}$, we reduce it to $\beta_I = 10^{-10}$ during the interval $[t_1, t_1 + t_2]$ and reinstate the standard value afterwards; we monitor the epidemic's evolution over six months. Figures 4.2–4.6 show the results of different choices for t_1 and t_2. Containment measures are effective as long as they are implemented, if they are taken early enough, before the epidemic attains its peak.

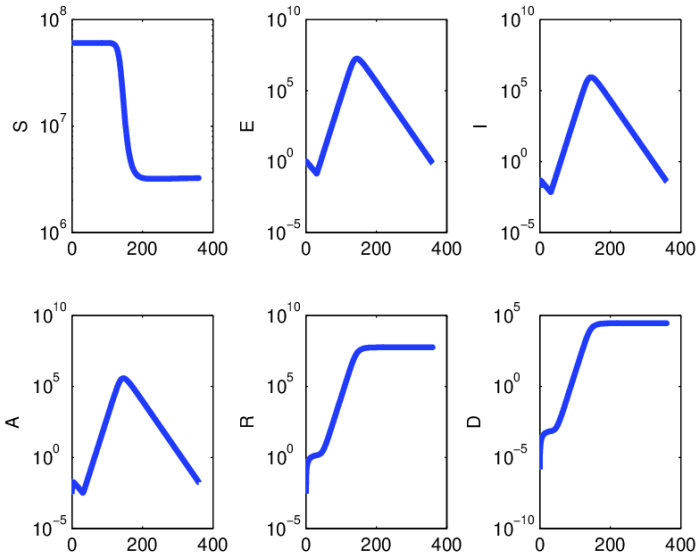

Figure 4.8: On a semilogarithmic scale, the total populations with the lock-down policy, implemented from time 1 up to time 30, with the milder reduced contact rate $\beta_I = 10^{-8}$, after which $\beta_I = 10^{-7}$ resumes. The simulation runs over a one year timespan for the simplified model (4.16). Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

Since reducing the transmission by one order of magnitude means that to infect a susceptible with rate β_I, it is necessary for only one infected; with $\beta_I/10$, 10 infected would be necessary. Thus since the lock-down is not perfect, as for instance, some essential activities like food production are still going on, a hypothetical reasonable estimate for the contact reduction is three orders of magnitude. A comparison with a different, milder reduction, $\beta_I = 10^{-8}$ is made, showing essentially no difference in the results, see Figure 4.8.

4.1.4.2 Epidemic with Total Isolation

We changed also the policy to an improbable absolute confinement of every individual in the population, reducing the transmission to exactly zero. The results show no change with respect to those of the lock-down policy. We report only Figure 4.6, which is identical to Figure 4.2. The same occurs in the cases contemplated by Figures 4.3–4.5.

4.1.4.3 The Simplified No-Demographics Model

We repeated the simulations for the model (4.16) in which we set $\Lambda = d_p = 0$. In the simulations we observed some small changes in the susceptibles behavior, with respect to the full model with vital dynamics. Figures 4.9 and 4.10 are the counterparts of the Figures 4.2 and 4.3. The ultimate impact of the epidemic is essentially the same; compare in particular, the curves of recovered and deceased. For the total isolation case, Figure 4.11 shows the same features; compare it with Figure 4.6. Similar considerations hold for the various remaining cases, and therefore, the pictures are not reported.

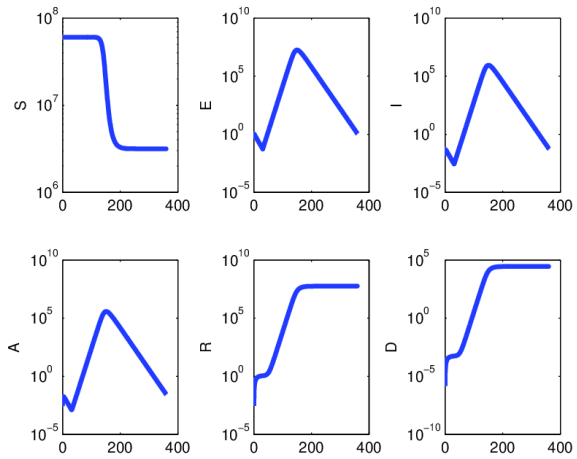

Figure 4.9: Using a semilogarithmic scale for the vertical axis, we show the results of starting the restrictions at time $t_1 = 1$, setting $\beta_I = 10^{-10}$ and lifting them at time $t_2 = 30$, returning to $\beta_I = 10^{-7}$ one month later, over a one year timespan for the simplified model with no demographics (4.16) where we take $\Lambda = 0$, $d_p = 0$. Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

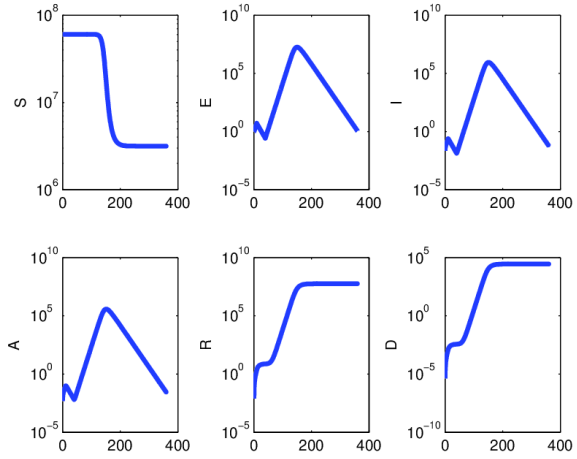

Figure 4.10: Using a semilogarithmic scale for the vertical axis, we show the results of starting the restrictions at time $t_1 = 10$, setting $\beta_I = 10^{-10}$ and lifting them at time $t_2 = 30$, returning to $\beta_I = 10^{-7}$ one months later, over a one year timespan for the simplified model with no demographics (4.16) where we take $\Lambda = 0$, $d_p = 0$.

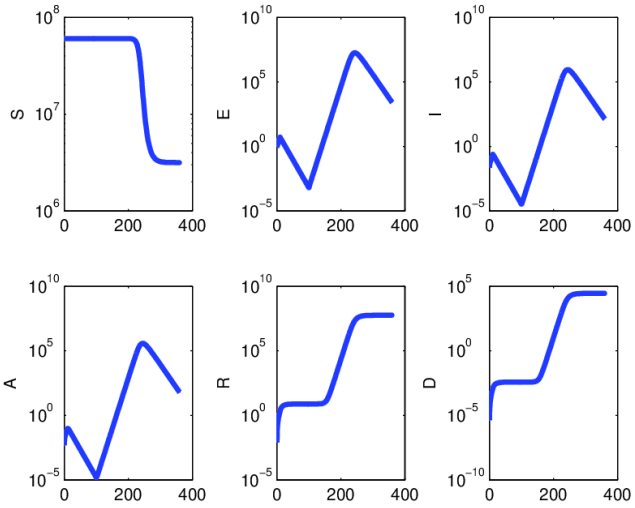

Figure 4.11: Using a semilogarithmic scale for the vertical axis, we show the results of absolute isolation, $\beta_I = 0$ starting at time $t_1 = 10$, setting $\beta_I = 0$ and lifting it at time $t_2 = 90$, returning to $\beta_I = 10^{-7}$ three months later, over a one year timespan for the model with no demographics (4.16) where $\Lambda = d_p = 0$.

4.1.4.4 Investigation of Different Timings for Restrictions' Introduction and Lifting

A further study has been carried out to assess the impact of the time until taking action on the containment measures. All the possible different combinations of simple restriction or total isolation as well as the presence or the absence of demographic effects give essentially the same results. Therefore we present only the results for some selected alternatives, giving the plots in semilogarithmic or total population values, but stressing that for the options not considered, the figures would be the same. In case the first restriction measure is taken too late, specifically at time $t = 120$, and followed by lifting it either one month or three months later, the epidemic occurs and the measures have no effect whatsoever; see Figure 4.12, where measures are kept for three months.

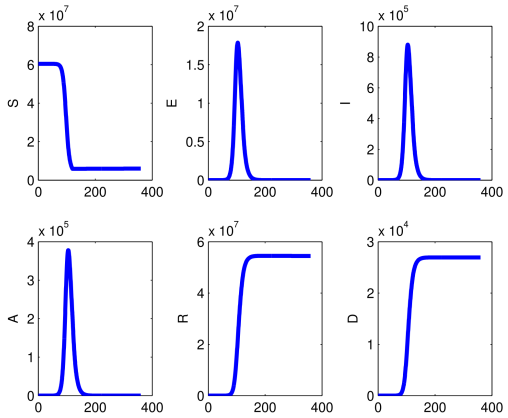

Figure 4.12: The total populations with the lock-down policy, implemented from time 120 up to time 210, with the reduced contact rate $\beta_I = 10^{-10}$, after which $\beta_I = 10^{-7}$ resumes. The simulation runs over a one year timespan for the model (4.16). Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

Beginning the restrictions after three months from the start of the epidemic and removing them one month afterwards, causes a second peak about two months later; i.e., six months after the onset of the disease spreading (Figure 4.13), with a higher number of affected individuals. If instead the lock-down is implemented for three months, the second peak is delayed further, occurring about three months later, Figure 4.14. Although the pictures are shown on different population scales, absolute values and semilogarithmic, a comparison of the heights of the peaks for the various types of infected subpopulations indicates no difference. Hence, these policies cannot significantly influence the number of people ultimately affected by the disease.

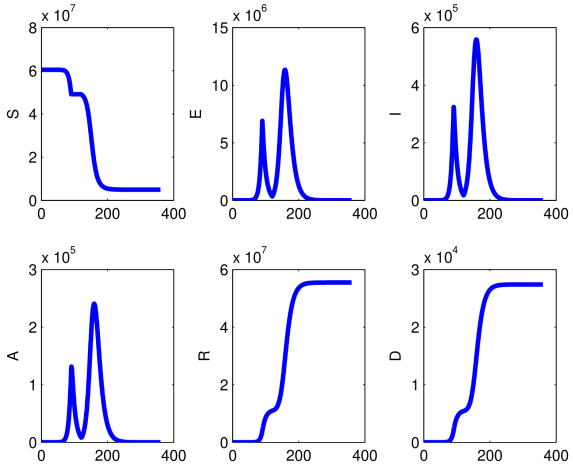

Figure 4.13: The total populations with the lock-down policy, implemented from time 90 up to time 120, with the total isolation policy $\beta_I = 0$, after which $\beta_I = 10^{-7}$ resumes. The simulation runs over a one year timespan for the simplified model (4.16) with no demographics, $\Lambda = d_p = 0$. Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

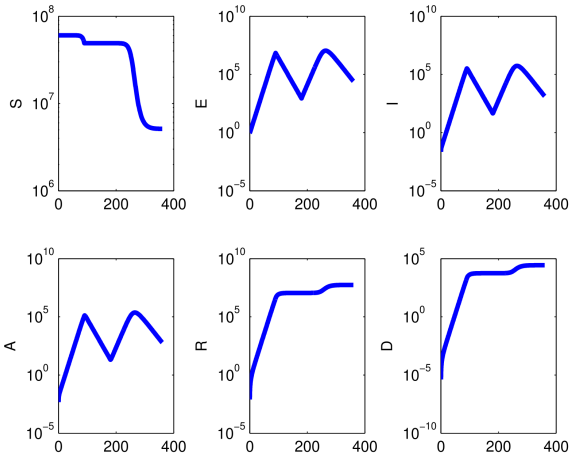

Figure 4.14: The semilogarithmic plot of the epidemic's spread with the lock-down policy, implemented from time 90 up to time 180, with the reduced contact rate $\beta_I = 10^{-10}$, after which $\beta_I = 10^{-7}$ resumes. The simulation runs over a one year timespan for the model (4.16) with demographics. Left to right and top to bottom, the subpopulations are: S, E, I, A, R and D, the disease-related deceased class.

4.1.4.5 The Intermittent Lock-Down Policy

We finally simulated a policy that attempts to assess the number of infectives at regular times, with a of period one week. If they exceed a threshold, taken to be 10, the lock-down is implemented for a week, and then lifted. Figures 4.15 and 4.16 show the results for the case with vital dynamics and in the case of $\Lambda = d_p = 0$. Note that susceptibles in both cases are at a constant value, the vertical scale being extremely small. The infected are kept below the threshold, and the periodic recurrences of the epidemic somewhat change its final impact, as the curves of recovered are reduced by about two orders of magnitude, and above all, the ones of the deceased decrease by about four orders, with respect to the ones found with the one-time lock-down policy. The other relevant change is that here the phenomenon is observed over a longer timespan. Thus the cumulative effects are spread out over a much longer time. This will have some importance to lessening the burden on hospitals. Figure 4.17 shows the results if the check policy starts immediately at time 1 rather than after a week. Comparing the population values with the intermittent policy with the one time lock-down, done early enough and implemented for one month, the final outcomes are milder than the latter. Thus the intermittency allows the control of the outbreaks. Susceptibles are almost depleted in the one-time policy; with the intermittent one, however, they are essentially spared from getting the disease; compare Figures 4.18 and 4.19.

The intermittency has also been checked with different time intervals. Comparing Figures 4.20–4.23, it is seen that the more frequent the checks are implemented, the lower are the peaks in the exposed class, which in turn leads to a smaller cumulative number of recovered and fatalities, at least comparing the policies for the one- and two-weeks alternatives, Figures 4.20 and 4.21. For the longer intervals between the checks, again the peaks are higher, the longer the timespan, but it is observed that as time elapses, their heights tend to decrease; see Figures 4.22 and 4.23.

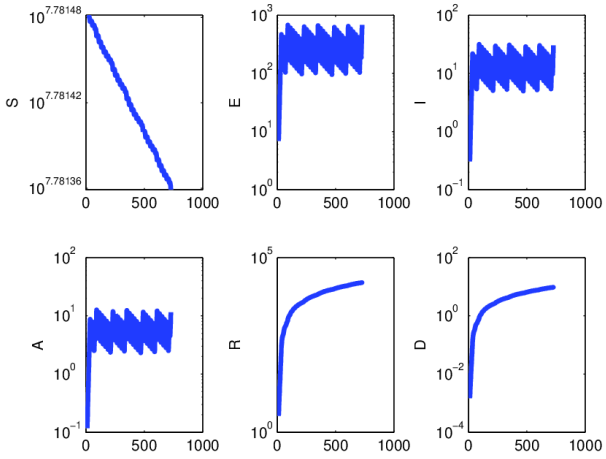

Figure 4.15: Using a semilogarithmic scale for the vertical axis, we show the results of the intermittent lock-down policy. Here the population is checked every week, starting after a week. If the number of infected is above a small threshold (here taken to be 10) the reduced contact rate $\beta_I = 10^{-10}$ is resumed for a week. The simulation runs over two years timespan for the model with demographics (4.16).

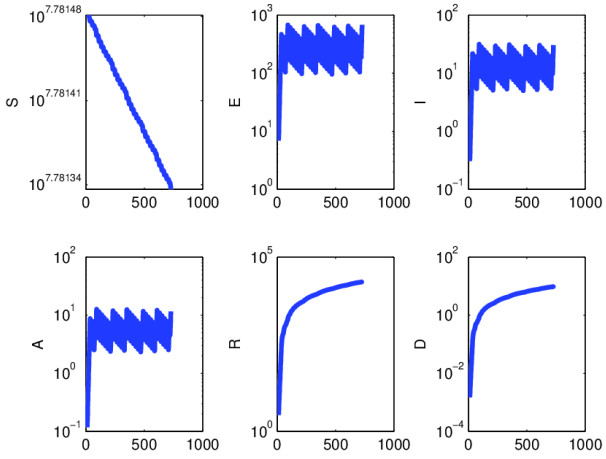

Figure 4.16: Using a semilogarithmic scale for the vertical axis, we show the results of the intermittent lock-down policy. Here the population is checked every week, starting after a week. If the number of infected is above a small threshold (here taken to be 10) the reduced contact rate $\beta_I = 10^{-10}$ is resumed for a week. The simulation runs over two years timespan for the simplified model with no demographics (4.16) where we take $\Lambda = 0$, $d_p = 0$.

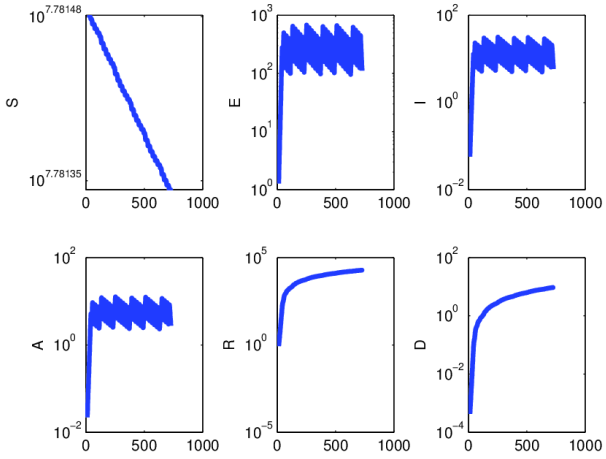

Figure 4.17: Using a semilogarithmic scale for the vertical axis, we show the results of the intermittent lock-down policy, implemented from time 1. Here the population is checked every week. If the number of infected is above a small threshold (here taken to be 10) the reduced contact rate $\beta_I = 10^{-10}$ is resumed for a week. The simulation runs over two years timespan for the simplified model with no demographics (4.16) where we take $\Lambda = 0$, $d_p = 0$.

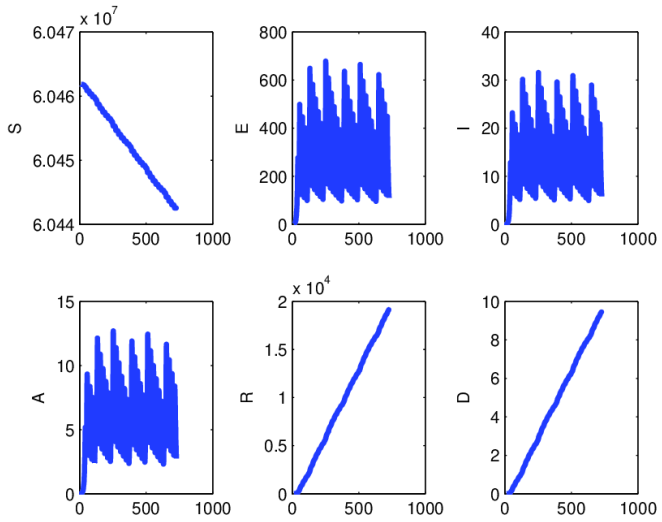

Figure 4.18: The total populations with the intermittent lock-down policy, implemented from time 1. Here the population is checked every week. If the number of infected is above a small threshold (here taken to be 10) the reduced contact rate $\beta_I = 10^{-10}$ is resumed for a week. The simulation runs over two years timespan for the simplified model with no demographics (4.16) where we take $\Lambda = 0$, $d_p = 0$.

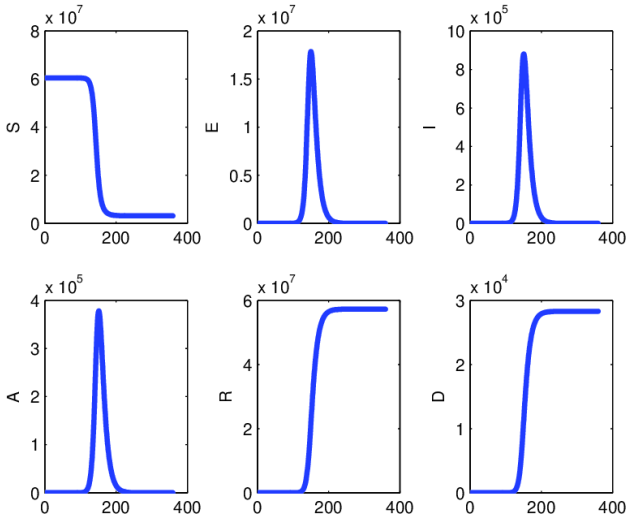

Figure 4.19: The total populations with the lock-down policy, implemented from time 1 up to time 30, with the reduced contact rate $\beta_I = 10^{-10}$, after which $\beta_I = 10^{-7}$ resumes. The simulation runs over a one year timespan for the simplified model with no demographics (4.16) where we take $\Lambda = 0$, $d_p = 0$.

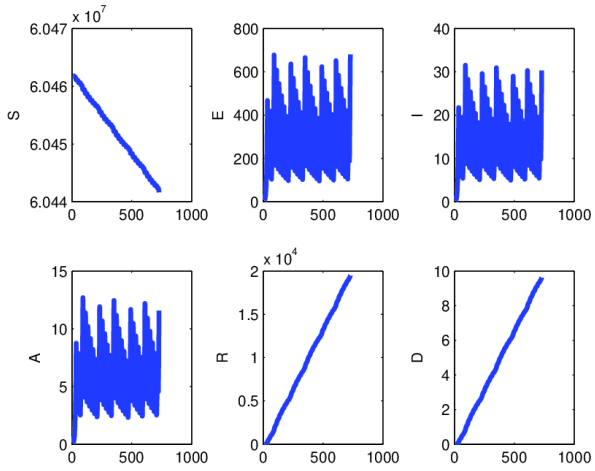

Figure 4.20: The population values with the lock-down policy, implemented after the first week with the reduced contact rate $\beta_I = 10^{-10}$, after which $\beta_I = 10^{-7}$ resumes. The check for possible repeated implementation is implemented every week afterwards. The simulation runs over a two year timespan for the model (4.16) with no demographics, i.e., $\Lambda = d_p = 0$.

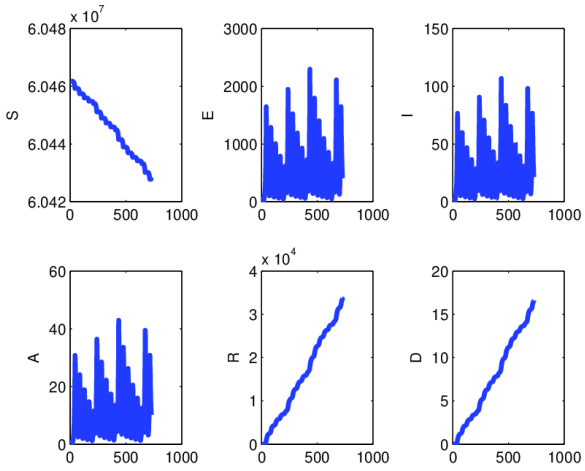

Figure 4.21: The population values with the lock-down policy, implemented after the first two weeks with the reduced contact rate $\beta_I = 10^{-10}$, after which $\beta_I = 10^{-7}$ resumes. The check for possible repeated implementation is implemented every two weeks afterwards. The simulation runs over a two year timespan for the model (4.16) with no demographics, i.e., $\Lambda = d_p = 0$.

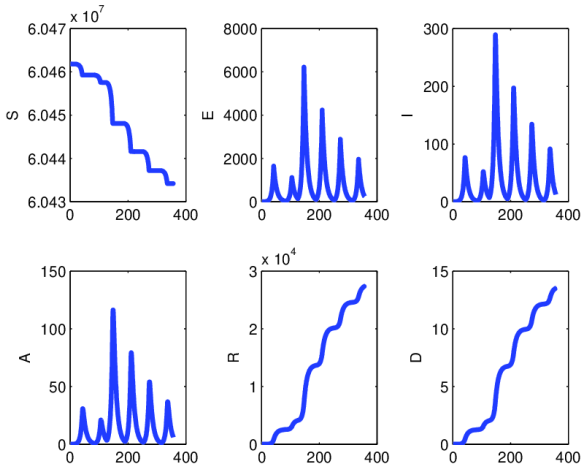

Figure 4.22: The population values with the lock-down policy, implemented after the first thee weeks with the reduced contact rate $\beta_I = 10^{-10}$, after which $\beta_I = 10^{-7}$ resumes. The check for possible repeated implementation is implemented every three weeks afterwards. The simulation runs over a two year timespan for the model (4.16) with no demographics, i.e., $\Lambda = d_p = 0$.

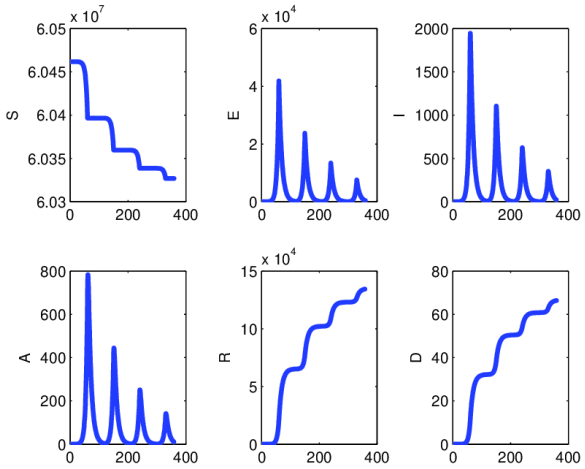

Figure 4.23: The population values with the lock-down policy, implemented after the first month with the reduced contact rate $\beta_I = 10^{-10}$, after which $\beta_I = 10^{-7}$ resumes. The check for possible repeated implementation is implemented every month afterwards. The simulation runs over a two year timespan for the model (4.16) with no demographics, i.e., $\Lambda = d_p = 0$.

4.1.5 Numerical Simulations

The calculation of the value of R_0 according to (4.6) with the parameter values used in the numerical simulations gives $R_0 = 3.1402$, in line with the current estimates [54, 89].

4.1.5.1 Simulations Methodology

We use a simple own-developed driver code calling the Matlab intrinsic routine ode45, implementing the classical Runge–Kutta 45 integration method for ordinary differential equations.

At first, we consider only the demographic simulation and show that the population is essentially at the same level during a year. This fact is substantiated also by the simulation results, for which there is scant difference between those of the model (4.16) and the ones obtained by using its no-demographic counterpart, where Λ and d_p are both set to zero.

We then perform three sets of simulations describing different possible scenarios. The first one considers lock-down, i.e., decreasing the contact rate significantly, but not to zero, as some essential activities are still open. Then the total isolation policy, for which the contact rate is set to zero. Finally an intermittent closure policy, for which when infectives reappear in a significant way, temporary lock-down measures resume again.

4.1.5.2 Data Acquisition

We use data published on official websites about the epidemic's spread in Italy collected between 29 January and 28 March 2020, a period that spans 61 days, incremented by more recent information [90].

Using the day as the base time unit, we assume that the average incubation period lies in the interval between two and 14 days, with a mean of 8 days. Based on the percentage of the reported symptomatic infected patients, the proportion of symptomatic in the infected class α is estimated to be in the interval $[0.01, 0.3]$. The correction k for asymptomatics to diffuse the disease is set in the range $k \in [0:005; 0:2]$. There have been 27,359 deaths between 15 February and 29 April [90], with changes in the number of fatalities every day. Dividing the fatal cases by the timespan, one gets 370 daily fatalities, which gives a rate 0.0027. Using this value in the simulation, puts the total losses to about 10^5. But we observed that apparently children hardly get the disease, the younger and adult people have it generally in a mild form and fatalities occur mainly for the elderly people, compare with Figure 3 of [82]. In view of the fact that there is no age structure in this model, we corrected this value by taking a third of the above result to set the disease mortality rate at the final value $\mu = 0.001$, which gives a reasonable estimate for the losses in the timespan, in rough agreement with the actual tallies. We neglect altogether mortality for the asymptomatics, setting $\nu = 0$. Based on the officially published data we estimate $\gamma_p = 0.1764$, $\gamma_p' = 0.6024$. For the initial values, the total population is obtained from the report published by the official cite of worldometers [91], $S = 60461826$. To avoid demographic effects, we set the susceptible recruitment rate Λ in order that on the timespan of the simulation the total population N does not change much.

4.1.5.3 The Pure Demographic Case

We simulate first the population model without disease. In so doing, we varied the parameter Λ until a satisfactory behavior of N, the total population was found. With $\Lambda = 500$ there is little variation of N during a whole year, the population remains roughly stable around the level $60,400,000$, see Figure 4.24. In this way the demographic effects are sort of removed, and we can concentrate mainly on the epidemics. Actually, the number of newborns per day in Italy would be about four times higher, but as mentioned, we just would like here to hide the demographics from the simulations and not have a picture more adherent to reality.

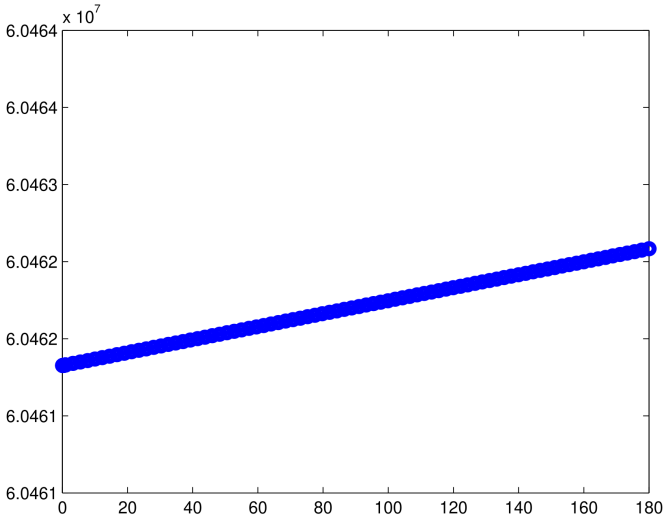

Figure 4.24: The susceptible population behavior over a year, without disease. It does not vary much as the vertical scale is rather small, the range of variation being around 3000, over a population of 60×10^6.

4.1.5.4 Epidemics Spread in the Absence of Measures

Here we introduced the disease, with incidence $\beta_I = 10^{-7}$. The result is shown in Figure 4.25 for absolute numbers, and in Figure 4.7 in semilogarithmic scale. In this case no measures are assumed to be taken to counteract the epidemics. These results are reported in order be able to compare the simulations with restrictions to what would happen if the containment measures were not taken.

4.1.5.5 Containment Measures for the Epidemics

Finally, we considered the introduction of the distancing policy. It is assumed to start at time t_1 and end at time $t_1 + t_2$. Two forms of containment measures are considered, substantially reducing the contact rate, or even setting it equal to zero, meaning the extreme measure of total individuals isolation.

In particular, we present the experience of using the reference value of the contact rate $\beta_I = 10^{-7}$, then reducing it to $\beta_I = 10^{-10}$ during the interval $[t_1, t_1+t_2]$. We then reset it to its previous reference value after time $t_1 + t_2$. We monitored the epidemics evolution over six months.

The alternative, milder choice $\beta_I = 10^{-8}$ is also used, for comparison.

The simulations are then repeated with total isolation, setting $\beta_I = 0$ during the implementation of

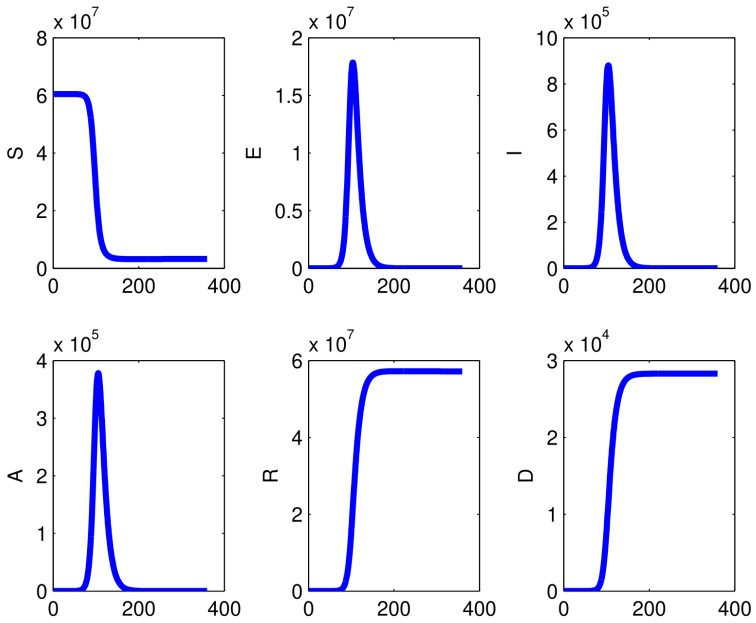

Figure 4.25: The epidemic's effect on the population in the absence of measures for $\beta_I = 10^{-7}$, over a period of one year. Left to right and top to bottom, the total population sizes: S, E, I, A, R and D, the disease-related deceased class.

the restrictions.

A comparison of the results with the model obtained by disregarding the demographic parameters, i.e., setting $\Lambda = d_p = 0$ is also performed in the same way as done for the model (4.16).

Different timings for taking both the first restriction measure and for lifting it are then investigated, using all the above alternatives.

Finally an intermittent restrictive policy is examined, for which when the infected are observed to trespass a threshold, distancing measures are taken. Here again lock-down or total isolation produce essentially the same results. The use of different timings for the introduction of the restrictions is also scrutinized.

4.2 A Mathematical Study of a Coronavirus Model with the Caputo Fractional-Order Derivative

4.2.1 Introduction

Among the new tools that have recently come into the limelight in scientific research, fractional derivatives play an important role, in view of the fact that, in a sense, they embed memory effects in dynamical systems [71, 24, 39, 70]. This concept has been successfully applied in mathematical physics [16], but more recently it has also been used in other contexts. In the biological framework, ecological models incorporating this type of operator have been introduced in [52], and for epidemic situations, in [65]. In view of the Covid-19 pandemic that has been affecting humanity for almost two years, in the last months several papers have been published on this topic. Some of them attempt to set up and analyse models for this epidemic based on the concept of fractional derivatives.

The simplest epidemiological model, SI, consists of two classes, namely susceptibles S and infectives I. If possible disease recovery is allowed, the class of healed individuals is introduced as R. These individuals are immune from the disease, at least temporarily. The model thus becomes type SIR. If, additionally, the recovered individuals lose disease immunity, they again become prone to being infected and thus they return to the class of susceptibles. In such cases, therefore, disease relapses are allowed, and the SIRS model is obtained. A further step forward consists of introducing another compartment, hosting the individuals that have been exposed to the disease. It is indeed well-known that, in the case of measles, individuals that have contracted the disease do not show symptoms until about at least a week after being infected. Meanwhile, they are very much able to transmit the disease, especially in the very first few days after infection. The exposed class therefore has paramount importance in transmissible disease modeling. The simplest nontrivial compartment model that shows this feature is the SEIR model. It has been taken into consideration, together with a fractional derivative approach, in [2, 67]. Reference [42] also considers this formulation, but in addition time delays are explicitly built into the model. Another extension of the SEIR system is considered in [66], where the class P of "deprived and marginalised" individuals is also considered. The latter are individuals that are less able to cope with strict distancing measures and therefore contribute to the further spread of the disease. Apparently, they are "recruited" from the

infected by a simple linear transition. In other words, the surviving infected exit this class either by recovering or by becoming part of P. In [5], instead, three additional classes are introduced, thereby forming the SEIQRDP model. Apart from the class D of deceased individuals, quarantined individuals Q are introduced, as well as the "insusceptible", P. In the model, disease mortality is allowed only among quarantined, thereby most likely implying that infected that die of the disease are accounted for as having been recognized as disease carriers, and therefore put in isolation before dying. The Atagana–Baleanu fractional derivative is employed instead of the Caputo fractional derivative in [69]. Here, the infected may migrate to the quarantined Q class. Individuals in isolation may possibly become confirmed cases and therefore are lumped into the new class C. Notably, individuals belonging to both Q and C classes are assumed not to be able to disseminate the disease further, which may be a strong assumption. In Italy, at least in the early phases of the pandemic, most of the contagions involved doctors and nurses working in hospitals. This indicates that virus leakage was nevertheless possible in supposedly confined environments. After collecting data for various compartments from two countries, in [4] parameters are estimated, on the basis of which, initially a standard dynamical system and later on some fractional models, are built. In particular, the Caputo, Caputo–Fabrizio, Atangana–Baleanu and the fractal–fractional nonlocal operators are employed. Five classes of infected are considered, of which the first one essentially represents the exposed in our above terminology. The remaining ones consider symptomatic individuals that have or have not been tested and found to be positive or not. In [3], again the same previous five classes of infected individuals are considered, those having been tested or not, or those under treatment. The model also introduces a time-dependent transmission rate that tries to incorporate the social distancing measures, including the wearing of masks, and social contacts restrictions, that is, shop closures, curfew and so forth. This attempts to model the ways of fighting the epidemic diffusion that have been enforced by many governments worldwide, although the implementation times differed from country to country. Specifically, in [3], a model is proposed that extends the possible disease transmission mechanism of [4] to two other compartments which were not able to spread it. In addition to the equilibria analysis, a numerical scheme for the integration of the fractional system is developed. In both [3, 4], the major novelty at the modeling level appears to be the introduction of the compartment of the vaccinated, V. In [14], an early model for treatment is also formulated using standard derivatives.

In all the papers considered above, however, no real asymptomatic class appears in the model. By this terminology, we mean people that are unrecognized carriers, in that they do not show symptoms. This class has enormous importance, given the fact that individuals in it believe that are not infectious and therefore think that they may mingle without restraint with susceptibles. However, not being recognized as disease-carriers, they contribute to the fast diffusion of the epidemic. A model with standard derivatives taking asymptomatics into account has been formulated in [36]. Symptomatic and asymptomatic infectious are partitioned into two different classes. The model is formulated via standard derivatives. Instead, in [74] a fractional operator model is presented, but the main aim of the paper consists of devising a suitable stable numerical scheme, which essentially relies on the use of the Laplace transform. The basic reproduction number is evaluated and, if smaller than one, it is shown that the epidemic is eradicated. Parameters for the simulations are taken from the literature or estimated by data fitting. The asymptomatic class is also considered in [59], where the main aim is the study of a numerical algorithm based on the Riesz wavelets is proposed.

In [55], quarantined individuals coming from the exposed class, the symptomatic and asymptomatic infected, the isolated and treated are considered in addition to the standard classes of the SEIR model. Notably, the model does not seem to account for disease mortality. For infected I the parameter ρ, according to the parameter list, should be interpreted to be the same as γ. It describes the migration from class I to treatment. At least both the infected and treated individuals should experience disease mortality. Indeed, if by the term "treated" the authors mean hospitalized, not including disease mortality does not appear to match observations. As a matter of fact, in the case of covid, hospitalized mortality has had a very big impact on societies worldwide. A similar remark may perhaps be made on the class P of "isolated" individuals into which the "quarantined" (being so after exposure) and infected migrate. After all, these people are still affected by the disease. In the model, the isolated and quarantined are assumed to be able to propagate the disease. However, treated individuals are not. In such cases, the same remark on the Italian hospitals' situation mentioned above may apply. The paper investigates the existence of the solutions and the feasibility and stability of the system equilibria.

We have therefore chosen a simple model that is formulated via fractional derivatives in the line of the above research lines. It includes only the basic epidemiological classes, because the aim of modeling is to elucidate, if possible, how very complex behaviors are generated, using the minimal feasible

assumptions. These must contain the basic mechanisms underlying the variables' relationships, but should not remove the system's basic features (Occam's razor).

The model we propose differs in some more important or smaller aspects from each one of the systems presented in the above papers. In some cases it is simpler, which may be a shortcoming if real data need to be analysed. On the other hand, however, it may represent an advantage in that it is well-known that minimal models sometimes help in highlighting system features whose real origin may be obscured in more complicated ones.

This section is organized as follows. The next subSection 4.2.2 contains the model description. The basic analytical properties of the system are presented in subSection 4.2.3. A numerical simulation is presented in subSection 4.2.4 together with a brief final discussion.

4.2.2 Material and Methods

We consider the following fractional-order epidemiological model incorporating a spread of corona virus. We consider the following classes of individuals: susceptibles S, namely the individuals who have not yet been exposed to the virus; exposed E, people who have been infected by the virus but are in the incubation period, in which they cannot yet spread the disease; symptomatic infected I, individuals that manifest symptoms and can communicate the disease; asymptomatic infected A, those persons that can communicate the disease even without having explicit symptoms; the removed class R, which includes the people that recovered from the disease. We further let $N(t)$ denote the total population. Thus, $N(t) = S(t) + E(t) + I(t) + A(t) + R(t)$. The model reads as follows:

$$\begin{aligned} D^q S(t) &= \Lambda - \beta_I S(I + kA) - d_p S, \\ D^q E(t) &= \beta_I S(I + kA) - (1-\alpha)\omega_p E - \alpha\omega_p' E - d_p E, \\ D^q I(t) &= (1-\alpha)\omega_p E - (\gamma_p + d_p + \mu) I + \xi A, \\ D^q A(t) &= \alpha\omega_p' E - (\gamma_p' + d_p + \nu) A - \xi A, \\ D^q R(t) &= \gamma_p I + \gamma_p' A - d_p R, \end{aligned} \tag{4.16}$$

where D^q is the standard Caputo differentiation with $q \in (0, 1)$. For the benefit of the reader, we recall the definition of the Caputo fractional derivative of order q [24, 39]:

$$D^q x(t) = \frac{1}{\Gamma(n-q)} \int_0^t (t-s)^{n-q-1} x^{(n)}(s)\, ds, \qquad n-1 < q < n, \quad n \in \mathbb{N}.$$

In the above model, all individuals experience natural mortality at rate d_p; susceptibles are recruited at constant rate Λ, these being the only two demographic features of the model. The epidemic part of the model considers disease transmission among susceptibles and both types of infected, at rate β_I, through mass action. Note that the factor k modulates the possible difference in the ability to spread the disease from asymptomatic people versus symptomatic ones. After contagion, a susceptible migrates into the class of the exposed, from which, after activation of the disease, it moves on to the infected compartments, at possibly different rates ω_p and ω_p'; α instead tells the proportion of exposed that will never show symptoms, that is, they move to class A. From this class, at rate ξ, individuals may still be able to become symptomatic and migrate to the I class. Both types of infected individuals may recover at rates γ_p and γ_p' and are subject to disease-related mortality, for which we assume two possibly different rates, μ for symptomatic and ν for asymptomatic people. All the parameters are non negative and their meaning is summarized in Table 4.1. The basic mechanisms underlying the model are shown in Figure 4.1. The system (4.16) is completed by the following initial conditions

$$\begin{gathered} S(0) \geq 0, \quad E(0) \geq 0, \quad I(0) \geq 0, \\ A(0) \geq 0, \quad \text{and} \quad R(0) \geq 0. \end{gathered} \tag{4.17}$$

4.2.3 Results

This subsection studies the existence, uniqueness, non-negativity and boundedness of the solutions of a fractional order epidemiological model (4.16). In addition, the stability analysis of fractional order epidemiological model (4.16) is also performed.

4.2.3.1 Existence and Uniqueness

The sufficient condition for the existence and uniqueness of the solution of a fractional order system (4.16) are as follows:

Theorem 4.8. *For each non-negative initial conditions, there exists a unique solution of fractional order system* (4.16).

Proof. We seek a sufficient condition for the existence and uniqueness of the solutions of fractional

order system (4.16) in the region $\Omega \times (0, T]$ where

$$\Omega = \{(x, y, z, u, v) \in \mathbb{R}^2 : \max(|x|, |y|, |z|, |u|, |v|) \leq \rho\}.$$

The approach used in [52] is adopted. Consider a mapping

$$G(X) = (G_1(X), G_2(X), G_3(X), G_4(X), G_5(X))$$

and

$$\begin{aligned} G_1(X) &= \Lambda - \beta_I x(z + ku) - d_p x, \\ G_2(X) &= \beta_I x(z + ku) - (1 - \alpha)\omega_p y - \alpha\omega_p' y - d_p y, \\ G_3(X) &= (1 - \alpha)\omega_p y - (\gamma_p + d_p + \mu)z + \xi u, \\ G_4(X) &= \alpha\omega_p' y - (\gamma_p' + d_p + \nu)u - \xi u, \\ G_5(X) &= \gamma_p z + \gamma_p' u - d_p v. \end{aligned} \tag{4.18}$$

For any X, $\overline{X}$, it follows from (4.18) that

$$\begin{aligned} \big|\big|G(X) - G(\overline{X})\big|\big| &= \big|G_1(X) - G_1(\overline{X})\big| + \ldots + \big|G_5(X) - G_5(\overline{X})\big| \\ &= |\Lambda - \beta_I x(z + ku) - d_p x - \Lambda + \beta_I \overline{x}(\overline{z} + k\overline{u}) + d_p \overline{x}| \\ &\quad + \big|\beta_I x(z + ku) - [(1 - \alpha)\omega_p + \alpha\omega_p' + d_p]y \\ &\quad -\beta_I \overline{x}(\overline{z} + k\overline{u}) + [(1 - \alpha)\omega_p + \alpha\omega_p' + d_p]\overline{y}\big| \\ &\quad + |(1 - \alpha)\omega_p y - (\gamma_p + d_p + \mu)z + \xi u \\ &\quad -(1 - \alpha)\omega_p \overline{y} + (\gamma_p + d_p + \mu)\overline{z} - \xi\overline{u}| \\ &\quad + \big|\alpha\omega_p' y - (\gamma_p' + d_p + \nu + \xi)u \\ &\quad -\alpha\omega_p' \overline{y} + (\gamma_p' + d_p + \nu + \xi)\overline{u}\big| \\ &\quad + \big|\gamma_p z + \gamma_p' u - d_p v - \gamma_p \overline{z} - \gamma_p' \overline{u} + d_p \overline{v}\big| \end{aligned}$$

$$
\begin{aligned}
&= \beta_I \left|x(z-\overline{z}) + \overline{z}(x-\overline{x})\right| + k\beta_I \left|x(u-\overline{u}) + \overline{u}(x-\overline{x})\right| \\
&\quad + d_p \left|x-\overline{x}\right| + \beta_I \left|x(z-\overline{z}) + \overline{z}(x-\overline{x})\right| \\
&\quad + k\beta_I \left|x(u-\overline{u}) + \overline{u}(x-\overline{x})\right| \\
&\quad + \left[(1-\alpha)\omega_p + \alpha\omega_p' + d_p\right] \left|y-\overline{y}\right| \\
&\quad + (1-\alpha)\omega_p \left|y-\overline{y}\right| + (\gamma_p + d_p + \mu) \left|z-\overline{z}\right| + \xi \left|u-\overline{u}\right| \\
&\quad + \alpha\omega_p' \left|y-\overline{y}\right| + (\gamma_p' + d_p + \nu + \xi) \left|u-\overline{u}\right| \\
&\quad + \gamma_p \left|z-\overline{z}\right| + \gamma_p' \left|u-\overline{u}\right| + d_p \left|v-\overline{v}\right| \\
&\leq \left[2\beta_I\rho(1+k) + d_p\right] \left|x-\overline{x}\right| \\
&\quad + \left[2(1-\alpha)\omega_p + 2\alpha\omega_p' + d_p\right] \left|y-\overline{y}\right| \\
&\quad + (2\beta_I\rho + 2\gamma_p + d_p + \mu) \left|z-\overline{z}\right| \\
&\quad + (2k\beta_I\rho + 2\xi + 2\gamma_p' + d_p + \nu) \left|u-\overline{u}\right| \\
&\quad + d_p \left|v-\overline{v}\right| \\
&\leq C \left|\left|X-\overline{X}\right|\right|,
\end{aligned}
$$

where

$$
\begin{aligned}
C &= \max\left(2\beta_I\rho(1+k) + d_p, 2(1-\alpha)\omega_p + 2\alpha\omega_p' + d_p,\right. \\
&\quad \left. 2\beta_I\rho + 2\gamma_p + d_p + \mu, 2k\beta_I\rho + 2\xi + 2\gamma_p' + d_p + \nu\right).
\end{aligned}
$$

Thus, $G(X)$ satisfies the Lipschitz condition. Consequently, the existence and uniqueness of the solution of the fractional order system (4.16) follows. □

4.2.3.2 Non-Negativity and Boundedness

The solutions of the fractional order system (4.16) represent the densities of the interacting populations and must therefore be non-negative and bounded. These features are ensured by the following results.

Theorem 4.9. *All the solutions of fractional order system (4.16), which start in $\mathbb{R}^5_+$ are uniformly bounded and non-negative.*

Proof. We follow the approach used by [52]. Define the function $N(t) = S(t)+E(t)+I(t)+A(t)+R(t)$. Hence, for each $d_p > 0$,

$$\begin{aligned} D^q N(t) + d_p N(t) &= \Lambda - \beta_I S(I + kA) - d_p S \\ &\quad +\beta_I S(I + kA) - (1-\alpha)\omega_p E - \alpha\omega_p' E - d_p E \\ &\quad +(1-\alpha)\omega_p E - (\gamma_p + d_p + \mu)I + \xi A \\ &\quad +\alpha\omega_p' E - (\gamma_p' + d_p + \nu)A - \xi A \\ &\quad +\gamma_p I + \gamma_p' A - d_p R \\ &\quad +d_p(S(t) + E(t) + I(t) + A(t) + R(t)) \\ &= \Lambda - \mu I - \nu A \\ &\leq \Lambda. \end{aligned}$$

By using the standard comparison theorem for fractional order [20],

$$N(t) \leq N(0)E_q\left(-d_p(t)^q\right) + \Lambda(t)^q E_{q,q+1}\left(-d_p(t)^q\right),$$

where E_q is the Mittag–Leffler function. According to Lemma 5 and Corollary 6 in [20],

$$N(t) \leq \frac{\Lambda}{d_p}, \quad t \to +\infty$$

Therefore, all the solutions of fractional order system (4.16) starting in $\mathbb{R}^5_+$ are confined to the region Σ, where

$$\Sigma = \{(S, E, I, A, R) \in \mathbb{R}^5_+ : \quad N(t) \leq \frac{\Lambda}{d_p} + \epsilon, \quad \epsilon > 0\}. \tag{4.19}$$

Next, we show that the solutions of the fractional order system (4.16) are non-negative.

From the first equation of system (4.16) we have

$$\begin{aligned} D^q S(t) &= \Lambda - \beta_I S(I + kA) - d_p S \\ &\geq -[\beta_I(I + kA) + d_p]S \\ &\geq -[\beta_I(1 + k)\frac{\Lambda}{d_p} + d_p]S \\ &\geq -C_1 S, \end{aligned}$$

where $C_1 = \beta_I(1+k)\frac{\Lambda}{d_p} + d_p$. According to the standard comparison theorem for fractional order [20], and the positivity of the Mittag–Leffler function $E_{q,1}(t) > 0$, for any $q \in (0,1)$ [84],

$$S \geq S(0)E_{q,1}(-C_1 t^q) \Rightarrow S \geq 0.$$

From the second equation of system (4.16) we find

$$\begin{aligned} D^q E(t) &= \beta_I S(I + kA) - (1-\alpha)\omega_p E - \alpha\omega_p' E - d_p E \\ &\geq -[(1-\alpha)\omega_p + \alpha\omega_p' + d_p]E \\ &\geq -C_2 E, \end{aligned}$$

where $C_2 = (1-\alpha)\omega_p + \alpha\omega_p' + d_p$. Therefore,

$$E \geq E(0)E_{q,1}(-C_2 t^q) \Rightarrow E \geq 0.$$

From the third equation of system (4.16) we get

$$\begin{aligned} D^q I(t) &= (1-\alpha)\omega_p E - (\gamma_p + d_p + \mu)I + \xi A \\ &\geq -(\gamma_p + d_p + \mu)I \\ &\geq -C_3 I, \end{aligned}$$

where $C_3 = \gamma_p + d_p + \mu$. Therefore,

$$I \geq I(0)E_{q,1}(-C_3 t^q) \Rightarrow I \geq 0.$$

From the fourth equation of system (4.16) we obtain

$$\begin{aligned} D^q A(t) &= \alpha\omega_p' E - (\gamma_p' + d_p + \nu)A - \xi A \\ &\geq -(\gamma_p' + d_p + \nu + \xi)A \\ &\geq -C_4 A, \end{aligned}$$

where $C_4 = \gamma_p' + d_p + \nu + \xi$. Therefore,

$$A \geq A(0)E_{q,1}(-C_4 t^q) \Rightarrow A \geq 0.$$

From the last equation of system (4.16) we have

$$\begin{aligned} D^q R(t) &= \gamma_p I + \gamma_p' A - d_p R \\ &\geq \gamma_p I + \gamma_p' A - d_p R \\ &\geq -d_p R. \end{aligned}$$

Therefore,

$$R \geq R(0) E_{q,1}(-d_p t^q) \Rightarrow R \geq 0.$$

Thus, it has been proved that the solutions of system (4.16) are non-negative. □

4.2.3.3 Equilibrium Points and Local Stability

In this subsection, we investigate the local stability of equilibrium points. The fractional-order system (4.16) has the following equilibrium points:

1. The coronavirus-free equilibrium $P_0(S_0, 0, 0, 0, 0)$, where $S_0 = \dfrac{\Lambda}{d_p}$. It is always feasible.
2. The coronavirus-symptomatic-infected-free equilibrium $P_I(S_I, E_I, 0, A_I, R_I)$, which is feasible if

$$\Lambda > \frac{d_p B_T H_T}{k\beta_I \omega_p'}, \quad \alpha = 1 \quad \text{and} \quad \xi = 0, \tag{4.20}$$

where

$$E_I = \frac{1}{B_T}\left(\Lambda - \frac{d_p B_T H_T}{k\beta_I \omega_p'}\right), \quad S_I = \frac{\Lambda - B_T E^*}{d_p},$$

$$A_I = \frac{\omega_p'}{H_T} E_I, \qquad R_I = \frac{\gamma_p'}{d_p}\frac{\omega_p'}{H_T} E_I,$$

and

$$\begin{cases} B_T &= (1-\alpha)\omega_p + \alpha\omega_p' + d_p, \\ C_T &= \gamma_p + \mu + d_p, \\ D_T &= \xi + kC_T, \\ H_T &= \gamma_p' + \nu + \xi + d_p. \end{cases} \tag{4.21}$$

3. The coronavirus endemic equilibrium $P^*(S^*, E^*, I^*, A^*, R^*)$, which is feasible if

$$\Lambda > \frac{d_p B_T C_T H_T}{\beta_I \left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}, \quad \text{and either} \quad \alpha \neq 1 \quad \text{or} \quad \xi \neq 0, \tag{4.22}$$

where

$$E^* = \frac{1}{B_T}\left(\Lambda - \frac{d_p B_T C_T H_T}{\beta_I \left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}\right), \quad S^* = \frac{\Lambda - B_T E^*}{d_p}, \tag{4.23}$$

$$I^* = \frac{(1-\alpha)\omega_p H_T + \alpha\omega_p'\xi}{C_T H_T} E^*, \quad A^* = \frac{\alpha\omega_p'}{H_T} E^* \tag{4.24}$$

$$R^* = \left(\frac{\gamma_p}{d_p}\frac{(1-\alpha)\omega_p H_T + \alpha\omega_p'\xi}{C_T H_T} + \frac{\gamma_p'}{d_p}\frac{\alpha\omega_p'}{H_T}\right) E^*. \tag{4.25}$$

Next, we will discuss the stability of the equilibrium points of system (4.16). At the point $P(S, E, I, A, R)$, the Jacobian matrix of system (4.16) is given by

$$J(P) = \begin{pmatrix} -\beta_I(I + kA) - d_p & 0 & -\beta_I S & -\beta_I S k & 0 \\ \beta_I(I + kA) & -B_T & \beta_I S & \beta_I S k & 0 \\ 0 & (1-\alpha)\omega_p & -C_T & \xi & 0 \\ 0 & \alpha\omega_p' & 0 & -H_T & 0 \\ 0 & 0 & \gamma_p & \gamma_p' & -d_p \end{pmatrix}. \tag{4.26}$$

Using the Jacobian matrix (4.26) and the Matignon condition [65, 70], the local stability of the equilibrium points of the fractional-order system (4.16) is investigated. We have the following results.

Theorem 4.10. *The coronavirus-free equilibrium P_0 of the fractional-order system (4.16) is locally asymptotically stable if*

$$\Lambda < \frac{d_p}{\beta_I}\frac{B_T C_T H_T}{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T}, \left(i.e.,\ R_0 = \beta_I S_0 \frac{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T}{C_T B_T H_T} < 1\right), \tag{4.27}$$

and unstable if

$$\Lambda > \frac{d_p}{\beta_I}\frac{B_T C_T H_T}{(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T}, \ (i.e.,\ R_0 > 1). \tag{4.28}$$

Here, recall that R_0 denotes the basic reproduction number.

Proof. From the proof of theorem (4.3) The eigenvalues of the Jacobian matrix $J(P_0)$ around the coronavirus-free equilibrium P_0 are $\lambda_1 = -d_p$ of multiplicity order two and the roots of the characteristic polynomial of the minor matrix of $J(P_0)$ given by

$$C(\lambda) = \lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0, \tag{4.29}$$

where a_i, $i = 0, \ldots, 2$ are given in (4.9).

and then From condition (4.27), we have also the following results:

$$a_i > 0, \quad i = 0, \ldots, 2 \quad \textit{and} \quad a_2 a_1 > a_0$$

From the Routh–Hurwitz criterion, all the roots λ_i of the characteristic Equation (4.29) have negative real parts. By using Matignon's condition [65, 70], it can be observed that $|arg(\lambda_i)| > q\frac{\pi}{2}$ for all $0 < q < 1$. Therefore, the coronavirus-free equilibrium point P_0 is locally asymptotically stable if condition (4.27) is satisfied. Under condition (4.28), we have $a_0 < 0$ and $\lim_{\lambda \to +\infty} C(\lambda) = +\infty$. Then a positive real root $\lambda^* > 0$ of the characteristic Equation (4.29) exists; from Matignon's condition [65, 70], it can be observed that $|arg(\lambda^*)| = 0 < q\frac{\pi}{2}$ for all $0 < q < 1$. Thus, the coronavirus-free equilibrium point P_0 is unstable. □

The coronavirus-free equilibrium point P_0 is locally asymptotically stable when the coronavirus-symptomatic-free equilibrium P_I and the coronavirus endemic equilibrium P^* do not exist.

Since we can deduce the stability of coronavirus symptomatic infected-free equilibrium P_I from the stability of coronavirus endemic equilibrium P^* by taking $\alpha = 1$ and $\xi = 0$, the stability of the coronavirus endemic equilibrium P^* is now discussed.

Theorem 4.11. *The coronavirus endemic equilibrium P^* of the fractional-order system (4.16) is locally asymptotically stable if*

$$\Lambda > \frac{d_p}{\beta_I} \frac{B_T C_T H_T}{(1-\alpha)\omega_p H_T + \alpha \omega_p' D_T}, \ (i.e., \ R_0 > 1). \tag{4.30}$$

Proof. The eigenvalues of the Jacobian matrix $J(P^*)$ at the equilibrium P^* are $-d_p < 0$ and the roots of the characteristic polynomial arising from the remaining minor of order four:

$$\lambda^4 + c_3\lambda^3 + c_2\lambda^2 + c_1\lambda + c_0 = 0, \tag{4.31}$$

where c_i, $i = 0, \ldots, 3$ are given in (4.12).

It is evident that $c_3 > 0$. From condition (4.30) and the proof of theorem (4.4), the following inequalities on the coefficients are also satisfied:

$$c_i > 0, \ i = 0, \ldots, 3 \quad \textit{and} \quad c_1(c_3c_2 - c_1) > c_0c_3^2$$

Then, according to the Routh–Hurwitz criterion, all the roots of the characteristic Equation (4.31) have negative real parts. By using Matignon's condition [65, 70], it can be observed that $|arg(\lambda_1)| = \pi > q\frac{\pi}{2}$ for all $0 < q < 1$. Therefore, the coronavirus endemic equilibrium point P^* is locally asymptotically stable if (4.30) is satisfied. □

From Theorem 4.11, we obtain the following result.

Remark 4.1. *The coronavirus symptomatic-infected-free equilibrium P_I of the system (4.16) is locally asymptotically stable if*

$$\Lambda > \frac{d_p}{\beta_I}\frac{B_T C_T H_T}{\omega'_p D_T}, \ (i.e., \ R_0 > 1). \tag{4.32}$$

Proof. The result can easily be deduced from Theorem 4.4 by taking $\alpha = 1$ and $\xi = 0$. □

4.2.3.4 Global Stability

The global asymptotic stability of the equilibria P_0, P_I and P^* of the fractional-order system (4.16) is now investigated by using a suitable constructed Lyapunov function, Lemma 4.6 in [30] and Lemma 3.1 in [79].

Theorem 4.12. *If*

$$\Lambda < \frac{d_p B_T C_T H_T}{\beta_I[(1-\alpha)\omega_p H_T + D_T \alpha \omega'_p]}, \ (i.e., \ R_0 < 1), \tag{4.33}$$

then the coronavirus-free equilibrium P_0 of the fractional-order system (4.16) is globally asymptotically stable in $\mathbf{R}^5_+$.

Proof. First, the four equations in (4.16) are independent of R, therefore the last equation in (4.16) can be omitted without loss of generality. Hence, let us consider the following function:

$$V_0(S, E, I, A) = \left(S - S_0 - S_0 \ln \frac{S}{S_0}\right) + E + \frac{B_T}{[(1-\alpha)\omega_p H_T + D_T \alpha \omega'_p]}(H_T I + D_T A).$$

It is easily seen that the above function is non-negative and also $V_0 = 0$ if and only if $S = S_0$, $E = 0$, $I = 0$ and $A = 0$. Further, calculating the q-order derivative of V_0 along the positive solutions of

(4.16), we find:

$$\begin{aligned}
D^q V_0(S,E,I,A) &\leq \frac{1}{S}(S-S_0)D^qS + D^qE + \frac{B_T(H_TD^qI + D_TD^qA)}{[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']} \\
&= \frac{1}{S}(S-S_0)(-\beta_I S(I+kA) - d_p(S-S_0)) + \beta_I S(I+kA) - B_TE \\
&\quad + \frac{B_TH_T((1-\alpha)\omega_pE - C_TI + \xi A)}{[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']} + \frac{B_TD_T(\alpha\omega_p'E - H_TA)}{[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']} \\
&= -\frac{d_p}{S}(S-S_0)^2 + \beta_I S_0(I+kA) \\
&\quad - \frac{B_TC_TH_TI}{[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']} - \frac{B_T(-\xi + D_T)H_TA}{[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']} \\
&= -\frac{d_p}{S}(S-S_0)^2 + \left(\beta_I S_0 - \frac{B_TC_TH_T}{[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']}\right)(I+kA) \\
&= -\frac{d_p}{S}(S-S_0)^2 + \frac{\beta_I}{d_p}\left(\Lambda - \frac{d_pB_TC_TH_T}{\beta_I[(1-\alpha)\omega_pH_T + D_T\alpha\omega_p']}\right)(I+kA).
\end{aligned}$$

From condition (4.33), we can show that the coefficient of the term $I + kA$ in the last equality are negative. Thus, we have $D^qV_0 \leq 0$ for all $(S,E,I,A) \in \mathbb{R}^4_+$ and $D^\alpha V_0 = 0$ if and only if $(S,E,I,A) = (S_0,0,0,0)$. Thus, the only invariant set contained in $\mathbb{R}^4_+$ is $\{(S_0,0,0,0)\}$. Hence, by Lemma 4.6 of [30], it is enough to prove the convergence of the solutions (S,E,I,A) to $(S_0,0,0,0)$. From the last equation of (4.16) we can easily show that R converges also to 0. Therefore, P_0 is globally asymptotically stable in $\mathbb{R}^5_+$ if $R_0 < 1$. □

Theorem 4.13. *If*

$$\Lambda > \frac{d_pB_TH_T}{\beta_Ik\omega_p'}, \ (i.e., \ R_0 > 1), \tag{4.34}$$

then the coronavirus-symptomatic-infected-free equilibrium P_I of the fractional-order system (4.16) is globally asymptotically stable in $\mathbb{R}^5_+/\mathbb{R}_+ \times \{(0,0,0)\} \times \mathbb{R}_+$.

Proof. Consider the function

$$\begin{aligned}
V_1(S,E,I,A) &= S - S_I - S_I\ln\frac{S}{S_I} + E - E_I - E_I\ln\frac{E}{E_I} \\
&\quad + \frac{\beta_IS_I}{C_T}I + \frac{k\beta_IS_I}{H_T}\left(A - A_I - A_I\ln\frac{A}{A_I}\right).
\end{aligned}$$

This function is positive and $V_1(S,E,I,A) = 0$ if and only if $(S,E,I,A) = (S_I,E_I,0,A_I)$.

By calculating the q-order derivative of V_1 along the solution trajectories of system (4.16) and using

Lemma 3.1 in [79], we obtain

$$\begin{aligned} D^q V_1(S,E,I,A) &\leq \left(1-\frac{S_I}{S}\right)(\Lambda-\beta_I S(I+kA)-d_p S) \\ &\quad +\left(1-\frac{E_I}{E}\right)(\beta_I S(I+kA)-B_T E) \\ &\quad +\frac{\beta_I S_I}{C_T}(-C_T I) \\ &\quad +\frac{k\beta_I S_I}{H_T}\left(1-\frac{A_I}{A}\right)\left(\omega_p' E - H_T A\right) \\ &= \left(1-\frac{S_I}{S}\right)(\beta_I S_I k A_I + d_p S_I - \beta_I S(I+kA) - d_p S) \\ &\quad +\left(1-\frac{E_I}{E}\right)\beta_I S(I+kA) - B_T E + \beta_I S_I k A_I \\ &\quad -\beta_I S_I I \\ &\quad +\frac{k\beta_I S_I}{H_T}\left(1-\frac{A_I}{A}\right)\omega_p' E - k\beta_I S_I A + \frac{k\beta_I S_I}{H_T}\omega_p' E_I \\ &= -\frac{d_p}{S}(S-S_I)^2 + \beta_I S_I k A_I\left(1-\frac{S_I}{S}\right) \\ &\quad -\beta_I E_I \frac{SI}{E} - k\beta_I E_I \frac{SA}{E} - \frac{k\beta_I S_I}{H_T}\omega_p' A_I \frac{E}{A} \\ &\quad +\beta_I S_I k A_I + \frac{k\beta_I S_I}{H_T}\omega_p' E_I. \end{aligned} \tag{4.35}$$

Now, substituting

$$x=\frac{S}{S_I}, \quad y=\frac{E}{E_I}, \quad z=I, \quad u=\frac{A}{A_I},$$

in inequality (4.35), we obtain

$$\begin{aligned} D^q V_1(S,E,I,A) &\leq -\frac{d_p}{S}(S-S_I)^2 + \beta_I S_I k A_I\left(2-\frac{1}{x}-\frac{xu}{y}\right) \\ &\quad -\beta_I S_I \frac{xz}{y} + \frac{k\beta_I S_I}{H_T}\omega_p' E_I\left(1-\frac{y}{u}\right). \end{aligned}$$

From the fourth equation of (4.16), we have

$$\omega_p' E_I - H_T A_I = 0. \tag{4.36}$$

Multiplying the Equation (4.36) by

$$\frac{k\beta_I S_I}{H_T} F_1(x,y,z,u),$$

where $F_1(x, y, z, u)$ is a function to be determined later, yields

$$\frac{k\beta_I S_I}{H_T}\omega_p' E_I F_1(x, y, z, u) - \beta_I S_I k A_I F_1(x, y, z, u) = 0. \tag{4.37}$$

Then, we obtain

$$\begin{aligned} D^q V_1(S, E, I, A) \leq & -\frac{d_p}{S}(S - S_I)^2 + \beta_I S_I k A_I \left(2 - \frac{1}{x} - \frac{xu}{y} - F_1(x, y, z, u)\right) \\ & -\beta_I S_I \frac{xz}{y} + \frac{k\beta_I S_I}{H_T}\omega_p' E_I \left(1 - \frac{y}{u} + F_1(x, y, z, u)\right). \end{aligned} \tag{4.38}$$

The function $F_1(x, y, z, u)$ is chosen such that the coefficient of E_I is equal to zero. In this case, we obtain

$$F_1(x, y, z, u) = \frac{y}{u} - 1.$$

Thus, inequality (4.38) is equivalent to

$$D^q V_1(S, E, I, A) \leq -\frac{d_p}{S}(S - S_I)^2 + \beta_I S_I k A_I \left(3 - \frac{1}{x} - \frac{xu}{y} - \frac{y}{u}\right) - \beta_I S_I \frac{xz}{y}.$$

By the arithmetic mean-geometric mean inequality we have $\left(3 - \frac{1}{x} - \frac{xu}{y} - \frac{y}{u}\right) \leq 0$ for all $x \geq 0$, $y \geq 0$ and $u \geq 0$. Hence $D^q V_1(S, E, I, A) \leq 0$, and $D^q V_1(S, E, I, A) = 0$ if and only if $S = S_I$, $I = 0$ and $u = y$ (i.e., $\frac{E}{E_I} = \frac{A}{A_I}$). Since S must remain constant at S_I, $D^q S$ is zero. This implies that $A = A_I$ and $E = E_I$. Thus, by Lemma 4.6 in [30], it follows that the coronavirus-symptomatic-infected-free equilibrium P_I is globally asymptotically stable in $\mathbb{R}^5_+/\mathbb{R}_+ \times \{(0, 0, 0)\} \times \mathbb{R}_+$. □

Theorem 4.14. *If*

$$\Lambda > \frac{d_p B_T C_T H_T}{\beta_I \left[(1-\alpha)\omega_p H_T + \alpha\omega_p' D_T\right]}, \quad (i.e.,\ R_0 > 1), \quad \text{and either} \quad \alpha \neq 1 \quad \text{or} \quad \xi \neq 0, \tag{4.39}$$

the fully endemic equilibrium P^* of the fractional-order system (4.16) is globally asymptotically stable in $\mathbb{R}^5_+/\mathbb{R}_+ \times \{(0, 0, 0)\} \times \mathbb{R}_+$.

Proof. Consider the function

$$\begin{aligned} V_2(S, E, I, A) = & S - S^* - S^* \ln\frac{S}{S^*} + E - E^* - E^* \ln\frac{E}{E^*} \\ & + \frac{\beta_I S^*}{C_T}\left(I - I^* - I^* \ln\frac{I}{I^*}\right) + \frac{\beta_I S^* D_T}{C_T H_T}\left(A - A^* - A^* \ln\frac{A}{A^*}\right). \end{aligned}$$

This function is positive and $V_2(S, E, I, A) = 0$ if and only if $(S, E, I, A) = (S^*, E^*, I^*, A^*)$.

By calculating the q-order derivative of V_2 along the solution of system (4.16) and using Lemma 3.1

in [79], we obtain

$$\begin{aligned}
D^q V_1(S,E,I,A) &\leq \left(1-\frac{S^*}{S}\right)(\Lambda-\beta_I S(I+kA)-d_p S)\\
&\quad+\left(1-\frac{E^*}{E}\right)(\beta_I S(I+kA)-B_T E)\\
&\quad+\frac{\beta_I S^*}{C_T}\left(1-\frac{I^*}{I}\right)((1-\alpha)\omega_p E-C_T I+\xi A)\\
&\quad+\beta_I S^*\left(\frac{D_T}{C_T H_T}\right)\left(1-\frac{A^*}{A}\right)\left(\alpha\omega_p' E-H_T A\right)\\
&= \left(1-\frac{S^*}{S}\right)(\beta_I S^*(I^*+kA^*)+d_p S^*-\beta_I S(I+kA)-d_p S)\\
&\quad+\left(1-\frac{E^*}{E}\right)\beta_I S(I+kA)-B_T E+\beta_I S^*(I^*+kA^*)\\
&\quad+\frac{\beta_I S^*}{C_T}\left(1-\frac{I^*}{I}\right)((1-\alpha)\omega_p E+\xi A)\\
&\quad-\frac{\beta_I S^*}{C_T}C_T I+\frac{\beta_I S^*}{C_T}[(1-\alpha)\omega_p E^*+\xi A^*]\\
&\quad+\frac{\beta_I S^* D_T}{C_T H_T}\left(1-\frac{A^*}{A}\right)\alpha\omega_p' E-\frac{\beta_I S^* D_T}{C_T H_T}H_T A+\frac{\beta_I S^* D_T}{C_T H_T}\alpha\omega_p' E^*\\
&= -\frac{d_p}{S}(S-S^*)^2+\beta_I S^* I^*\left(1-\frac{S^*}{S}\right)+\beta_I S^* kA^*\left(1-\frac{S^*}{S}\right)\\
&\quad-\beta_I E^*\frac{SI}{E}-k\beta_I E^*\frac{SA}{E}-\frac{\beta_I S^*}{C_T}(1-\alpha)\omega_p I^*\frac{E}{I}\\
&\quad-\frac{\beta_I S^*}{C_T}\xi I^*\frac{A}{I}-\frac{\beta_I S^* D_T}{C_T H_T}\alpha\omega_p' A^*\frac{E}{A}+\beta_I S^*(I^*+kA^*)\\
&\quad+\frac{\beta_I S^*}{C_T}[(1-\alpha)\omega_p E^*+\xi A^*]+\frac{\beta_I S^* D_T}{C_T H_T}\alpha\omega_p' E^*. \qquad (4.40)
\end{aligned}$$

Now, replacing

$$x=\frac{S}{S^*},\quad y=\frac{E}{E^*},\quad z=\frac{I}{I^*},\quad u=\frac{A}{A^*},$$

in inequality (4.38), we obtain

$$\begin{aligned}
D^q V_1(S,E,I,A) &\leq -\frac{d_p}{S}(S-S^*)^2+\beta_I S^* I^*\left(2-\frac{1}{x}-\frac{xz}{y}\right)\\
&\quad+\beta_I S^* kA^*\left(2-\frac{1}{x}-\frac{xu}{y}\right)+\frac{\beta_I S^*}{C_T}(1-\alpha)\omega_p E^*\left(1-\frac{y}{z}\right)\\
&\quad+\frac{\beta_I S^*}{C_T}\xi A^*\left(1-\frac{u}{z}\right)+\frac{\beta_I S^*(kC_T+\xi)}{C_T H_T}\alpha\omega_p' E^*\left(1-\frac{y}{u}\right).
\end{aligned}$$

From the third and fourth equations of (4.16), we have

$$C_T I^* - (1-\alpha)\omega_p E^* - \xi A^* = 0, \tag{4.41}$$

$$\alpha\omega_p' E^* - H_T A^* = 0. \tag{4.42}$$

Multiplying the Equations (4.41) and (4.42) respectively by

$$\frac{\beta_I S^*}{C_T} F_2(x,y,z,u), \quad \frac{\beta_I S^*(kC_T+\xi)}{C_T H_T} F_3(x,y,z,u),$$

where $F_2(x,y,z,u)$ and $F_3(x,y,z,u)$ are functions to be determined later, yields

$$\left(C_T I^* - (1-\alpha)\omega_p E^* - \xi A^*\right) \frac{\beta_I S^*}{C_T} F_2(x,y,z,u) = 0, \tag{4.43}$$

$$\left(\alpha\omega_p' E^* - H_T A^*\right) \frac{\beta_I S^*(kC_T+\xi)}{C_T H_T} F_3(x,y,z,u) = 0. \tag{4.44}$$

Then, we have

$$\begin{aligned} D^q V_1(S,E,I,A) \leq & -\frac{d_p}{S}(S-S^*)^2 + \beta_I S^* I^* \left(2 - \frac{1}{x} - \frac{xz}{y} + F_2(x,y,z,u)\right) \\ & + \beta_I S^* k A^* \left(2 - \frac{1}{x} - \frac{xu}{y} - F_3(x,y,z,u)\right) \\ & + \frac{\beta_I S^*}{C_T}(1-\alpha)\omega_p E^* \left(1 - \frac{y}{z} - F_2(x,y,z,u)\right) \\ & + \frac{\beta_I S^*}{C_T}\xi A^* \left(1 - \frac{u}{z} - F_2(x,y,z,u) - F_3(x,y,z,u)\right) \\ & + \frac{\beta_I S^*(kC_T+\xi)}{C_T H_T}\alpha\omega_p' E^* \left(1 - \frac{y}{u} + F_3(x,y,z,u)\right). \end{aligned} \tag{4.45}$$

The functions $F_2(x,y,z,u)$ and $F_3(x,y,z,u)$ are chosen such that the coefficients of $\omega_p' E^*$ and I^* are equal to zero. In this case, we obtain

$$F_2(x,y,z,u) = \frac{1}{x} + \frac{xz}{y} - 2,$$

and

$$F_3(x,y,z,u) = \frac{y}{u} - 1.$$

Thus, inequality (4.45) is equivalent to

$$\begin{aligned} D^q V_1(S,E,I,A) \leq & -\frac{d_p}{S}(S-S^*)^2 + \beta_I S^* k A^* \left(3 - \frac{1}{x} - \frac{xu}{y} - \frac{y}{u}\right) \\ & + \frac{\beta_I S^*}{C_T}(1-\alpha)\omega_p E^* \left(3 - \frac{y}{z} - \frac{1}{x} - \frac{xz}{y}\right) \\ & + \frac{\beta_I S^*}{C_T}\xi A^* \left(4 - \frac{u}{z} - \frac{1}{x} - \frac{xz}{y} - \frac{y}{u}\right). \end{aligned}$$

By the arithmetic mean-geometric mean inequality we have $\left(3-\frac{1}{x}-\frac{xu}{y}-\frac{y}{u}\right) \leq 0$, $\left(3-\frac{y}{z}-\frac{1}{x}-\frac{xz}{y}\right) \leq 0$ and $\left(4-\frac{u}{z}-\frac{1}{x}-\frac{xz}{y}-\frac{y}{u}\right) \leq 0$ for all $x \geq 0$, $y \geq 0$, $z \geq 0$ and $u \geq 0$. Hence, $D^q V_1(S,E,I,A) \leq 0$, and $D^q V_1(S,E,I,A) = 0$ if and only if $S = S^*$ and $u = z = y$ (i.e., $\frac{E}{E^*} = \frac{I}{I^*} = \frac{A}{A^*}$). Since S must remain constant at S^*, $D^q S$ is zero. This implies that $A = A^*$, $I = I^*$ and $E = E^*$. Thus, by Lemma 4.6 in [30], it follows that the fully endemic equilibrium P^* is globally asymptotically stable in $\mathbb{R}^5_+/\mathbb{R}_+ \times \{(0,0,0)\} \times \mathbb{R}_+$. □

Remark 4.2. *If the initial conditions start from $\mathbb{R}_+ \times \{(0,0,0)\} \times \mathbb{R}_+$, then the solution converges to the coronavirus-free equilibrium point P_0.*

4.2.4 Discussion

The proposed epidemic model for Covid-19 containing a fractional derivative formulation has been analysed. The results show that the model is sound, because trajectories are confined to a compact set and the subpopulations corresponding to the various compartments into which the whole population is partitioned remain bounded. Unboundedness would indeed be biologically impossible. The model exhibits the endemic equilibrium P^* at which the disease persists. It also contains the disease-free point with only susceptible individuals, P_0, for which the pandemic is finally eradicated. This equilibrium should be the goal of the policies attempting epidemic diffusion confinement. There is also an "intermediate equilibrium", P_I, which does not contain symptomatic infected, but it still harbors the disease among the asymptomatic individuals, so that it is in reality still endemic. The susceptible-only point P_0 is incompatible with both P_I and P^*, the latter being unfeasible when the former is stably attained. Note also that P_I is a kind of particular case of coexistence P^*, which arises if asymptomatics will never develop symptoms and all the exposed migrate into the asymptomatic class. In Section 4.2.3.4, global stability for each equilibrium in suitable conditions is shown. This result is relevant but also to be expected, in view of the incompatibility of multiple equilibria discussed above.

Figures 4.26–4.28 show these three theoretical types of possible model behaviors. The comparison of these results with publicly available datasets on Covid-19 is not really our goal. In part, this is also due to the discussion that follows below, indicating that the population equilibrium levels change with the changes of the fractional derivative order.

Note that, of the two endemic points P^* and P_I, at equilibrium P_I the disease remains hidden in the population. However, it still has its pernicious effects, since people will still "silently" die of it, at rate ν. In a sense, this equilibrium is worse than the explicit endemic one P^*, because the latter keeps on showing to the people that the disease is not eradicated and therefore warns the population to maintain suitable safety measures.

Finally, we observe that the stability results obtained analytically for the fractional operator model in this case do coincide with those of the model formulated using standard derivatives. Therefore, theoretically, the memory effects on this dynamical system are essentially scantly relevant, and the use of a classical standard formulation appears to be adequate. However, to further analyse in practice the effect of the order of the fractional derivatives, we have investigated how it may possibly affect the equilibrium levels. Simulations of the population values attained at equilibrium are also reported as a function of the fractional derivative order, in Figures 4.29–4.31, which correspond to the time series of the Figures 4.26–4.28 mentioned above. It is clearly seen that the order q of the fractional derivative does influence the final stage of the compartment levels. In Figure 4.29, for the endemic equilibrium P^*, all compartments show a population decrease when q falls below 0.5, with the exception of S, which slightly increases. The same trend is also observed for the other endemic point P_I, in Figure 4.31, although in this case the compartments are arranged differently in the two frames, to better show the details. For the disease-free point P_0, in Figure 4.30, a low value of q decrements the susceptibles and increases the other compartments. These are very small, but in fact should vanish. However, the simulations have all been carried out with the same final time $T =$ 10,000, so that the result indicates that a low q entails a longer time for disease eradication.

A possible line of research to be pursued in the future is to compare the real-world scenario data with the simulation outcomes to assess the optimal fractional order to be used in the model, or if instead the standard derivatives are sufficient.

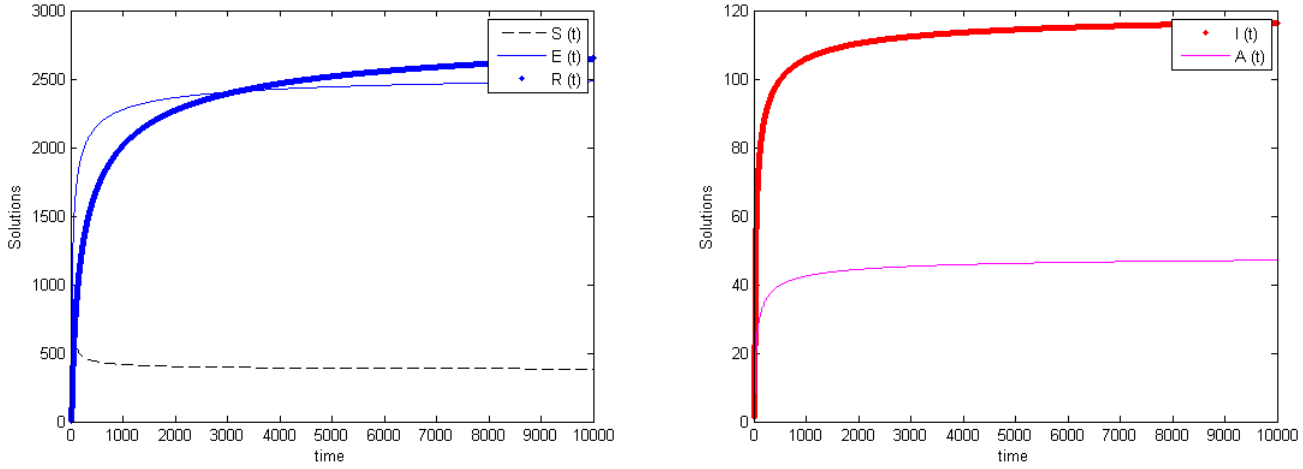

Figure 4.26: The model behavior for $R_0 = 1.1421 > 1$. (**Left**) exposed and recovered settle at a level near 2500, susceptibles drop to about 500; (**Right**) infected stabilize at 120 individuals, asymptomatic instead at 40 individuals. This corresponds to the endemic equilibrium P^*. The parameter values are $\Lambda = 500$, $\beta_I = 0.01$, $k = 0.1$, $d_p = 0.082$, $\alpha = 0.15$, $\omega_p = 0.1$, $\omega_p' = 0.1$, $\xi = 0.1$, $\mu = 0.001$, $\gamma_p = 1.764$, $\gamma_p' = 0.6024$, $\nu = 0.0005$.

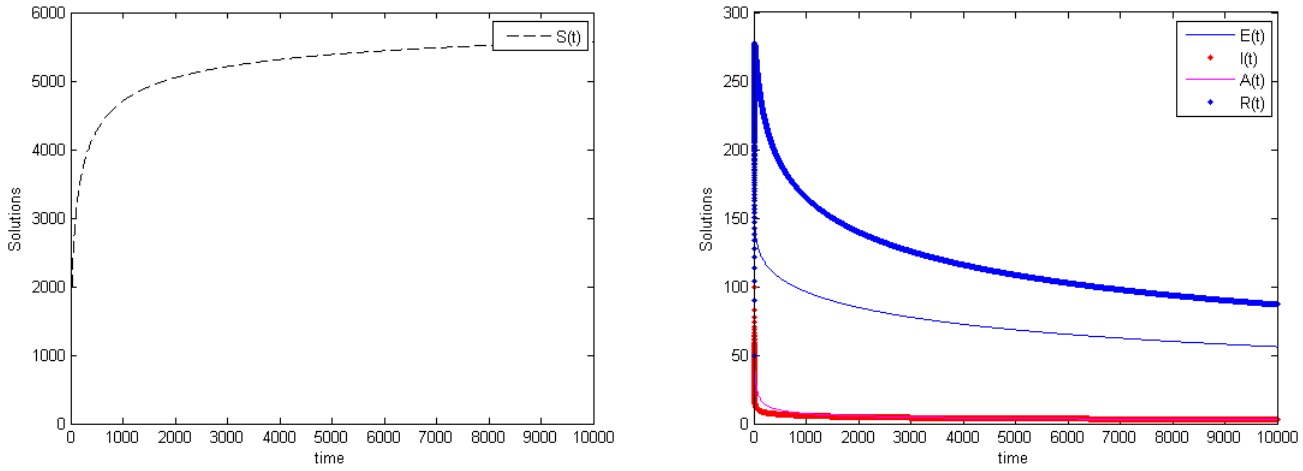

Figure 4.27: The model behavior for $0 < R_0 = 0.0571 < 1$. (**Left**) susceptibles reach the level of 5500; (**Right**) infected and asymptomatic individuals are reduced to the single digits, essentially vanishing, recovered and exposed individuals remain confined respectively around the levels 100 and 50. In this situation, the system approaches the disease-free equilibrium P_0. The parameter values are $\Lambda = 500$, $\beta_I = 0.0005$, $k = 0.1$, $d_p = 0.082$, $\alpha = 0.15$, $\omega_p = 0.1$, $\omega_p' = 0.1$, $\xi = 0.1$, $\mu = 0.001$, $\gamma_p = 1.764$, $\gamma_p' = 0.6024$, $\nu = 0.0005$.

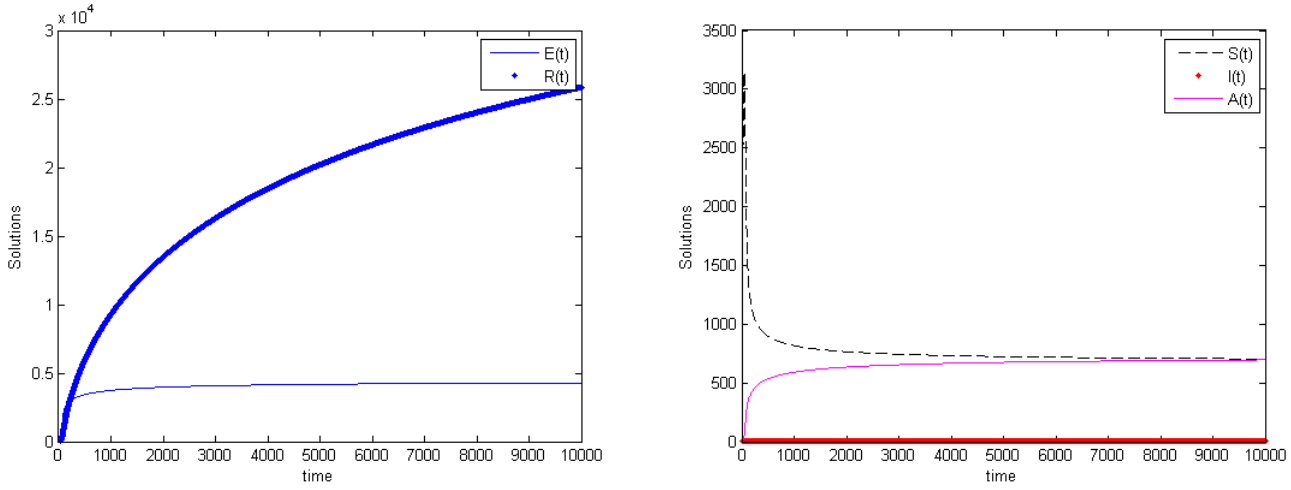

Figure 4.28: The model behavior for $R_0 = 1.2677 > 1$. (**Left**) recovered attain the level of 25,000, exposed instead about 4000; (**Right**) infected stabilize at around the 200 level, susceptibles and asymptomatic individuals remain confined around the level 100. Once again the system settles at the endemic equilibrium, but this time we have $\xi = 0$ and $\alpha = 1$, so that the point attained is P_I. The parameter values are $\Lambda = 500$, $\beta_I = 0.01$, $k = 0.1$, $d_p = 0.0082$, $\alpha = 1$, $\omega_p = 0.1$, $\omega_p' = 0.1$, $\xi = 0$, $\mu = 0.001$, $\gamma_p = 1.764$, $\gamma_p' = 0.6024$, $\nu = 0.0005$.

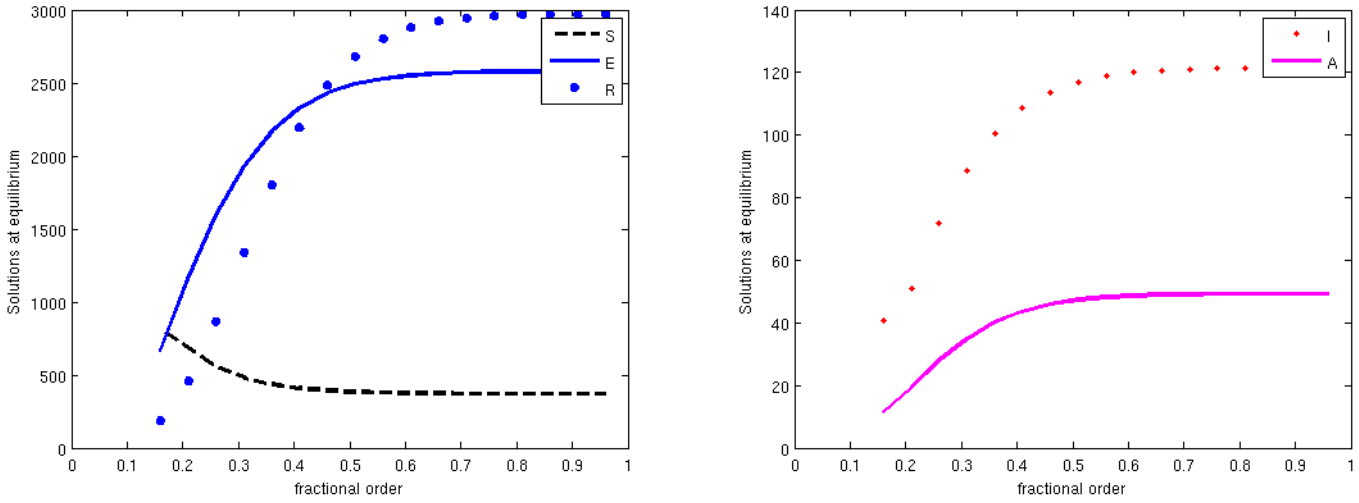

Figure 4.29: The model behavior for $R_0 = 1.1421 > 1$ as q varies in $[0, 1]$. (**Left**) exposed and recovered; (**Right**) susceptibles, infected and asymptomatic. The situation corresponds to the endemic equilibrium P^*. The parameter values are the same of Figure 4.26.

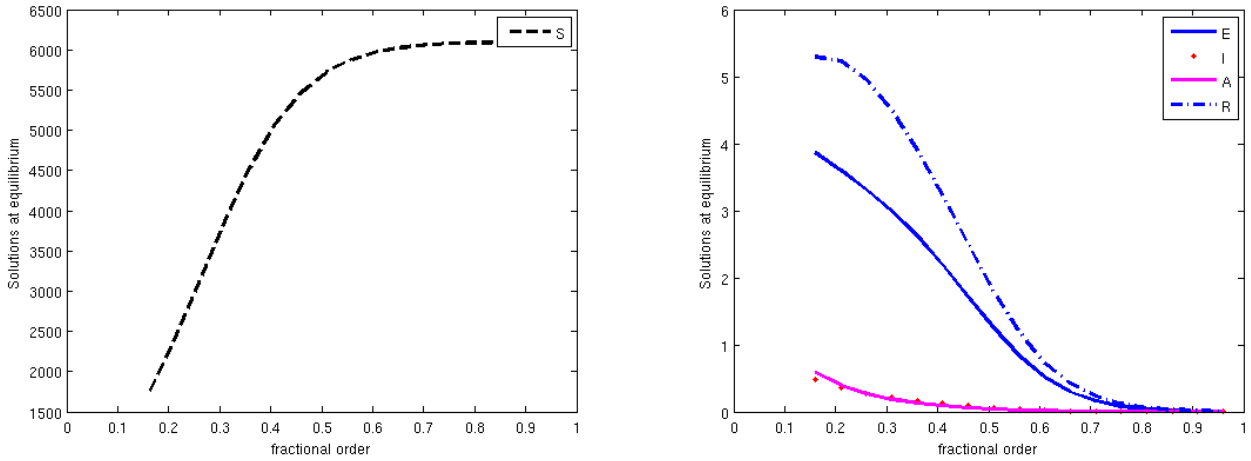

Figure 4.30: The model behavior for $0 < R_0 = 0.0571 < 1$ as q varies in $[0, 1]$. (**Left**) susceptibles; (**Right**) exposed, infected, asymptomatics and recovered. In this situation the system approaches the disease-free equilibrium P_0. All the simulations have been stopped at the same final time, $T = 10{,}000$. For low values of the fractional derivative order, the populations E, I, A and R are not zero, but this feature is intentionally left in the figure. Thus, it denotes the different speeds at which the populations vanish as a function of the fractional derivative order. The parameter values are the same as those in Figure 4.27.

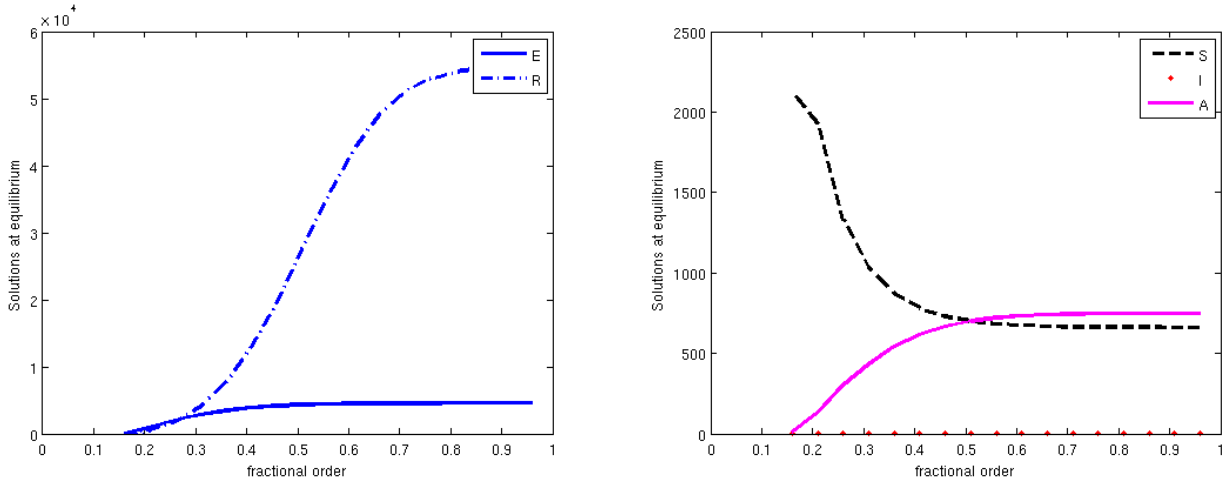

Figure 4.31: The model behavior for $R_0 = 1.2677 > 1$ as q varies in $[0, 1]$. (**Left**) exposed and recovered; (**Right**) susceptibles, infected and asymptomatic. Once again the system settles at the endemic equilibrium, but this time we have $\xi = 0$ and $\alpha = 1$, so that the point attained is P_I. The parameter values are the same as those in Figure 4.28.

Chapter 5

Appendix

5.1 Gershgorin Circle Theorem

Gershgorin Circle TheoremAlso called the Gershgorin Disk Theorem.It allows possible to conclude the stability of a matrix without having recourse to the explicit calculation of the eigenvalues.

Definition 5.1. ***[Stability module, spectral radius]***

Let A be a matrix square matrix and we denote by $spec(A)$ the set of eigenvalues of matyrix A. We call module of stability of the matrix A the number defined by:

$$\alpha(A) = \max\{\mathrm{Re}(\lambda); \lambda \in \mathrm{Spec}(A)\}$$

The matrix A is said stable if $\alpha(A) < 0$

We say spectral radius the real number $\rho(A)$ defined by

$$\rho(A) = \max_{\lambda \in \mathrm{Spec}(A)} |\lambda|$$

We say that a matrix A is stable if its eigenvalues have a strictly negative real parts. It is also called the matrix of Hurwitz.

Definition 5.2. ***[Gershgorin Disk]****[76], [92]*

Let $A = (a_{ij}) \in \mathcal{M}_a(K)$. For all $i \in [1, n]$ denote

$$D_i = B_f\left(a_{ii}, r_i = \sum_{j=1, j\neq i}^{n} |a_{ij}|\right) = \left\{x \in K : |a_{ii} - x| \neq r_i = \sum_{j=1, j\neq i}^{n} |a_{ij}|\right\}$$

The ith Gershgorin disk of A, with B_f is a closed ball.

Theorem 5.1. ***[Gershgorin Theorem]***

Let $A = (a_{ij}) \in \mathcal{M}_n(K)$. The set of all eigenvalues of A lie in the union of the Gerschgorin disks D_i ie : λ is eigenvalue of $A \Rightarrow \lambda \in \cup_{i=1}^{n} D_i$

5.2 Calculation of the reproductive number $\mathcal{R}_0$ using the next generation matrix

As seen before, the basic reproductive number R_0, is defined as the expected number of new infections from one infected individual in a fully susceptible population through the entire duration of the infectious period. This is the method of *Van den Driessche* et *Watmough* [23], [77]. Here, the basic reproduction number R_0 is obtained calculating the spectral radius of next generation matrix .
In this method, the next generation matrix is constructed by a subsystem taking into account the states-at-infection and the states-of-infectiousness We consider a deterministic model for disease transmission with n compartments (dimensions). We let x where x_j denotes the number of individuals in compartment j at time t. For ease of notation, we order the compartments such that the first k compartments correspond to the states with infection. Let $\mathcal{F}_j(x)$ to be the rate of new infections entering compartment j. and $\mathcal{V}_j^+$ is the rate of transfer into compartment j by any other means, V_j^- is the rate of transfer out of compartment j.
We rewrite the model as:

$$\dot{x}_j = \mathcal{F}_j(x) + \mathcal{V}_j^+(x) - \mathcal{V}_j^-(x),$$

if we suppose $V_j(x) = V_j^+(x) - V_j^-(x)$ the system become:

$$\dot{x}_j = \mathcal{F}_j(x) + \mathcal{V}_j(x).$$

We list 5 reasonable assumptions for these functions below.

1. $x \geq 0, \mathcal{F}_j(x) \geq 0, V_j^+(x) \geq 0, V_j^-(x) \geq 0$ This implies that no rate of movement can be negative.
2. If $x_j = 0$ then $V_j^- = 0$.In particular if we define $X_s = \{x \geq 0; x_j = 0, i = 1, \cdots, n\}$ and if $x \in X_s$ then $\mathcal{V}_j^- = 0$.If there are no individuals in a compartment, there can be no movement of individuals out of that compartment.

3. If $j \leq k$ then $\mathcal{F}_j(x) = 0$. This means by definition that it cannot fit infected people into non-infected compartments.

4. if x_0 disease-free states then $\mathcal{F}_j(x_0) = 0$ and for $j > k$, $\quad V_j^+(x_0) = 0$.If there is no infection in the population, there can be no input into the infectious populations. For example, there can be no density-independent, non per-capita immigration of infectious individuals. This ensures that the disease-free subspace is invariant.

For a disease-free equilibrium point x_0, and $f(x)$ satisfy assumptions. we define matrices $J_{\mathcal{F}}$ and $J_{\mathcal{V}}$ by

$$J_{\mathcal{F}} = \left(\frac{\partial \mathcal{F}_i}{\partial x_j}\right), \quad J_{\mathcal{V}} = \left(\frac{\partial \mathcal{V}_i}{\partial x_j}\right), \quad 1 \leq i\,, j \leq k$$

such that :$J_{\mathcal{F}}$ is non-negative and $J_{\mathcal{V}}$ is inversible.

Then $-J_{\mathcal{F}} J_{\mathcal{V}}^{-1}$ is said the next generation matrix

Definition 5.3. *[23] The basic reproductive number $\mathcal{R}_0$ is the spectral radius of the next generation matrix*

$$\mathcal{R}_0 = \rho\left(-J_{\mathcal{F}} J_{\mathcal{V}}^{-1}\right)$$

5.3 K-th additive compound of the matrix

Definition 5.4. ***[k-th additive compound of the matrix]****[88] [62].*

Let Abe a matrix in $\mathcal{M}_n(R)$, let k be a positive integer, We denote by $A^{[k]}$ the k-th compound of the matrix of A, the matrix $\mathcal{M}_N(R)$ where $N = C_m^k$ defined by

$$A^{[k]} = D_+\left((l + hA)^k\right)_{|h=0},$$

where D_+ denotes defferentiation with respect to h.

The second additive compound matrix of$A$

$$\text{for} n = 2 \quad \text{by} \quad A^{[2]} = a_{11} + a_{22}$$

$$\text{for } n = 3 \quad \text{by} \quad A^{[2]} = \begin{pmatrix} a_{11} + a_{22} & a_{23} & -a_{13} \\ a_{32} & a_{11} + a_{33} & a_{12} \\ -a_{31} & a_{21} & a_{22} + a_{33} \end{pmatrix}$$

$$\text{for } n=4 \quad \text{by} \quad A^{[2]} = \begin{pmatrix} a_{11}+a_{22} & a_{23} & a_{24} & -a_{13} & -a_{14} & 0 \\ a_{32} & a_{11}+a_{33} & a_{34} & a_{12} & 0 & -a_{14} \\ a_{42} & a_{43} & a_{11}+a_{44} & 0 & a_{12} & a_{13} \\ -a_{31} & a_{21} & 0 & a_{22}+a_{33} & a_{34} & -a_{24} \\ -a_{41} & 0 & a_{21} & a_{43} & a_{22}+a_{44} & a_{23} \\ 0 & -a_{41} & a_{31} & -a_{42} & a_{32} & a_{33}+a_{44} \end{pmatrix}$$

Example: Let us consider the system (2.1) of chapter two 2. We have from the theorem of **Gershgorin**, the following result:

Theorem 5.2. *If* $d_{NB}-d_{BT}>0$, $d_T-kd_{TH}>0$ *and* $[\frac{b_T}{T_H^*}-a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^*], [\frac{b_N}{N^*}-d_{NB}N^*]>0$. *the equilibrium point* E^* *in the case* $L=2$ *is asymptotically stable.*

Proof. The Jacobian of the system at the equilibrium E^* in the case $L=2$ it becomes, using the first three of equilibrium equations to simplify some of the diagonal elements:

$$J_2(E^*) = \begin{pmatrix} -\frac{b_B}{B^*} & -d_{BN}B^* & -d_{BT}B^* & 0 \\ -d_{NB}N^* & -\frac{b_N}{N^*} & 0 & 0 \\ -d_{TB}T^*+ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* & 0 & -d_T-d_{TB}B^* & ka_{T_H}\frac{B^{*2}}{s+B^{*2}} \\ a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* & 0 & 0 & -\frac{b_T}{T_H^*} \end{pmatrix} \tag{5.1}$$

The second additive compound matrix is given by : $J^{[2]}(E^*) =$

$$\begin{pmatrix} -\frac{b_B}{B^*}-\frac{b_N}{N^*} & 0 & 0 & ..... \\ 0 & -\frac{b_B}{B^*}-d_T-d_{TB}B^* & ka_{T_H}\frac{B^{*2}}{s+B^{*2}} & ..... \\ 0 & 0 & -\frac{b_B}{B^*}-\frac{b_T}{T_H^*} & ..... \\ d_{TB}T^*-ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* & -d_{NB}N^* & 0 & ..... \\ -a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* & 0 & -d_{NB}N^* & ..... \\ 0 & -a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* & -d_{TB}T^*+ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* & ..... \end{pmatrix}$$

$$
\begin{pmatrix}
..... & d_{BT}B^* & 0 & 0 \\
..... & -d_{BN}B^* & 0 & 0 \\
..... & 0 & -d_{BN}B^* & -d_{BT}B^* \\
..... & -\frac{b_N}{N^*} - d_T - d_{TB}B^* & ka_{T_H}\frac{B^{*2}}{s+B^{*2}} & 0 \\
..... & 0 & -\frac{b_N}{N^*} - \frac{b_T}{T_H^*} & 0 \\
..... & 0 & 0 & -d_T - d_{TB}B^* - \frac{b_T}{T_H^*}
\end{pmatrix}
$$

It is easy to see that the diagonal elements of $J^{[2]}$ are negative and more; the matrix $J^{[2]}$ is a dominant diagonal in line, because:

$$
\begin{aligned}
J_{11} + \sum_{j=2}^{6} |J_{1j}| &= -\frac{b_B}{B^*} - \frac{b_N}{N^*} + d_{BT}B^* \\
&= -\frac{b_B}{B^*} - d_N - B^*(d_{NB} - d_{BT}) < 0 \\
J_{22} + \sum_{j=1\ j\neq 2}^{6} |J_{2j}| &= -\frac{b_B}{B^*} - d_T - d_{TB}B^* + ka_{T_H}\frac{B^{*2}}{s+B^{*2}} + d_{BN}B^* \\
&= -\frac{b_B}{B^*} - (d_T - kd_{TH}) - B^*(d_{TB} - d_{BN}) - \frac{kb_T}{T_H^*} < 0 \\
J_{33} + \sum_{j=1\ j\neq 3}^{6} |J_{3j}| &= -\frac{b_B}{B^*} - \frac{b_T}{T_H^*} + B^*(d_{BN} + d_{BT}) < 0 \\
J_{44} + \sum_{j=1\ j\neq 4}^{6} |J_{4j}| &= -d_{TB}T^* + ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* + d_{NB}N^* - \frac{b_N}{N^*} - d_T - d_{TB}B^* + ka_{T_H}\frac{B^{*2}}{s+B^{*2}} \\
&= -k[\frac{b_T}{T_H^*} - a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^*] - [\frac{b_N}{N^*} - d_{NB}N^*] - d_{TB}T^* - d_{TB}B^* - (d_T - kd_{TH}) < 0 \\
J_{55} + \sum_{j=1\ j\neq 5}^{6} |J_{5j}| &= a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* + d_{NB}N^* - \frac{b_N}{N^*} - \frac{b_T}{T_H^*} \\
&= -[\frac{b_T}{T_H^*} - a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^*] - [\frac{b_N}{N^*} - d_{NB}N^*] < 0 \\
J_{66} + \sum_{j=1}^{5} |J_{6j}| &= a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* - d_{TB}T^* + ka_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^* - d_T - d_{TB}B^* - \frac{b_T}{T_H^*} \\
&= a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^*(k+1) - d_{TB}T^* - d_T - d_{TB}B^* - \frac{b_T}{T_H^*} \\
&= -(k+1)[\frac{b_T}{T_H^*} - a_{T_H}\frac{2B^*s}{(s+B^{*2})^2}T_H^*] - d_{TB}T^* - (d_T - kd_{TH}) - d_{TB}B^* - ka_{T_H}\frac{B^{*2}}{s+B^{*2}} < 0
\end{aligned}
$$

Consequently, the matrix $J^{[2]}$ is stable according to the Gershgorin's theorem . So the first condition of (5.1) is satisfied. In addition The second condition of theorem (5.1); $det(J_{E^*}) > 0$ is also satisfied. Hence the result.

□

Conclusion and Perspectives

In this thesis work, we focused our interest on the study of the stability of certain models from biology that occur around the world.

In the first chapter we have give a reminder of the fundamental mathematical tools necessary for the analysis of the systems subject to our study.

Then, in the rest of the chapters, we considered three mathematical models, the first is a model of chronic lymphoid leukemia with B-CLL cells, where we found the necessary conditions for the existence of solutions and the conditions for their stability. Then we studied an impulsive model on the control of agroecosystems, we have studied the existence of trivial and non-trivial periodic solutions and their stability.

We have also considered at the level of the fourth chapter, a model of spread of the epidemic of coronavirus. It is a SEIAR model. We have establish the model in two cases with ordinary derivatives and fractional derivatives. We have proved the existence and the uniqueness of the equilibrium points of the system, then, we show the stability of the equilibrium point where we used the direct Lyapunov's methode, LASalle's invariance principle and the Routh − Hurwitz criterion. Then we determined the basic reproduction rate. Finally, we performed numerical simulations to illustrate the stability results.

It would be interesting for our next work For more realistic modeling:

− To establish the stability of the equilibrium point by other methods.

− To establish the case of models with delay, with diffusion or more with fractional derivatives.

− To work with systems structured in age...

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Abstract:

The purpose of this work is to contribute to the study of some mathematical models of ecology and epidemiology from biology and medicine in the case of ordinary and impulsive differential equations, by highlighting the study of the stability of their equilibrium points.

Key words: dynamical systems; stability; lyapunov's methods; impulsive differential equations; periodic solutions; compartment model; epidemics; leukemia; basic reproduction number.

Résumé:

L'objectif de ce travail est de contribuer à l'étude de quelques modèles mathématiques d'écologie et d'épidémiologie issus de la biologie et de la médecine dans le cas d'équations différentielles ordinaires et impulsives, en mettant en évidence l'étude de la stabilité de leurs points d'équilibres.

Mots clés: Systèmes dynamiques; Stabilité; Méthodes de Lyapunov; Equations différentielles Impulsives; Solutions périodiques; Modèle de compartiment; Epidémies; Leucémie; Taux de reproduction de base.

الملخص

الهدف من هذا العمل هو المساهمة في دراسة بعض النماذج الرياضية لعلم البيئة وعلم الأوبئة من علم الأحياء والطب في حالة المعادلات التفاضلية العادية والمندفعة ، من خلال دراسة استقرار نقاط توازنهم

الكلمات الافتتاحية

الأنظمة الديناميكية استقرار؛ نظرية ليابونوف؛ معادلات تفاضلية دافعة؛ سرطان الدم؛ حلول دورية؛ نموذج المقصورة؛الأوبئة؛ معدل التكاثر الأساسي.