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A continuous SIR mathematical model of the spread of infectious illnesses that takes human immunity into account

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A mathematical model of infectious disease contagion that accounts for population stratification based on immunity criteria is proposed. Our goal is to demonstrate the effectiveness of this idea in preventing different epidemics and to lessen the significant financial and human costs these diseases cause. We determined the fundamental reproduction rate, and with the help of this rate, we were able to examine the stability of the free equilibrium point and then proposed two control measures. The Pontryagin's maximum principle is used to describe the optimal controls, and an iterative approach is used to solve the optimality system. Finally, numerical simulations are carried out in MATLAB to verify the theoretical analysis.

Keywords: *dynamic system; human immunity; infectious diseases; stability; free equilibrium; optimal control.*

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1. Introduction

Immunity consists of a collection of cells and chemicals that protect the human body from pathogens. However, there are two distinct types of reactions to bacterial invasion. Innate (natural) immunity occurs to the same degree, although the infectious agent is recognized several times. While acquired (adaptive) responses result from repeated exposure to a particular pathogen. The natural innate immune system is comprised of phagocytic cells (macrophages, neutrophils, and monocytes), natural killer cells, and cells that deal with inflammatory mediators (mast cells, eosinophils, and basophils) [1]. The molecular parts of natural responses consist of acute-phase proteins, complements, and cytokines at the molecular level (the interferon for instance). Adaptive immunity is characterized by the proliferation of antigen-specific T and B cells when their receptors attach to antigen. The latter is presented to lymphocytes by specialized cells known as antigen-presenting cells, and the entire cell works in concert to respond to the antigen. The B cells responsible for eliminating external bacteria (antigen-specific antibodies) collaborated with T cells to produce antibodies and could also eradicate intracellular infections by activating macrophages and targeting infected cells. Consequently, innate and adaptive immune responses frequently collaborate to eliminate pathogens and viral diseases [2, 3].

These cells develop from pluripotent stem cells in the foetal liver and bone marrow. They are then distributed throughout the extracellular fluid. T cells must migrate to the thymus to complete their maturation, whereas B cells mature within the bone marrow. In the secondary lymphoid tissues, acquired immunity is generated (spleen, lymph nodes, and mucosa-associated lymphoid tissue). Lymphocyte activation by antigen occurs in the spleen and lymph nodes in discrete B- and T-cell compartments of lymphoid tissue [4, 5].

Two forms of immunity make up acquired immune responses: Targeting intracellular pathogens, tumour cells, and damaged cells, cellular immunity is triggered by the T-activity. Lymphocyte's Immunity is given by B-lymphocyte responses, which produce antigen-specific antibodies as distinct proteins. This category targets extracellular pathogens (bacteria, fungi, parasites). The mucosa-associated lymphoid tissues consisting of Peyer's patches, tonsils, and adenoids protect mucosal surfaces [6, 7].

In order to establish an infection, the pathogen must first overcome several surface barriers (enzymes and mucus) that are antimicrobial or inhibit attachment of the microbe. This is because the keratinized surface of the skin and the mucus-lined body cavities do not provide a suitable habitat for the majority of microorganisms. Microbes must thus penetrate the ectoderm. Consequently, if the organism breaches this initial barrier, it will confront two more layers of protection (innate and acquired immunological responses) [8, 9]. The inflammatory immune response is an example of innate immunity since it prevents the entry of invading microorganisms through the skin, respiratory system, or digestive tract. If infections are able to penetrate epithelial surfaces, they will encounter macrophages in sub-epithelial tissues, which will not only attempt to absorb them but also create cytokines to amplify the inflammatory response [10]. An adaptive acquired immune response, on the other hand, utilizes the capabilities of certain cells and their products (immunoglobulins and cytokines) to create a response to invading pathogens and displays characteristics. Active immunity is acquired since it arises from the immune system's reaction to an antigen. Passive immunity results from the transmission of immune cells or antibodies from a previously vaccinated individual. In the event of a skin abrasion, for instance, numerous bacteria are attracted to the wound. However, the cells of the immune system are already on watch. When tissue integrity is compromised, damaged cells produce cytokines that signal the beginning of the inflammatory process to other immune cells. The "message" for macrophages and neutrophils is cytokines. They rush to the damaged region by passing through the capillary walls. Beginning of the process of eliminating bacteria that have entered the wound. Neutrophils and macrophages kill them [11, 12].

Using humoral and cellular processes, adaptive antiviral immunity aims to neutralize, rid the body of the virus and its antigens, and eliminate infected cells. Antigen initially travels from the inflammatory site to the local lymphoid organ via antigen-presenting cells (APC) or the bloodstream. Antiviral immunity begins with the presentation of a complex consisting of a viral antigen fragment and HBA class II gene products to T cells in thymus-dependent regions of lymphoid organs. On the T helper side of recognition, an antigen-specific receptor and CD4 T cells engage with the Human Leukocyte Antigen (HLA class II genes) of the accessory cell. The membrane or free form of GH-1 (Growth Hormone 1) must engage with the relevant T-helper receptors for T-helper activation. TY helper cells are separated into two populations after several divisions: TK2 cells drive the establishment of humoral immune response, while TY cells are essential for the activation of cytotoxic T lymphocytes (CTL). The humoral reaction has two phases: inductive and productive. B-lymphocytes can serve as particular APCs (Armored Personnel Carrier) that process and deliver antigen to T-helper cells in the presence of MHC (Major Histocompatibility Complex) class II molecules during the inductive phase. After recognizing an antigen, T cells begin to create cytokines that encourage the transformation of B lymphocytes into antibody-producing cells. During the productive phase of the humoral immune response, effector plasma cells are produced, which, in response to a particular stimulus from an antigen and a non-specific stimulus from T cells, begin to generate antibodies with a single specificity. This type of cell has a lifespan of 4 to 7 days before undergoing apoptosis [1, 13, 14].

Antibodies generated during viral infections possess a broad antiviral action range. It is a protective role related mostly to their neutralizing action against extracellularly situated viruses. Due to the cytopathogenic features of certain viruses (such as arbo-, entero-, and rhinoviruses), antibodies can destroy the virus following the death of target cells. Virus-neutralizing antibodies, though, only act directly on the virus when it kills one cell and transfers to another. In other instances (adenovirus infection, herpes), antibodies primarily serve as witnesses to the immune response to the virus and do not inhibit its long-term survival. Antibodies, by agglutinating viral particles, produce conformational changes in the surface proteins of the virion, preventing their interaction with cell receptors and blocking the entrance of virions into the cell (deproteinization, pinocytosis). Opsonization of the resultant complex (viral particles with antibodies) with complement and anti-idiotypic antibodies that develop later in the infectious phase and bind the immunoglobulin epitopes of the complex enhances phagocytosis and pathogen destruction [15].

When viruses (such as herpes viruses and cytomegaly) move from cell to cell via cytoplasmic bridges without touching circulating antibodies, cellular processes connected with the activation of particular

CTLs, T-effectors, and macrophages are principally responsible for the establishment of immunity. During the first phase of the immune response, the antigen collected by the APC is transformed into an immunogenic form and released to the cell surface. The next step involves presenting the antigen complex with the MHC Class I molecule to killer T-effectors in conjunction with a co-receptor molecule. The duration of antiviral immunity varies considerably. Infections such as chickenpox, measles, mumps, and rubella are thus characterized by a relatively stable immune system and few recurrences. In other instances, viruses are changed to resist the neutralizing impact of antibodies and other particular immune defense mechanisms, resulting in a less sustained immunological response. For instance, there is a continual drift of surface antigenic viral proteins and a shift in circulating strains in influenza. Viruses that employ the tactic of inhibiting molecules by interfering with T-cell recognition cause viral persistence [15, 16].

Immunodeficiency illnesses are characterized by a decline in the quantitative indicators and functional activity of the immune system's major components, resulting in a breach of the body's defense against harmful microorganisms and manifested by an increase in infectious morbidity. Using the Human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) as an example. HIV damages immune system cells that would ordinarily attack pathogens. As the number of immune system cells declines, the susceptibility of the human body to infection continuously increases [17].

The virus is attached to cells via the CD4 molecule. T4 cells, together with monocytes and macrophages, are hence targets of HIV infection. Although this infection is cytopathic to T cells, monocytes continue to survive and provide the virus with food and shelter. Within a healthy immune system, the number of antigen-specific T4 cells increases. Vaccination increases not just T4 cells but also the cell population that the virus assaults in cases of HIV infection. In addition, the activation of T4 cells results in viral copy. Consequently, immunization may generate an increase rather than a decrease in the number of infected cells alongside virus-specific serum antibodies. The infection may lead to the destruction of T4 cells by destroying cell membranes, introducing a large quantity of nonintegrated viral DNA, or triggering terminal differentiation of viral T4 cells, hence shortening their lifespan [18]. The primary way of treatment is so-called highly active antiretroviral therapy, which involves the concurrent use of three or four different medications. Depending on the virus's mutagenicity, a more specific dose is calculated. For maximal long-term cupping, a different medication combination is advised. Indicators of a high-quality therapy include a decrease in viral load and an increase in CD4+ cells in the blood, which signals immunological function [19].

Every second, the body undergoes cellular mutations; hence, mechanisms exist to eliminate them. As a result of mutations, however, certain cancer cells gain the ability to evade immune system responses and "mask" themselves during inspections. This masking technique activates the immune brake. Cancer cells evade the immune system's reaction and continue to proliferate. The human body considers them as "its own" up to a certain extent [20]. The immune system will begin to attack the illness if the activity of this brake is slowed down. This notion is the foundation of immunotherapy, which assists the immune system in overcoming a malignant tumour. Immunotherapy forces the body's immune system to attack abnormal cells with greater vigour by unblocking it. The core of cellular immunotherapy is that the patient takes their own immune cells, activates them against the tumour's components, multiplies a new activated "clone" in the laboratory, and then returns it to their body. This helps to diminish or eradicate the tumour. The purpose of this therapy and other immune system modulators or drugs, which often include interferon, interleukins, and growth factors, is to enhance the functioning of the immune system in general [21]. Some control systems can be found in the following references [22–24].

The remaining parts of the paper are organized as follows. In section 2, we provide a continuous mathematical model SIR that takes human immunity into consideration. Some preliminary results are given in section 3. In section 4 we study the local stability of the free equilibrium point. Furthermore, we provide a numerical simulation without control to our model in section 5. The optimal control problem of the considered model is studied in section 6. Results and discussion are provided to ensure the effectiveness of the control strategies in section 7. Section 8 is given to conclude our paper.

2. Presentation of the model

Throughout history, the globe has been plagued by a number of contagious epidemics that have claimed many people. Despite advances in science and medicine, these disease outbreaks continue to represent a significant danger to human communities and the world's economies, particularly for those with weak immune systems. We suggest a basic SIR model in which the first two compartments are split into two additional compartments.

We obtain the following model

$$\begin{cases} \dot{S}(t) = \Lambda_1 - (\mu + \theta_1)\, S(t) - (\alpha_1\, J(t) + \alpha_2\, K(t))\, S(t) + \theta_2 T(t), \\ \dot{T}(t) = \Lambda_2 + -\mu T(t) - (\beta_1\, J(t) + \beta_2\, K(t))\, T(t) + \theta_1\, S(t) - \theta_2 T(t), \\ \dot{J}(t) = (-\mu - \eta_1 - \sigma_1)\, J(t) + (\alpha_1\, J(t) + \alpha_2\, K(t))\, S(t), \\ \dot{K}(t) = (-\mu - \eta_2 - \sigma_2)\, K(t) + (\beta_1\, J(t) + \beta_2\, K(t))\, T(t), \\ \dot{R}(t) = -\mu R(t) + \sigma_1 J(t) + \sigma_2\, K(t), \end{cases} \tag{1}$$

where $S(0) = S_0 > 0$, $T(0)T_0 > 0$, $J(0) = J_0 > 0$, $K(0) = K_0 > 0$ and $R(0) = R_0 > 0$.

Table 1. Compartments meaning.

Compartment	Meaning
S	Susceptible individuals without immunity
T	Susceptible individuals with immunity
J	Infected individuals without immunity
K	Infected individuals with immunity
R	Recovered individuals

Table 2. Parameters meaning.

Compartment	Meaning
Λ_1	The incidence of susceptible individuals without immunity
Λ_2	The incidence of susceptible individuals with immunity
μ	The natural death rate
θ_1	The rate of susceptible individuals without immunity retrieving their natural imminence
θ_2	The rate of susceptible individuals with immunity losing their natural imminence
α_1	The rate of persons without immunity who became infected by coming into contact with an unimmunized infected person
α_2	The rate of persons without immunity who became infected by coming into contact with an immune infected person
β_1	The rate of immunized people who became infected by coming into contact with an infected, non-immune person
β_2	The rate of immunized people who became infected by coming into contact with an infected and immunized person
σ_1	The rate of individuals without immunity who recovered from the disease
σ_2	The rate of individuals with immunity who recovered from the disease
η_1	The mortality rate of infected without immunity due to the virus
η_2	The mortality rate of infected immune due to the virus

3. Results

In this section we will give some preliminary results.

Theorem 1. *If $S(0) \geqslant 0$, $T(0) \geqslant 0$, $J(0) \geqslant 0$, $K(0) \geqslant 0$ and $R(0) \geqslant 0$, the solutions $S(t)$, $T(t)$, $J(t)$, $K(t)$ and $R(t)$ of the proposed system (1) are positive for all $t \geqslant 0$.*

Proof. For $t > 0$, we have the following results:

$$\left.\frac{dS}{dt}\right|_{S=0} = \Lambda_1 + \theta_2 T \geqslant 0, \qquad \left.\frac{dT}{dt}\right|_{T=0} = \Lambda_2 + \theta_1 S \geqslant 0, \qquad \left.\frac{dJ}{dt}\right|_{J=0} = \alpha_1 K S \geqslant 0,$$
$$\left.\frac{dK}{dt}\right|_{K=0} = \beta_2 J T \geqslant 0, \qquad \left.\frac{dR}{dt}\right|_{R=0} = \sigma_1 J + \sigma_2 K \geqslant 0.$$

Consequently, the positivity of all solutions starting in $\mathbb{R}^6_+$ is guaranteed for all $t > 0$. This completes the proof. ∎

Theorem 2. *For any given $(S(0), T(0), J(0), K(0), R(0))$, there exists a unique solution of the proposed system* (1).

Proof. Let

$$X = \begin{pmatrix} S(t) \\ T(t) \\ J(t) \\ K(t) \\ R(t) \end{pmatrix} \quad \text{and} \quad \psi(X) = \begin{pmatrix} \frac{dS(t)}{dt} \\ \frac{dT(t)}{dt} \\ \frac{dJ(t)}{dt} \\ \frac{dK(t)}{dt} \\ \frac{dR(t)}{dt} \end{pmatrix}$$

so, that the system (1) becomes the following:

$$\psi(X) = AX + B(X), \tag{2}$$

where

$$A = \begin{pmatrix} -(\mu+\theta_1) & \theta_2 & -0 & 0 & 0 \\ \theta_1 & -(\mu+\theta_2) & 0 & 0 & 0 \\ 0 & 0 & -(\mu+\sigma_1+\eta_1) & 0 & 0 \\ 0 & 0 & 0 & -(\mu+\sigma_1+\eta_1) & 0 \\ 0 & 0 & \sigma_1 & \sigma_2 & -\mu \end{pmatrix}$$

and

$$B(X) = \begin{pmatrix} \Lambda_1 - (\alpha_1 J(t) + \alpha_2 K(t))S(t) \\ \Lambda_2 - (\beta_1 J(t) + \beta_2 K(t))T(t) \\ (\alpha_1 J(t) + \alpha_2 K(t))S(t) \\ (\beta_1 J(t) + \beta_2 K(t))T(t) \\ 0 \end{pmatrix}$$

on the other hand, we have

$$B(X_1) - B(X_2) = \begin{pmatrix} -\alpha_1 J_1 S_1 + \alpha_1 J_2 S_2 - \alpha_2 K_1 S_1 + \alpha_2 K_2 S_2 \\ -\beta_1 J_1 T_1 + \beta_1 J_2 T_2 - \beta_2 K_1 T_1 + \beta_2 K_2 T_2 \\ \alpha_1 J_1 S_1 - \alpha_1 J_2 S_2 + \alpha_2 K_1 S_1 - \alpha_2 K_2 S_2 \\ \beta_1 J_1 T_1 - \beta_1 J_2 T_2 + \beta_2 K_1 T_1 - \beta_2 K_2 T_2 \\ 0 \end{pmatrix}$$

then

$$\begin{aligned}
&\|B(X_1) - B(X_2)\| \\
&\quad = 2\big|\alpha_1 J_1 S_1 - \alpha_1 J_2 S_2 + \alpha_2 K_1 S_1 - \alpha_2 K_2 S_2\big| + 2\big|\beta_1 J_1 T_1 - \beta_1 J_2 T_2 + \beta_2 K_1 T_1 - \beta_2 K_2 T_2\big| \\
&\quad = 2\big|\alpha_1 J_1 S_1 - \alpha_1 J_1 S_2 + \alpha_1 J_1 S_2 - \alpha_1 J_2 S_2 + \alpha_2 K_1 S_1 - \alpha_2 K_1 S_2 + \alpha_2 K_1 S_2 - \alpha_2 K_2 S_2\big| \\
&\qquad + 2\big|\beta_1 J_1 T_1 - \beta_1 J_1 T_2 + \beta_1 J_1 T_2 - \beta_1 J_2 T_2 + \beta_2 K_1 T_1 - \beta_2 K_1 T_2 + \beta_2 K_1 T_2 - \beta_2 K_2 T_2\big| \\
&\quad = 2\big|\alpha_1 J_1 (S_1 - S_2) + \alpha_1 S_2 (J_1 - J_2) + \alpha_2 K_1 (S_1 - S_2) + \alpha_2 S_2 (K_1 - K_2)\big| \\
&\qquad + 2\big|\beta_1 J_1 (T_1 - T_2) + \beta_1 T_2 (J_1 - J_2) + \beta_2 K_1 (T_1 - T_2) + \beta_2 T_2 (K_1 - K_2)\big| \\
&\quad \leqslant 2\tfrac{\Lambda}{\mu} \left(\alpha_1 |S_1 - S_2| + \alpha_1 |J_1 - J_2| + \alpha_2 |S_1 - S_2| + \alpha_2 |K_1 - K_2|\right) \\
&\qquad + 2\tfrac{\Lambda}{\mu} \left(\beta_1 |T_1 - T_2| + \beta_1 |J_1 - J_2| + \beta_2 |T_1 - T_2| + \beta_2 |K_1 - K_2|\right) \\
&\quad \leqslant M \|X_1 - X_2\|,
\end{aligned}$$

where

$$M = \frac{\Lambda}{\mu} \max(\alpha_1, \alpha_2, \beta_1, \beta_2)$$

and also

$$\|\psi(X_1) - \psi(X_2)\| \leqslant C\|X_1 - X_2\|,$$

where $C = \max(M, \|A\|) < \infty$. Thus, it follows that the function ψ is a Lipschitz continuous function, so, the system admit a unique solution [25]. ■

Theorem 3. *The set* $\Gamma = \left\{(S,T,J,K,R) \in \mathbb{R}^5_+ / 0 \leqslant N = S+T+J+K+R \leqslant \frac{\Lambda}{\mu}\right\}$ *positively invariant under the system* (1) *with the initial conditions* $S(0) \geqslant 0, T(0) \geqslant 0, J(0) \geqslant 0, K(0) \geqslant 0$ *and* $R(0) \geqslant 0$.

Proof. We have

$$\begin{aligned}\frac{dN}{dt} &= \frac{dS}{dt} + \frac{dT}{dt} + \frac{dJ}{dt} + \frac{dK}{dt} + \frac{dR}{dt} \\ &= -\mu N + \Lambda - \eta_1 J - \eta_2 K \\ &\leqslant -\mu N + \Lambda,\end{aligned}$$

then

$$N(t) \leqslant \frac{\Lambda}{\mu} + N(0)e^{-\mu t},$$

where $\Lambda = \Lambda_1 + \Lambda_2$. Since

$$\lim_{t \to +\infty} N(0)e^{-\mu t} = 0,$$

$$0 \leqslant N = S + T + J + K + R \leqslant \frac{\Lambda}{\mu}.$$

The last inequality completes the proof. ■

4. The local stability of the free equilibrium point

Theorem 4. *The free equilibrium point of the system* (1) *is given by*

$$E_0\left(\frac{\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2}{\mu(\mu + \theta_1 + \theta_2)}, \frac{\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1}{\mu(\mu + \theta_1 + \theta_2)}, 0, 0, 0\right).$$

Proof. To find the disease-free equilibrium point, we set the right-hand side of model (2) to zero, evaluating it at $J = K = 0$ and solving for uninfected and non-carrying state variables. ■

The basic reproduction number $\mathcal{R}_0$ is defined in this work as the number of secondary infections produced by an infected individual in a completely susceptible population.

Theorem 5. *The basic reproduction rate associated with the system* (1) *is given by*

$$\mathcal{R}_0 = \max_{i=1,2}(\mathcal{R}_i) \tag{3}$$

with

$$\mathcal{R}_1 = \frac{(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)\alpha_1}{\mu(\mu + \theta_1 + \theta_2)(\mu + \eta_1 + \sigma_1)}$$

and

$$\mathcal{R}_2 = \frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_2}{\mu(\mu + \theta_1 + \theta_2)(\mu + \eta_2 + \sigma_2)}.$$

Proof. To obtain the basic reproduction number, we used the new generation matrix method formulated by Bani–Yaghoub et al. [26]. Through the system of equations in model (1), then by the next generation matrix principle, we obtained:

$$f = \begin{pmatrix} -\alpha_1 JS - \alpha_2 KS \\ -\beta_1 JT - \beta_2 KT \\ \alpha_1 JS + \alpha_2 KS \\ \beta_1\, JT + \beta_2 KT \end{pmatrix} \quad \text{and} \quad v = \begin{pmatrix} -\Lambda_1 + (\mu+\theta_1)S - \theta_2 T \\ -\theta_1 S + \mu T + \theta_2 T - \Lambda_2 \\ -(-\mu - \eta_1 - \sigma_1)J \\ -(-\mu - \eta_2 - \sigma_2)K \end{pmatrix},$$

then

$$F = \begin{pmatrix} 0 & 0 & -\frac{(-\mu\Lambda_1 - \Lambda_1\theta_2 - \Lambda_2\theta_2)\alpha_1}{-\mu^2 - \mu\theta_1 - \mu\theta_2} & -\frac{(-\mu\Lambda_1 - \Lambda_1\theta_2 - \Lambda_2\theta_2)\alpha_2}{-\mu^2 - \mu\theta_1 - \mu\theta_2} \\ 0 & 0 & -\frac{(-\mu\Lambda_2 - \Lambda_1\theta_1 - \Lambda_2\theta_1)\beta_1}{-\mu^2 - \mu\theta_1 - \mu\theta_2} & -\frac{(-\mu\Lambda_2 - \Lambda_1\theta_1 - \Lambda_2\theta_1)\beta_2}{-\mu^2 - \mu\theta_1 - \mu\theta_2} \\ 0 & 0 & \frac{(-\mu\Lambda_1 - \Lambda_1\theta_2 - \Lambda_2\theta_2)\alpha_1}{-\mu^2 - \mu\theta_1 - \mu\theta_2} & \frac{(-\mu\Lambda_1 - \Lambda_1\theta_2 - \Lambda_2\theta_2)\alpha_2}{-\mu^2 - \mu\theta_1 - \mu\theta_2} \\ 0 & 0 & \frac{(-\mu\Lambda_2 - \Lambda_1\theta_1 - \Lambda_2\theta_1)\beta_1}{-\mu^2 - \mu\theta_1 - \mu\theta_2} & \frac{(-\mu\Lambda_2 - \Lambda_1\theta_1 - \Lambda_2\theta_1)\beta_2}{-\mu^2 - \mu\theta_1 - \mu\theta_2} \end{pmatrix}$$

and

$$V = \begin{pmatrix} \mu + \theta_1 & -\theta_2 & 0 & 0 \\ -\theta_1 & \mu + \theta_2 & 0 & 0 \\ 0 & 0 & \mu + \eta_1 + \sigma_1 & 0 \\ 0 & 0 & 0 & \mu + \eta_2 + \sigma_2 \end{pmatrix},$$

therefore

$$F \cdot V^{-1} = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)\alpha_1}{(\mu^2 + \mu\theta_1 + \mu\theta_2)(\mu + \eta_1 + r_1)} & 0 \\ 0 & 0 & 0 & \frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_2}{(\mu^2 + \mu\theta_1 + \mu\theta_2)(\mu + \eta_2 + \sigma_2)} \end{pmatrix}$$

since $\mathcal{R}_0 = \rho(F \cdot V^{-1})$, we obtain that $\mathcal{R}_0$ is given by the relation (3). Which completes the demonstration. ∎

Theorem 6. *If $\mathcal{R}_0 < 1$ then the free equilibrium point E_0 is stable and otherwise it is unstable.*

Proof. The Jacobian matrix associated with the system (1) at the free equilibrium point E_0 is written as

$$J(E_0) = \begin{bmatrix} -\mu - \theta_1 & \theta_2 & -\frac{\alpha_1(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)}{\mu(\mu + \theta_1 + \theta_2)} & -\frac{\alpha_2(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)}{\mu(\mu + \theta_1 + \theta_2)} & 0 \\ \theta_1 & -\theta_2 - \mu & -\frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_1}{\mu(\mu + \theta_1 + \theta_2)} & -\frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_2}{\mu(\mu + \theta_1 + \theta_2)} & 0 \\ 0 & 0 & \frac{\alpha_1(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)}{\mu(\mu + \theta_1 + \theta_2)} - \mu - \sigma_1 - \eta_1 & \frac{\alpha_2(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)}{\mu(\mu + \theta_1 + \theta_2)} & 0 \\ 0 & 0 & \frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_1}{\mu(\mu + \theta_1 + \theta_2)} & \frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_2}{\mu(\mu + \theta_1 + \theta_2)} - \mu - \sigma_2 - \eta_2 & 0 \\ 0 & 0 & \sigma_1 & \sigma_2 & -\mu \end{bmatrix}.$$

Since, $-\mu$ is an eigenvalue of multiplicity 2 of the matrix $J(E_0)$ and that this eigenvalue is strictly negative. We are interested in the sign of the eigenvalues of the sub-matrix $\tilde{J}(E_0)$ given by

$$\tilde{J}(E_0) = \begin{pmatrix} \frac{\alpha_1(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)}{\mu(\mu + \theta_1 + \theta_2)} - \mu - \sigma_1 - \eta_1 & \frac{\alpha_2(\mu\Lambda_1 + \Lambda_1\theta_2 + \Lambda_2\theta_2)}{\mu(\mu + \theta_1 + \theta_2)} \\ \frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_1}{\mu(\mu + \theta_1 + \theta_2)} & \frac{(\mu\Lambda_2 + \Lambda_1\theta_1 + \Lambda_2\theta_1)\beta_2}{\mu(\mu + \theta_1 + \theta_2)} - \mu - \sigma_2 - \eta_2 \end{pmatrix},$$

the characteristic polynomial of the matrix $\tilde{J}(E_0)$ is given by

$$P(\lambda) = \lambda^2 - [(\mu + \eta_1 + \sigma_1)(\mathcal{R}_1 - 1) + (\mu + \eta_2 + \sigma_2)(\mathcal{R}_2 - 1)]\,\lambda + (\mu + \eta_1 + \sigma_1)(\mathcal{R}_1 - 1)(\mu + \eta_2 + \sigma_2)(\mathcal{R}_2 - 1),$$

then

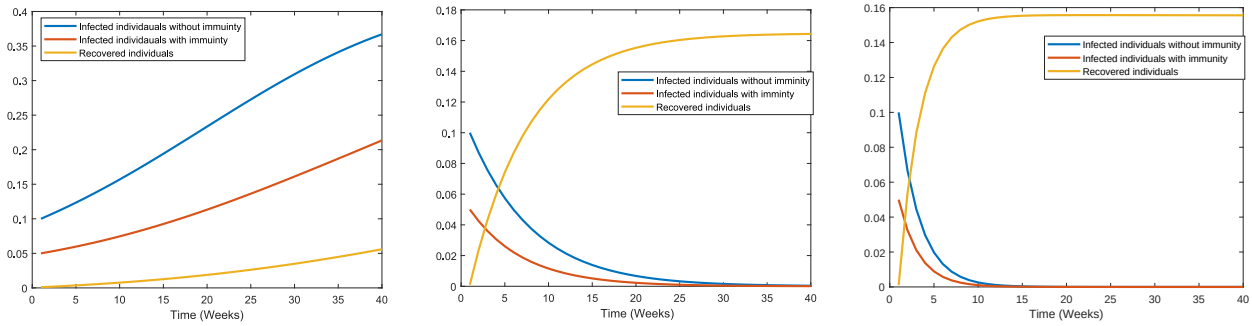
$$P(\lambda) = 0 \Longleftrightarrow \lambda = (\mathcal{R}_1 - 1)(\mu + \eta_1 + \sigma_1) \quad \text{or} \quad \lambda = (\mathcal{R}_2 - 1)(\mu + \eta_2 + \sigma_2).$$

If $\mathcal{R}_0 < 1$, we have $\mathcal{R}_1 < 1$ and $\mathcal{R}_2 < 1$.

Thus two remaining eigenvalues of the matrix $J(E_0)$ are strictly negative, hence we complete the proof of the theorem. ∎

5. Numerical Simulation without controls

In this section, we restrict ourselves to simulating how many people were infected and recovered over the course of 40 weeks. According to Fig. 1*c* (the case where $\mathcal{R}_0 = 0.6906$), the number of infected with immunity and without immunity tends to 0 in 20 weeks, and in the case where $\mathcal{R}_0 = 0.0298$, we see that the number of infected with immunity and without immunity tends to 0 in almost 10 weeks, but in the case where $\mathcal{R}_0 > 1$, we see that the infected tend to bigger values during these 40 weeks (see Fig. 1*a*). The results of the simulation provided a strong confirmation of Theorem 6's theoretical findings.



a $(\mathcal{R}_0 > 1)$ ***b*** $(\mathcal{R}_0 = 0.6906)$ ***c*** $(\mathcal{R}_0 = 0.0298)$

Fig. 1. The evolution of the three compartments: infected without immunity, infected with immunity and recovered persons in the different cases.

6. Optimal control

6.1. Presentation of the controls

We recommend two control techniques to help prevent the risks associated with epidemics that negatively impact society, keeping in mind that those with normal immunity are better protected against epidemic complications than those with low immunity.

The first tactic (control u) entails encouraging individuals with low immune systems to engage in activities that boost immunity, such as participating in sports, maintaining a nutritious diet, and quitting smoking.

The second tactic (control v) is giving patients with weak immune systems additional medical attention and setting up recuperation areas for those who have serious problems. As a result, we obtain the following controlled system,

$$\begin{cases} \dot{S}(t) = \Lambda_1 - (\mu + \theta_1 - u(t))S(t) - (\alpha_1 J(t) + \alpha_2 K(t))S(t) + \theta_2 T(t), \\ \dot{T}(t) = \Lambda_2 - \mu T(t) - (\beta_1 J(t) + \beta_2 K(t))T(t) + (\theta_1 + u(t))S(t) - \theta_2 T(t), \\ \dot{J}(t) = (-\mu - \eta_1 - \sigma_1 - v(t))J(t) + (\alpha_1 J(t) + \alpha_2 K(t))S(t), \\ \dot{K}(t) = (-\mu - \eta_2 - \sigma_2)K(t) + (\beta_1 J(t) + \beta_2 K(t))T(t), \\ \dot{R}(t) = -\mu R(t) + \sigma_1 J(t) + \sigma_2 K(t) + v(t)J(t). \end{cases} \tag{4}$$

6.2. Objective functional

The objective function J is described as follows

$$J(u, v) = J(t_f) - R(t_f) + \int_0^{t_f} \left(J(t) - R(t) + \frac{1}{2} A u(t)^2 + \frac{1}{2} B v(t)^2 \right) dt, \tag{5}$$

where the parameters $A > 0$ and $B > 0$ are based on the benefits and costs of treatment. Our goal is to minimize the objective function defined in equation (5) by minimizing the number of infected who

have low immunity and also the number of deaths from disease with optimal cost. In other words, we are looking for an optimal control pair (u^*, v^*) such that

$$J(u^*, v^*) = \min\{J(u, v)/(u, v) \in \mathcal{U}\} \tag{6}$$

with $\mathcal{U}$ is the set of controls defined by

$$\mathcal{U} = \{(u, v)\colon u, v \text{ measurable}, 0 < u_{\min} \leqslant u(t) \leqslant u_{\max} < 1, 0 < v_{\min} \leqslant v(t) \leqslant v_{\max} < 1, \forall t \in [0, t_f]\}. \tag{7}$$

6.3. Sufficient conditions

The existence of optimal control can be derived using a result of Fleming and Rishel [27, 28].

Theorem 7. *Consider the control problem of system* (4). *There exists an optimal control* $(u^*, v^*) \in \mathcal{U}$ *such that*

$$J(u^*, v^*) = \min\{J(u, v)/(u, v) \in \mathcal{U}\}.$$

6.4. Necessary conditions

Pontryagin's maximum principle [28–30] transforms (4)–(6) and (7) into a problem of minimizing a Hamiltonian, H, point-wise with respect to u and v:

$$H(t) = J(t) - R(t) + \frac{1}{2}Au(t)^2 + \frac{1}{2}Bv(t)^2 + \sum_{i=1}^{5} \zeta_i(t) f_i(S, T, J, K, R),$$

where f_i is the right side of the difference equation of the state variable (4).

In the following theorem we present the necessary conditions for the existence of an optimal control.

Theorem 8. *Given optimal controls* u^*, v^* *and solutions* S^*, T^*, J^* *and* R^* *of corresponding state system* (4), *there exists* ζ_i, $i = 1, \ldots, 5$ *the adjoint variables that satisfy the following equations*

$$\begin{aligned}
\frac{d\zeta_1}{dt} &= -[\zeta_1(-\alpha_1 J - \alpha_2 K - \mu - u - \theta_1) + \zeta_2(\theta_1 + u) + \zeta_3(\alpha_1 J + \alpha_2 K)],\\
\frac{d\zeta_2}{dt} &= -[\zeta_1\theta_2 + \zeta_2(-\beta_1 J - \beta_2 K - \mu - \theta_2) + \zeta_4(\beta_1 J + \beta_2 K)],\\
\frac{d\zeta_3}{dt} &= -[1 - \zeta_1\alpha_1 S - \beta_1\zeta_2 T + \zeta_3(\alpha_1 S - \mu - \sigma_1 - v - \eta_1) + \beta_1\zeta_4 T + \zeta_5(\sigma_1 + v)],\\
\frac{d\zeta_4}{dt} &= -[-\zeta_1\alpha_2 S - \zeta_2\beta_2 T + \zeta_3\alpha_2 S + \zeta_4(\beta_2 T - \mu - \sigma_2 - \eta_2) + r_2\zeta_5],\\
\frac{d\zeta_5}{dt} &= -[-\mu\zeta_5 - 1]
\end{aligned}$$

with the conditions of transversality at time N

$$\zeta_1(t_f) = 0, \quad \zeta_2(t_f) = 0, \quad \zeta_3(t_f) = 1, \quad \zeta_4(t_f) = 0, \quad \zeta_5(t_f) = -1.$$

Moreover, we obtain the optimal control (u^*, v^*) *as*

$$u(t) = \min\left\{\max\left\{u_{\min}, \tfrac{S(t)(\zeta_1(t) - \zeta_2(t))}{A}\right\}, u_{\max}\right\}, \tag{8}$$

$$v(t) = \min\left\{\max\left\{v_{\min}, \tfrac{J(t)(\zeta_3(t) - \zeta_5(t))}{B}\right\}, v_{\max}\right\}. \tag{9}$$

Proof. For $t \in [0, t_f]$, both adjoint equations and transversality conditions can be obtained by using the Pontryagin maximum principle [29, 31] such that

$$\begin{aligned}
&\frac{d\zeta_1}{dt} = -\frac{\partial\mathcal{H}}{\partial S}, && \frac{d\zeta_2}{dt} = -\frac{\partial\mathcal{H}}{\partial T}, && \frac{d\zeta_3}{dt} = -\frac{\partial\mathcal{H}}{\partial J},\\
&\frac{d\zeta_4}{dt} = -\frac{\partial\mathcal{H}}{\partial K}, && \frac{d\zeta_5}{dt} = -\frac{\partial\mathcal{H}}{\partial M}, && \frac{d\zeta_6}{dt} = -\frac{\partial\mathcal{H}}{\partial R}.
\end{aligned}$$

In addition, the optimal controls (u^*, v^*) can be determined from the optimality conditions

$$\frac{\partial \mathcal{H}}{\partial u} = Au - S\zeta_1 + \zeta_2 S = 0, \quad \frac{\partial \mathcal{H}}{\partial v} = Bv - \zeta_3 J + \zeta_5 J = 0.$$

Thus, we obtain

$$u^*(t) = \frac{S(\zeta_1 - \zeta_2)}{A}, \quad v^*(t) = \frac{J(\zeta_3 - \zeta_5)}{B}.$$

By the bounds in $\mathcal{U}$ of the controls, it is convenient to obtain u^* and v^* in the form of (8) and (9). ■

7. Numerical Simulation and Discussion

We present in this section numerical simulations for the optimization problem given above. Writing the program in MATLAB, we simulate the work using different data. The optimization systems are solved using a discrete iterative process that converges after an appropriate test similar to FBSM. First, the state system is solved with the initial assumption forward in time, and then the adjoint system is solved backward in time due to transversality conditions. Then, we update our optimal control values with the state and co-state resources that were derived in the previous steps. Finally, we run the previous steps until the standard tolerance is reached.

7.1. Protocol 1: Spreading knowledge about the value of exercise and a healthy diet for those with weakened immune systems

We only make use of the optimal control u.

Through television and online advertisements, as well as through awareness campaigns in hospitals and schools, we conduct awareness programs on the value of exercise and a healthy diet to boost people's immunity.

Figure 2 illustrates how well this plan works at reducing the number of infected people with low immunity, but Figure 3 demonstrates how poorly it performs in raising the number of patients who recover from their illnesses.

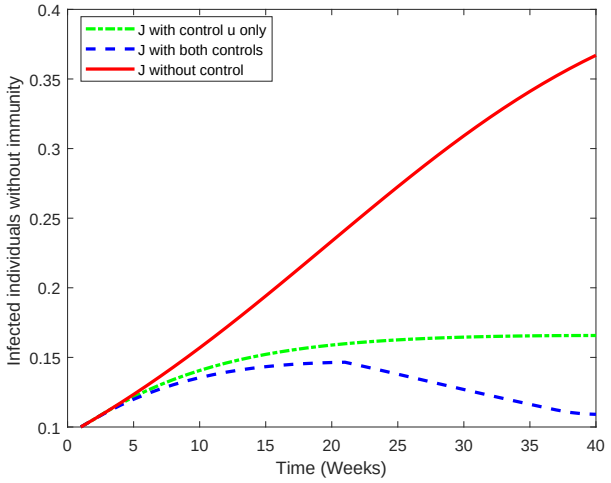


Fig. 2. The number of infected individuals without immunity using only the control u.

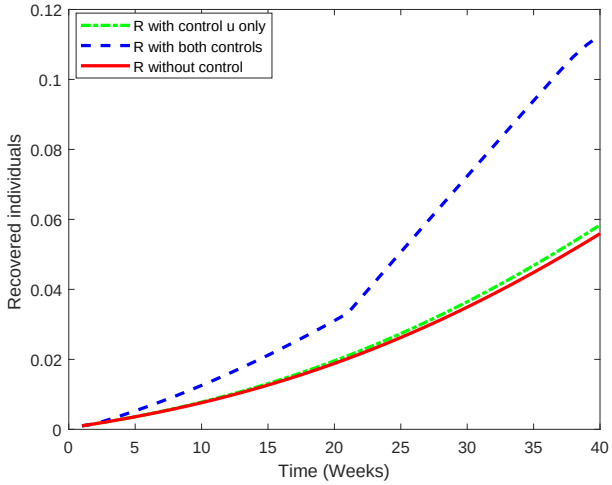


Fig. 3. The number of people who were recovered using only the control u.

7.2. Protocol 2: Healing infected people with inadequate immunity

We use only optimum control v.

Due to the fact that immune-compromised individuals are thought to be the most susceptible to the negative effects of any viral disease, we are implementing a strategy based on the medical care of this group and increasing the number of medical beds designated for them. Figures 5 and 4 show

that this strategy increases the number of sufficiently recovered and slightly decreases the number of infected patient.

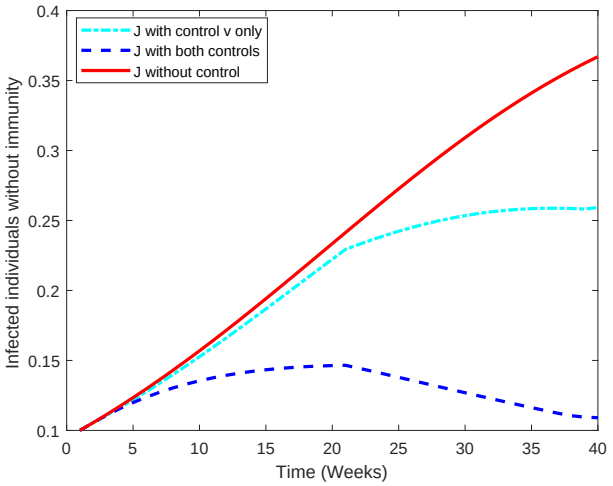


Fig. 4. The number of infected individuals without immunity using only the control v.

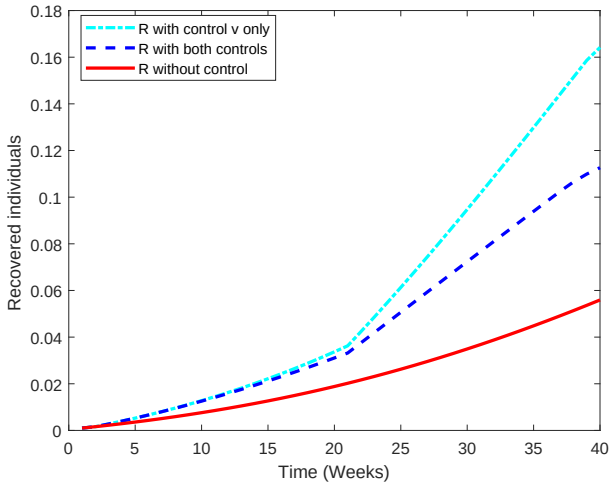


Fig. 5. The number of people who were recovered using only the control v.

7.3. Protocol 3: The combination of the above two strategies

In order to enhance the statistical performance of both proposed strategies, the two optimal commands $u(t)$ and $v(t)$ are applied simultaneously in this new strategy.

Figures 6, 7 show that after employing both strategies, we achieve the desired results, with a reduction in the number of infected individuals with low immunity and an increase in the number of individuals who are recovering from the disease. This demonstrates the efficacy of this method of population division based on immunity and control strategy.

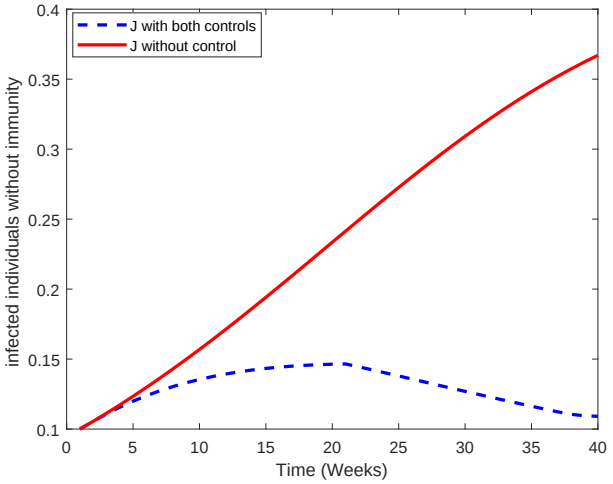


Fig. 6. The number of infected individuals without immunity.

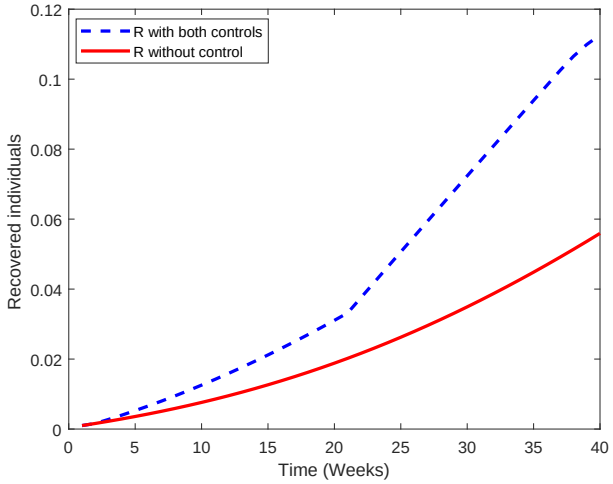


Fig. 7. The number of recovered individuals.

8. Conclusion

We proposed a mathematical SIR model that takes into account the division of the compartment of susceptible and infected people into two parts with immunity and without immunity because people with low immunity are the groups most affected by various epidemics and infectious diseases. We suggested two prevention measures: the first is an education campaign on the value of exercise and

a healthy diet for boosting immunity; the second is treatment and medical care for those with low immunity. With the aid of the control theory's research results, we were able to characterize the optimal controls. The proposed control strategies' efficacy and the population's division based on the immunity criterion were shown through numerical simulation of the results. The division based on immunity criteria will open a new approach for combating infectious diseases and will improve the outcomes. We will work on this strategy to combat monkey pox.

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Неперервна математична модель SIR поширення інфекційних хвороб з урахуванням імунітету людини

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У цій статті пропонується математична модель зараження інфекційними захворюваннями, яка враховує стратифікацію населення на основі критеріїв імунітету. Метою є продемонструвати ефективність цієї ідеї в запобіганні різним епідеміям і зменшити значні фінансові та людські витрати, які спричиняють ці захворювання. Визначено фундаментальну швидкість відтворення і за допомогою цієї швидкості перевірено стійкість вільної точки рівноваги, а потім запропоновано дві міри керування. Для опису оптимальних керувань використано принцип максимуму Понтрягіна, а для розв'язування системи керування — ітераційний підхід. Накінець, чисельне моделювання виконується в MATLAB для перевірки теоретичного аналізу.

Ключові слова: *динамічна система; імунітет людини; інфекційні хвороби; стійкість; вільна рівновага; оптимальне керування.*