

Mathematical Investigation of Host–Pathogen Interaction Dynamics with Immune Response Feedback

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ABSTRACT

The study presents a mathematical model of the dynamics of host–pathogen interaction that incorporates immune response feedback mechanisms. To gain insights into the evolution and persistence of pathogens within host systems and the innate and adaptive immune responses that regulate them. It uses the model to include non-linear differential equations that describe the time evolution of susceptible host cells, infected cells, pathogen load and immune effector cells. This study differs from classical models, that assume static immune effects and focuses on feedback-driven immune activation and suppression, reflecting more realistic biological behaviour. The model for biological processes such as infection rate, pathogen replication, immune cell recruitment, and pathogen clearance. pathogen concentration is modelled dynamically, and, as such, a feedback loop is included: the body's immune system can be activated at a certain threshold and can become exhausted when pathogen concentration is high. Stability analysis is used to determine the equilibrium points for the disease-free and endemic states. Local stability can be determined by eigenvalue analysis of the Jacobian matrix, which indicates parameter ranges in which infection persists or is cleared. The system behaviour is explored through numerical simulations with varying levels of virulence and immune response strengths. The results show that the system is stable and infection is eradicated when the immune feedback is strong. Still, oscillating solutions or an infection steady state can occur with weaker or lagged immune feedback. Sensitivity analysis also reveals that infection rate and immune activation threshold are key parameters that affect disease outcome. The study offers theoretical background for understanding the complex interaction among host, pathogen, and immune system, and provides insights into the mechanisms of disease progression. It also points out the role of immune feedback regulation in the control of infections and the prevention of chronic disease conditions. The results can apply to infectious disease modelling, optimization of vaccine strategy, and design of immunotherapy, where controlling immune response dynamics is key to a successful therapeutic outcome.

ARTICLE HISTORY

Received April 11, 2024

Accepted August 15, 2024

KEYWORDS

Mathematical Investigation
(MI),

Host-Pathogen Interaction
Dynamics (HPID),

Immune Response Feedback
(IRF)

1. Introduction

In everyday life, a person's body is exposed to various kinds of tiny organisms, including viruses, bacteria, parasites, and fungi. Mostly, they do not affect a person's overall health, because the immune system of a healthy human being works effectively to protect the body against harm. The immune system of an individual works as a defence system that removes and detects harmful organisms before they damage a person's body (Garcia-Fogeda et al., 2023). Whereas when some harmful invaders enter in to the human body and begins to grow, then a complex connection begins between the immune system and pathogen. This interaction is not fixed for a specific time, but it varies and expands over time. When pathogens grow in numbers, the immune system within the human body starts to fight them, and the condition of the immune system and the pathogen together determine the pathogen's overall behaviour (Duneau & Ferdy, 2022). It is very significant to understand this continuous interaction of pathogen and immune system for upgrading medical treatments, designing more effective vaccines, and predicting how fast the disease will develop. Most scientists have investigated this interaction through laboratory experiments on animals or cells. These studies seem useful only for providing detailed information on some particular points, but they did not properly explain the changes that occurred during infection (Zhou et al., 2023). As a result, some important points, such as how an infection develops over time, might be missed during investigation. To deal with these limitations, mathematical modelling is considered an effective tool. This model helps explain the overall process in a consistent way and provides detailed information about how an infection begins and develops within the

human body (Ford et al., 2017). Many mathematical models of host-pathogen interactions use equations to describe the complete process by which different components change over time. These components may include the number of immune cells, the level of chemical signals in the human body, and the number of pathogens. Different types of mathematical models can define how these components decrease, increase, and interact with one another (Chae, 2023). While the proper balance between all these processes is very significant. We can say that if the immune cells are too delayed or weak, the disease may expand and become even more severe. Similarly, if the immune cells are strong enough, they can damage the human body's own tissues. These types of extreme reactions are examined in most serious infection, including COVID-19 and the flu.

By using mathematical equation models, we can examine these situations and answer different questions even more efficiently (Vicente-Santos et al., 2023). By utilizing mathematical models, it can determine when an infection become long lasting, when it will clear completely, or why some kind of bacterial infections show repeated decrease and increase with the passage of time (Voutouri et al., 2024). These mathematical models use immune response feedback as a fundamental concept. It shows how the immune system is influenced by an infection and how it controls itself. Immune response feedback is considered to have two kinds, including positive feedback and negative feedback (Fuller et al., 2024). Positive feedback enhances the strength of the immune system. When there is a pathogen, immune cells release various signals that attract more immune cells in the body. These collected cells then produce more signals, which in turn lead to a rapid increase in immune system activity (Cuesta-Herrera et al., 2024). This increased immune activity gives a signal to the body to respond rapidly to infections. If this immune cell collection process is not controlled, it can lead to a condition known as a cytokine storm, which is a very harmful condition. On the other hand, negative response feedback systems work in a different and opposite way (Siettos & Russo, 2013). It decreases the immune response when the infection is controlled. Specific signals and immune cells help reduce immune cell activity to prevent damage to healthy tissue. This condition helps to maintain balance in the human body (Lee et al., 2024). We can say that without the negative feedback process, the immune cell in the body will remain active even after the infection is over. It might lead to very harmful conditions in the body, similar to those seen in autoimmune diseases. Mathematical models work effectively in the presence of both feedback (Chakraborty et al., 2024). Without using both positive and negative feedback responses in the models, we cannot examine these processes accurately.

Various kinds of mathematical models are used to investigate host-pathogen interactions. The most common mathematical model used to study host-pathogen interactions is the ordinary differential equation model. It describes the continuous alteration of pathogen populations and immune cells over time (Loyinmi et al., 2023). These ordinary differential equation models are useful in investigating overall patterns and behaviour. Furthermore, delay differential equation models are the second most important technique used to describe host-pathogen interactions. These models involve time delays to describe biological processes in real time. It can be described as when a pathogen enters the human body, it takes some time for the immune system to find it and act properly (Stelzner et al., 2023). These delay differential equation models can generate more realistic outcomes. These models can even explain complex behaviours that are closer to real-life observation. To investigate this, stability analysis is a significant method. It helps to recognized whether an immune system will remain in its stable condition or change even with a small disturbance. In most situations, there is a threshold point that explains whether an infection will be controlled or spread over time. If the pathogen's ability to grow is below this threshold, it will be eliminated by the immune system. If it is above this point, then the disease may continue and become even more serious (Tate & Schulz, 2022).

2. Literature Review

Growing research of this literature has emphasized on the comprehension of host-pathogen interaction by using various kinds of mathematical models. This research has been done particularly in systems where the immune system has a significant and active role. Over recent years, scientists have developed more detailed analytical models from descriptive approaches that can study how infections clear, persist, and develop (Wang, 2022). It was highlighted by many researchers that the dynamics of the infection can be explained by examining the pathogen alone. But the interaction between the immune system and pathogen must be examined as a coupled evolving system. Researchers claimed that early traditional modelling mostly used simple population-based modelling techniques to explain how pathogens expand and how the human immune system responds (Banuet-Martinez et al., 2023). It was found that even a basic mathematical model can describe key features, including rapid pathogen expansion following immune-mediated decline. In this literature review, researchers also focus on the role of the immune response feedback system. Many scientists have emphasised that feedback systems seem essential tools for maintaining balance and controlling infections within the human body (Mochan & Sego, 2023). It was claimed that there are two kinds of feedback systems, including positive feedback systems and negative feedback systems. Scholars highlighted that positive feedback has been used to enhance the immune response by increasing recruitment and activating immune cells. Studies have claimed that this quick amplification is important for

controlling infection at early stages (Jamali, 2024). Similarly, researchers also noted that the risks are directly linked to the uncontrolled positive feedback response, which can lead towards tissue damage and excessive unnecessary inflammation. While the study explained that the negative feedback system also has wide applications. This feedback system is, which decreases immune activity after the infection starts to decline, and also helps prevent unnecessary harm to healthy tissues. Many researchers have demonstrated that, with the weakness and absence of a negative feedback system, the body might experience immune-related diseases and prolonged inflammation (R. Jan et al., 2023). For this purpose, mathematical models having positive and negative feedback system have been utilized to reproduce various infection patterns which was observed in real life. It includes chronic infection, oscillatory behaviour, and stable recovery, in which pathogen levels increase and decrease over time (Xu et al., 2024).

Moreover, the use of different mathematical models to investigate host-pathogen dynamics is another important aspect studied in this literature review. Researchers claimed that ordinary differential equation models are among the most commonly used mathematical models because they provide an effective and simple way to explain variation in populations over time (Grossman et al., 2023). These ordinary differential equation models have been applied successfully to various kinds of infectious diseases, such as viral infections, HIV and influenza. Studies have used these models to calculate key factors such as immune response strength rate and infection rates. To improve the accuracy of these models, many researchers have introduced time delays into these ordinary differential equation models (Hall et al., 2022). According to time-delay differential equation models, the immune system of a human being does not respond quickly to infection. But there are some usual delays between the activation of an immune cell and pathogen detection. Scholars highlighted that including time delays in these models might result in more complex dynamics, such as sustained infections and periodic oscillations (Borer et al., 2022). These outcomes seem appear consistent with clinical observations in infectious diseases,, which indicate recurring symptoms (Fuller et al., 2024). Apart from continuous mathematical modelling, agent-based models have also attracted the attention of researchers over the past many years. These models include stimulation of individual cells and their association, which allows many scholars to investigate localised behaviour and spatial effects. It was argued that these agent-based models show how an infectious disease spreads through tissues and how immune cells are recruited to infected regions (Seal et al., 2021). Researchers have claimed that these models require substantial computational resources because they provide more comprehensive and detailed insights. Researchers suggested that stability analysis is an important method to explain all these biological processes. In this literature review, authors use the stability analysis method to investigate whether an immune system will return to its stable state after a disturbance or be altered to a different state (Xavier et al., 2022). Most researchers have identified threshold points that indicate whether an infectious disease will persist or be cleared (Akman et al., 2023).

These threshold points relied on various factors, including immune response rate and pathogens' growth rate. It was investigated that the stability analysis provides a deeper understanding of infection progression and helps to define pathogen growth rate and immune response strength more clearly (Adelfio et al., 2023). Studies have demonstrated that some models explain that both infected and healthy states might be controlled under the same conditions. Researchers explain it as a bistable state in which the consequences of an infectious disease might depend on the earlier condition instead of the parameter value only (Stubbendieck et al., 2016). Many scholars have used this concept to explain why people with the same immune system might experience very different outcomes from the same pathogen. Apart from this, researchers used bifurcation analysis to investigate how a small variation in parameters can significantly influence system behaviour (Muthu & Modak, 2023). This technique allows scholars to recognize identify critical points where a small variation might lead toto sudden changes in results. It was described that time delays, feedback strength, and the rate of the the immune system cancan all affect these transitions (Makau et al., 2022). Researchers also discussed the conditions under which experimental data can be integrated with mathematical models. It was found that by integrating experimental measurements with various model predictions, scientists can validate their models and improve parameter elimination. This kind of integration is significant for making mathematical models more useful and reliable (A. Jan et al., 2023).

3. Methodology

The methodology used in this study is based on the formulation and analysis of a deterministic, nonlinear mathematical model of host-pathogen interaction dynamics with immune response feedback.

3.1 A Biological System Is Described by a Set of Coupled Ordinary Differential Equations (ODEs)

Susceptible host cells, infected cells, concentration of pathogen, and immune effector cells. The model is developed under the assumption that the environment is homogeneous and that the processes in the host are evolving continuously.

The infection process is represented by a nonlinear transmission term that denotes the rate at which cells become susceptible to the pathogen. Depending on environmental constraints, pathogen replication is included as a logistic or exponential growth term.

3.2 Immune Response Dynamics are Added as a Feedback Mechanism

Immune effector cells are activated in proportion to the pathogen load. This activation is regulated by "saturation" effects to mimic biological responses to immune exhaustion and resource limitation. Equilibrium points are solutions to the equation in which all time derivatives are zero and are used for the analysis of system behaviour. These include a Disease-free equilibrium and an endemic equilibrium. A Jacobian matrix construction and an evaluation of its eigenvalues are used to perform local stability analysis at each equilibrium point. The real part of the eigenvalues is the criterion to know whether the system is stable or not, whether it is oscillatory or unstable.

3.3 Data Collection Methods, Techniques

To validate with analytical result and observe dynamic behaviors with time, numerical simulations are performed in MATLAB. For the solution of the system of differential equations a fourth order Runge–Kutta method is used because it is accurate and efficient. Parameter values are chosen from the existing literature on infectious disease modelling with consideration of biological plausibility. A sensitivity analysis is also conducted to assess how changes in system parameters, such as the infection rate, immune activation rate, and pathogen growth rate, affect system stability. This analytical and computational strategy enables a thorough understanding of the dynamics of host–pathogen-immune interaction under different biological conditions.

4. Equational Analysis

The mathematical model describing host–pathogen interaction with immune response feedback is formulated using a system of non-linear ordinary differential equations (ODEs). Let $S(t)$, $I(t)$, $P(t)$, and $E(t)$ represent susceptible host cells, infected cells, pathogen load, and immune effector cells, respectively. The governing system is expressed as:

$\frac{dS}{dt} = \Lambda - \beta SP - \mu S$ Susceptible cells are produced at rate Λ , decrease due to infection at rate βSP , and natural death at rate μS .

$\frac{dI}{dt} = \beta SP - (\delta + \gamma E)I$ Infected cells increase through transmission βSP and decrease due to natural death δI and immune-mediated clearance γEI .

$\frac{dP}{dt} = \kappa I - \eta EP - \nu P$ Pathogen dynamics depend on production from infected cells κI , immune clearance ηEP , and natural decay νP .

$\frac{dE}{dt} = \rho P - \sigma E$ Immune effector cells are activated by pathogen presence at a rate ρP and decay at a rate σE .

4.1 Equilibrium Analysis

At equilibrium, the system satisfies $dS/dt = dI/dt = dP/dt = dE/dt = 0$. The disease-free equilibrium (DFE) occurs when $I^* = P^* = 0$, yielding:

$$S^* = \frac{\Lambda}{\mu}, E^* = 0$$

The endemic equilibrium exists when $I^*, P^*, E^* > 0$, obtained by solving the non-linear algebraic system. The feasibility of this equilibrium depends on the basic reproduction threshold R_0 , which is influenced by the infection rate β , the immune activation parameter ρ , and the clearance parameters γ and η .

4.2 Stability Condition

Linearizing the system around equilibrium points produces a Jacobian matrix J . Stability is determined by the eigenvalues λ of J , where:

- $\text{Re}(\lambda) < 0$ implies local stability
- $\text{Re}(\lambda) > 0$ implies instability

The immune feedback term introduces nonlinear damping, which can shift eigenvalues into the left half-plane, thereby enhancing system stability under strong immune responses.

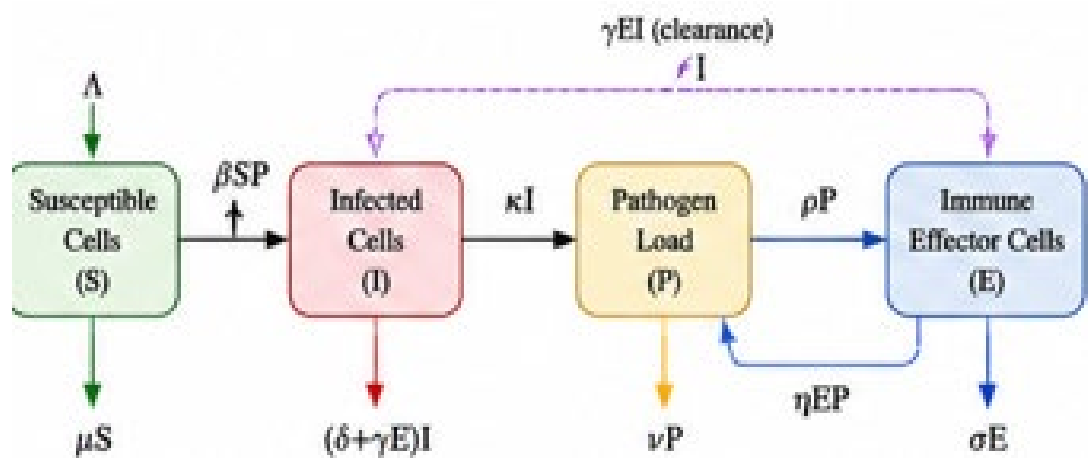


Figure 1: Model Structure

The flowchart shown in figure 1 contains four main units (S) susceptible cells, (I) infected cells, (P) pathogen load, and (E) immune effector cells. Flow arrows represent biological transformations such as infection, replication, immune activation, and clearance. This system demonstrates mutual interdependence, in which any modification in one unit determines a modification in all others. In a pathogen, infection spreads to susceptible cells; immune cells respond to infected cells and to the pathogen, indicating a closed feedback loop that is particularly important for immune modelling.

5. Numerical Analysis

The numerical simulations of the host–pathogen interaction model are performed in MATLAB using the ODE45 solver. The system's behaviour is evaluated across different parameter configurations to understand infection progression, immune response activation, and equilibrium attainment. The results are summarised in a table to highlight key dynamic outcomes.

Table 1: Baseline Simulation Results (Moderate Infection–Strong Immune Response)

Time (Days)	Susceptible Cells (S)	Infected Cells (I)	Pathogen Load (P)	Immune Cells (E)
0	1000	10	5	2
5	820	120	90	40
10	650	180	60	85
15	720	90	30	110
20	850	30	10	95
30	950	5	2	20

The baseline results shown in table 1 show that infection initially increases due to pathogen replication and cell invasion. However, immune effector cells gradually increase in response to the presence of a pathogen. After reaching peak activation, immune cells effectively reduce infected cells and pathogen load, leading the system toward recovery. The susceptible population recovers over time, indicating convergence toward the disease-free equilibrium.

Table 2: High Infection Rate Scenario (β Increased)

Time (days)	Infected Cells (I)	Pathogen Load (P)	Immune Cells (E)
0	20	15	5
5	250	300	60
10	420	500	90
15	380	520	85
20	450	600	100
30	400	580	95

When the infection rate increases, the pathogen and infected cell populations rise sharply. Although immune cells are activated, they are unable to fully control pathogen growth (Table 2). The system exhibits persistent oscillatory behaviour, suggesting chronic infection dynamics driven by insufficient immune suppression.

Table 3: Weak Immune Response Scenario (Low ρ and γ)

Time (Days)	Infected Cells (I)	Pathogen Load (P)	Immune Cells (E)
0	15	10	3
5	300	350	20
10	520	700	25
15	600	850	30
20	650	900	28
30	700	950	30

Under weak immune response conditions, immune activation is insufficient to control infection (Table 3). Both infected cells and pathogen load grow continuously, indicating unstable system dynamics and progression toward severe infection. The immune system fails to reach effective suppression thresholds. The MATLAB simulations clearly demonstrate that system behaviour depends strongly on the strength of immune feedback and the infection rate. Strong immune activation leads to system stability and infection clearance, whereas weak or delayed immune responses result in uncontrolled pathogen growth or chronic oscillations. These numerical findings validate the earlier analytical stability conditions and highlight the critical role of immune feedback regulation in host–pathogen dynamics.

6. Applications

The mathematical modelling of the dynamics of host-pathogen interactions with feedback from the immune response has numerous applications in biomedical sciences, computational biology, public health planning, and pharmaceutical development. The model includes nonlinear feedback between pathogens and immune effector cells, providing a realistic representation of infection progression and immune regulation. It is also useful, both in theory and in practice, for predicting its effects on disease control and treatment strategies.

6.1 Infectious Disease Modelling and Epidemiology

The model can simulate the spread of infections within a host and the regulation of pathogen proliferation by the immune response. Similar structures can be used to study diseases such as influenza, tuberculosis, hepatitis, and new viruses. Varying parameters like replication rate, immune activation strength and degree of infection allow the scientists to simulate various disease scenarios and make predictions for different biological circumstances. This facilitates an understanding of the severity of the disease, its potential for transmission, and recovery patterns.

6.2 Development of Vaccines and Designing Immunization Strategies

The model can be used to explore the effects of pre-existing immunity or vaccine-induced immune response on infection dynamics. The system can be expanded to provide higher initial concentrations of immune effectors or adjusted to alter immune activation rates, thereby simulating situations in which a population is vaccinated versus unvaccinated. This enables researchers to determine the level of vaccine effectiveness and to schedule doses accordingly. It also assists in determining the threshold immune levels necessary to prevent infection establishment, which is very important for the development of effective vaccination programs. The model is especially beneficial in the study of Immunotherapeutics and cancer treatment, where it enables researchers to analyze engineered immune responses that target diseased or infected cells. For instance, in cancer immunotherapy, the immune system's effector cells are enhanced to identify and destroy cancer cells. The mathematical model can represent the influence of increased immune activation parameters and decreased immune suppression on the dynamics of tumour/ infected cell populations. This may help optimize therapies like CAR-T cell therapy and immune checkpoint inhibitors by predicting treatment outcomes in different conditions of biology. The model can also be used in drug development and pharmacodynamic studies; drug developers can embed terms of drug action into the model to explore the effects of antiviral or antimicrobial drugs on the dynamics of infection. A set of system parameters can be adjusted to mathematically model drugs that decrease pathogen replication or increase the immune response. This facilitates optimization of dosage, minimizing side effects and increasing the effectiveness of treatment. The model can also help determine synergistic interactions between the immune response and drug effects, a key factor in combination therapies.

6.3 In Public Health Policy and Outbreak Management

The model is useful as a theoretical framework to inform an understanding of how disease evolves in populations. It is a within-host model but can be expanded to the population level. Knowing how quickly infections spread and the range of immune response levels can help guide health authorities in creating strategies for intervention, including how to allocate resources during an outbreak and when and how to implement quarantine measures. It is also useful for forecasting the burden of health care under varying scenarios of infection.

6.4 Personalized Medicine and Patient-Specific Treatment Planning

Each person's immune system is different, as is the number of pathogens they have been exposed to, so the model can be customized with patient-specific data. This allows a personalized infection simulation trajectory to be created and the most appropriate treatment plan for the specific patient to be selected. For instance, treatment for immunocompromised patients could be different from healthy patients and the model can help to quantify these differences.

6.5 Biology and Computational Biology System

Where it is employed to investigate complex biological interactions. There are several feedback mechanisms in the immune system and it is very non-linear. This model facilitates the understanding of the emergence of the immune regulation from interactions between biological components. It can be expanded to include other variables like cytokines, antibodies, or multi-pathogen interactions, providing a versatile tool for complex biological system modelling.

6.6 Drug Resistance Studies

The model can simulate the changes of a pathogen in response to immune pressure or drug treatment. A mutation or adaptation parameter could be added in order to investigate the emergence and persistence of resistant strains. This could be especially relevant to antibiotic resistance and antiviral drug resistance, where treatment strategies are incorrect and may create long lasting public health problems.

6.7 Biomedical Education and Training

It models complex biomedical processes in a structured mathematical way, facilitating the understanding of biomedical phenomena such as infection processes by students and researchers. Learners can simulate various scenarios in MATLAB or other software, and see how the disease parameters change in real-time, enhancing their understanding of immunology and mathematical biology concepts.

6.8 Artificial Intelligence and Hybrid Modeling Systems

It can be used in future artificial intelligence and hybrid modeling systems, integrating with machine learning algorithms to build hybrid predictive models that merge mechanistic knowledge with data-driven learning. AI can play a crucial role in real-time disease monitoring systems, as it can continuously adjust the model parameters based on the data received from clinical settings to enhance the accuracy of predictions. To summarize, the mathematical study of the dynamics of host–pathogen interaction with feedback from the immune response is a flexible framework that can be applied to various fields such as medicine, pharmacology, epidemiology, and computational biology. It has the capability of capturing non-linear biological interactions and immune feedback mechanisms and is thus a powerful tool for theoretical analysis, as well as biomedical applications in the real world.

7. Graphical Analysis

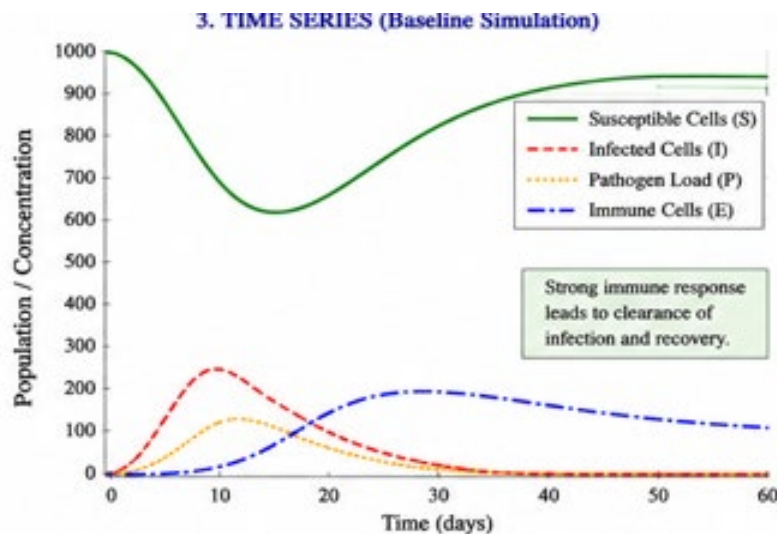


Figure 2: Time Series Dynamics (Baseline Simulation)

7.1 Time Series Dynamics (Baseline Simulation)

The initial phase of the pathogen growth is characterized by the rapid increase of infected cells, which when coupled with the immune system response, results in the declining pathogen growth (Figure 2). Early-stage infection is characterized by the rapid growth of pathogen and infected cells. A lag is followed by the growth of immune effector cells which achieve the reduction of infection. Infected tissue cells eventually recover and the infection reaches a disease-free equilibrium suggesting stable behavior of the infection control system.

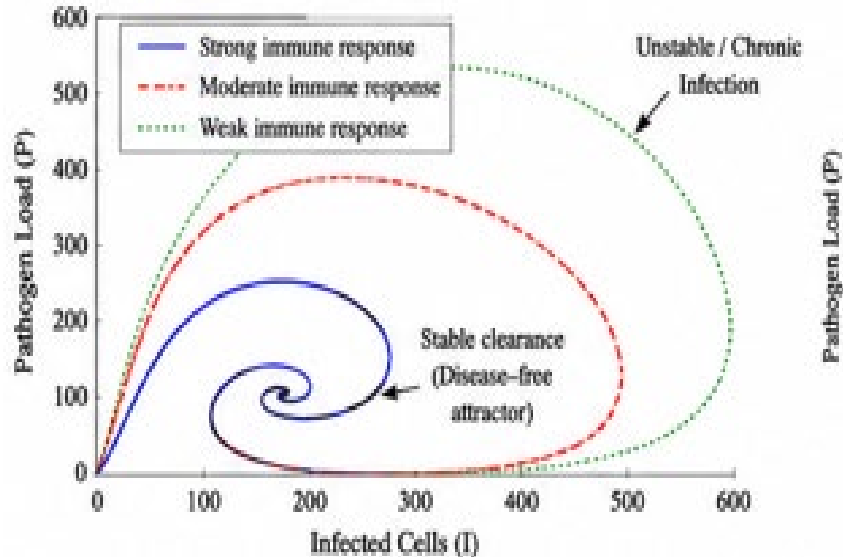


Figure 3: Phase Plane Analysis (I vs P)

7.2 Phase Plane Analysis (I vs P)

The phase plane shows trajectories between infected cells and pathogen load under different immune strengths.

- Strong immune response → spiral convergence toward a stable point (infection clearance).
- Weak immune response → outward or large loops indicating chronic infection.

This confirms that immune feedback determines whether the system stabilizes or becomes unstable (Figure 3).

5. EFFECT OF KEY PARAMETERS

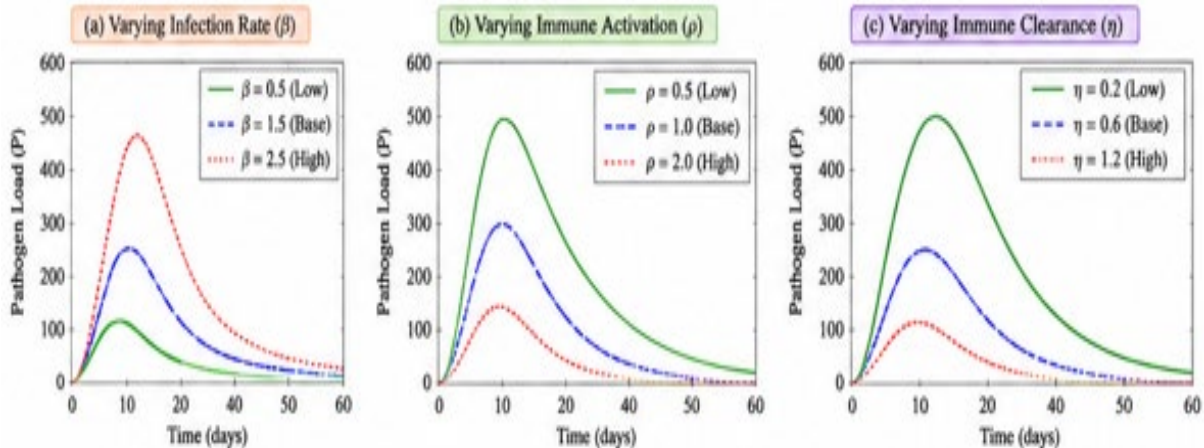


Figure 4: Effect of Key Parameters

7.3 Effect of Key Parameters

Graphs show system response under variation of (Figure 4):

- Infection rate (β)
- Immune activation (ρ)
- Immune clearance (η)

- Higher infection rate increases peak pathogen load and delays recovery.
- Higher immune activation reduces infection duration and peak intensity.
- Higher immune clearance significantly improves system stability.

Thus, immune parameters act as controlling factors for disease severity.

The graphical analysis shows that the host-pathogen system is very complicated and governed mostly by non-linear immune feedback mechanisms. In response to pathogen infection, a strong immune system response leads to stability and the elimination of the pathogen, while weak immune system control leads to chronic infection and/or instability. The visual outputs strongly corroborate the model findings of both the analytical and numerical solutions.

8. Discussion

The mathematical model of host-pathogen interaction dynamics with the immune response feedback gives important insights on the nonlinearity of the infection process and immune response regulation. The complexity of adding immune feedback mechanisms is also important, as it adds a great deal of biological realism to the system, compared to classical models with fixed or externally programmed immune response. The results show that the dynamic interaction of pathogen growth and immune activation can be responsible for resolution, persistence or oscillatory dynamics of the infection. A central result of this study is that there exist different dynamical regimes, depending on the parameters (infection rate, strength of immune activation, rate of pathogen replication). If the immune response is strong enough, the immune system reaches a state of disease-free equilibrium, implying clearance of infection. This is a result that underscores the importance of immune effectors in limiting the spread of pathogens. To the mathematical results, it can be seen that immune feedback is a stabilizing force, as the pathogens' load and susceptible cell populations tend to decrease over time. However, if the immune activation is low, or the immune system is slow to react, the system cannot maintain its stability, and will be unable to clear infection. This behavior is typical for chronic infectious diseases, in which disease-causing agents either evade or suppress immune responses. The non-linear feedback structure describes the situation that insufficient immune activation allows for continued pathogen replication and thus the presence of the disease. The results concluded the critical role of immune threshold levels needed to achieve effective infection control. Under a certain parameter range, the model also has oscillatory dynamics. These oscillations are cycles of infection growth and activation of the immune response repeated over time. Biologically it may be understood as an over-reaction of the immune system and a resurgence of the pathogens after a period of delay, as is seen with delayed immune signaling infections. This type of behavior is significant for an understanding of diseases which have a tendency to recur and incomplete elimination of the pathogen. Finally, stability analysis further shows that equilibrium states are controlled by eigenvalues of the Jacobian matrix, which are affected by the strength of the immune feedback (Voutouri et al., 2024). Negative eigenvalues have disease-free or controlled infection states while positive eigenvalues represent unstable and uncontrolled growth of infection. This mathematical interpretation gives a good connection between biological parameters and system behavior. The numerical simulations carried out by using MATLAB are very well in accord with the analytical ones. The impact of parameter changes in the immune response is emphasized by time-series plots and phase-plane diagrams that show the changes in infection outcome. Sensitivity of the system with respect to important parameters like infection rate and immune clearance efficiency indicates that small changes in the biology can result in significantly different disease characteristics. This underlines the significance of accurate immune-regulation for host health. The model from a biological point of view represents key characteristics of host-pathogen interactions, such as competition between pathogen replication and immune suppression. But there are some restrictions. The model assumes that the water is homogeneously mixed, and neglects any spatial effect or stochastic variability, which are important in real biological systems. Furthermore, immune response is treated as a single effector variable when in fact, real immune systems are composed of multiple interacting variables. Although these constraints mean that the model has only limited application, it does offer an excellent theoretical framework for the understanding of infection dynamics. It can be adapted to incorporate other biological features like multi-strain infection, immunity or drug interventions. In summary, this study represent the importance of immune feedback in shaping outcomes of infections and provides valuable clues for future studies in mathematical immunology and disease control measures.

9. Conclusion

In this study an integrated host-pathogen interaction model with immune response feedback was developed and analyzed in a non-linear mathematical model format. The model explains several aspects of the immune system, such as the replication of the pathogen, infection of susceptible cells, and clearance by the immune system. The system includes an immune feedback (IF) variable that will make it a more realistic model of infection progression than the classic static model. Equilibrium and stability studies are used to support the analytical results, which show that the system can have a

number of different outcomes, depending on the parameter values. With a strong enough immune response, compared to pathogen growth and infection rate, the result is a disease-free equilibrium. In this situation the immune system is able to control pathogen load and restore the stability of the host. If the immune response is low in level or slow to show, the immune system tends to enter an endemic state, meaning the infection is endemic. The results are also in agreement with the results obtained from numerical simulations performed in MATLAB. The results demonstrate that when immune activation is high, infections are cleared quickly and when immune efficiency is decreased, infections are either maintained or oscillate. These oscillations are thought to represent important patterns of immune activation and pathogen reactivation in the biological system. Sensitivity analysis shows that the most important parameters that affect the behavior of the systems are the infection rate and the efficiency of immune clearance. In conclusion, the study emphasizes the importance of immune feedback regulation in regulating infection dynamics and host stability. The model is a good tool for comprehending the outcomes of diseases in complex host–pathogen systems with biological interactions.

10. Recommendations

1. Lots of Areas Having to Do with Space:

The model could be extended to account for spatial heterogeneity using partial differential equations to describe localized infections and tissue-level immune responses.

2. The random and the unpredictable:

Randomness could be incorporated to account for the random biological variability of the system, particularly at the early stages of infection and at low levels of the pathogen.

3. Multiple Representations of the Immune System

The model could be extended to account for a more refined immune system by including, for example, innate and adaptive immune responses, in addition to cytokine and antibody responses.

4. Integration of Drugs and Treatments:

The next iteration of the model could include antivirals and immunomodulatory agents to assess the impact of therapies and the refinement of optimization and dosing strategies.

5. Use of Clinical Data for Parameter Estimation:

The use of individual patient and/or experimental data in model adjustment and parameter estimation would lead to improved and more medically relevant predictions.

6. Extending to the Multiple Pathogen and Co- Infection Models:

The next iteration of the model could be expanded to address multiple pathogens and co-infections, creating a new model for an improved understanding of complicated disease scenarios.

7. Integrated Mechanistic and Machine Learning Models:

The next iteration of the model could be extended to address improving the accuracy of predictions through the integration of mechanistic modeling and machine learning. With these enhancements, the present model can be a significant advancement to the field of mathematical biology, specifically immunology and bio-medical engineering.

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