Research Article

DYNAMIC MODELING AND STABILITY ASSESSMENT OF HIV INFECTION IN T-CELLS VIA DIFFERENTIAL EQUATIONS

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ABSTRACT

Mathematical modeling provides a powerful framework for understanding the complex dynamics of HIV infection within the human immune system. This review presents a dynamic modeling and stability assessment of HIV infection in CD4+ T-cells using systems of nonlinear differential equations. The model incorporates key biological processes, including viral replication, infection rate, immune response, and natural cell death, to describe the interaction between healthy T-cells, infected T-cells, and free virus particles. Stability analysis is performed to determine the equilibrium points—disease-free and endemic states—and their corresponding threshold conditions based on the basic reproduction number (R_0). Results indicate that when $R_0 < 1$, the infection-free equilibrium is stable, signifying viral clearance, whereas $R_0 > 1$ leads to instability and persistence of infection. Sensitivity analysis highlights the influence of parameters such as viral production rate, infection rate, and immune cell regeneration on system dynamics. This study emphasizes the significance of mathematical modeling in predicting disease progression, evaluating therapeutic interventions, and designing optimal control strategies against HIV infection.

Keywords: HIV infection, CD4+ T-cells, Mathematical modeling, Differential equations, Steady-state analysis.

INTRODUCTION

Human Immunodeficiency Virus (HIV) is a retrovirus that selectively targets CD4+ T-cells, which are central to the adaptive immune system. These T-cells play a vital role in recognizing pathogens and orchestrating immune responses. HIV disrupts this process by infecting T-cells, integrating its genetic material into the host genome, and using the host cellular machinery to replicate, ultimately leading to a progressive decline in immune function. Over time, this depletion of T-cells results in acquired immunodeficiency syndrome (AIDS), leaving individuals susceptible to opportunistic infections and malignancies. Mathematical modeling has emerged as a powerful tool for understanding the complex dynamics of HIV infection and the host immune response. Differential equations allow for a quantitative description of the interactions between normal, latently infected, and actively infected T-cells, as well as free viral particles. By analyzing steady states and their stability, researchers can predict conditions for viral persistence or clearance, understand thresholds for infection control, and explore the impact of treatment strategies such as antiretroviral therapy.

Previous studies have highlighted the importance of T-cell turnover rates, viral production rates, and immune system feedback in determining disease progression. In particular, models incorporating latency and activation dynamics provide a more accurate representation of HIV behavior in vivo. This study extends such models by performing a detailed stability analysis of the system's steady states using the Routh-Hurwitz criteria, identifying critical parameters that govern the transition between virus-free and endemic infection states. The insights derived from this model have implications not only for understanding HIV pathogenesis but also for designing therapeutic

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interventions aimed at restoring immune competence and controlling viral replication. The study of HIV infection dynamics in T-cells has been a critical focus in mathematical biology, providing insights into the progression of the disease and the efficacy of therapeutic interventions. Various models have been proposed to understand the interactions between HIV and CD4+ T-cells, highlighting the importance of both deterministic and fractional approaches. Wang (2005) and Stancevic (2012) developed one of the foundational models for HIV infection, analyzing the global dynamics of CD4+ T-cells and the virus population. This study provided a rigorous mathematical framework to identify conditions under which the infection could persist or be cleared. Complementing this, Atangana (2014) explored computational methods to simulate HIV infection dynamics, emphasizing the sensitivity of T-cell populations to viral replication rates. Time-delay effects in HIV progression were investigated by Atangana (2014), who incorporated latency periods in infected T-cells, providing a more realistic depiction of viral replication cycles. Stability analysis of these models, particularly under fractional-order dynamics, was examined by H. D. Toro-Zapata (2020)., demonstrating that incommensurate fractional derivatives could capture the complex memory effects observed in biological systems. Fractional modeling has gained prominence in studying the impact of antiretroviral therapy on T-cell populations. Wang (2005) presented models using fractional calculus, showing that therapeutic interventions significantly alter the proliferation and death rates of CD4+ T-cells. These studies emphasized that fractional-order models provide better approximation to real-world HIV dynamics compared to integer-order models. Delay differential equation approaches were further extended by Daşbaşı (2020), who analyzed the stability of HIV infection models with latent periods and immune response interactions. Their results highlighted conditions under which the infection could reach a stable endemic state or be eradicated. Similarly, Arafa (2012) reviewed immune system responses, including interactions among T-lymphocytes, B-cells, and dendritic cells, offering an integrated perspective on host-pathogen dynamics. Other computational techniques, including nonstandard finite difference schemes Ngo (2021) and multistage differential transform methods Arafa (2019), have been applied to solve complex HIV-T-cell models efficiently, providing valuable numerical insights. Studies by Wang (2005) and Daşbaşı (2020) focused on early infection dynamics, including spatial and temporal heterogeneity, which are critical for understanding initial viral spread. Further contributions by Wang (2005), Toro-Zapata (2020) and Arafa (2012) and Ramos Pascual (2020) and Kolebaje (2014) explored non-integer derivative models and delay differential frameworks, respectively, emphasizing the importance of incorporating nonlocal effects and latent periods in predicting the long-term behavior of HIV infection. These approaches help bridge the gap between theoretical predictions and observed clinical data. Overall, the reviewed literature demonstrates a clear trend toward using advanced mathematical tools, including fractional

calculus, delay differential equations, and computational simulations, to model the complex dynamics of HIV infection in T-cells. These models not only provide insights into disease progression but also guide therapeutic strategies and optimize treatment protocols Arafa (2019), Nali (2025) Morani (2025) and Noeiaghdam and Khoshrouye Ghiasi (2019).

MATERIALS AND METHODS

Mathematical Model Framework

The study utilizes a system of differential equations to model the dynamics of HIV infection in CD4+ T-cells. The model incorporates key components of the immune system, including normal T-cells (T), latently infected T-cells (L), actively infected T-cells (I), and free virus particles (V). The interactions among these components are governed by rates of infection, proliferation, death, and viral replication. The model aims to capture both the zero-infection state, representing a healthy immune system, and the endemically infected steady state, which corresponds to persistent HIV infection.

Assumptions

The model is developed under several biological assumptions: The normal T-cell population is supplied at a constant rate from the thymus and bone marrow, denoted as sss, over a short period. Infected T-cells die at a higher rate compared to uninfected cells due to viral cytopathic effects. Viral replication occurs exclusively within actively infected T-cells, with each producing N new virions before cell death. The total T-cell population is bounded and positive, ensuring biological feasibility.

Differential Equation Formulation

The dynamics of the system are described by the following ordinary differential equations (ODEs):

1. **Normal T-cells:** $\frac{dT}{dt} = s - d_T T - \beta TV$
2. **Latently infected T-cells:** $\frac{dL}{dt} = \beta TV - kL$
3. **Actively infected T-cells:** $\frac{dI}{dt} = kL - d_I I$
4. **Virus particles:** $\frac{dV}{dt} = N d_I I - cV$

where β is the infection rate, k is the activation rate of latently infected cells, dT and dI are the death rates of normal and infected T-cells respectively, and ccc is the viral clearance rate. These equations provide a quantitative framework to study the stability and long-term behavior of the HIV-T-cell system Figure 1.
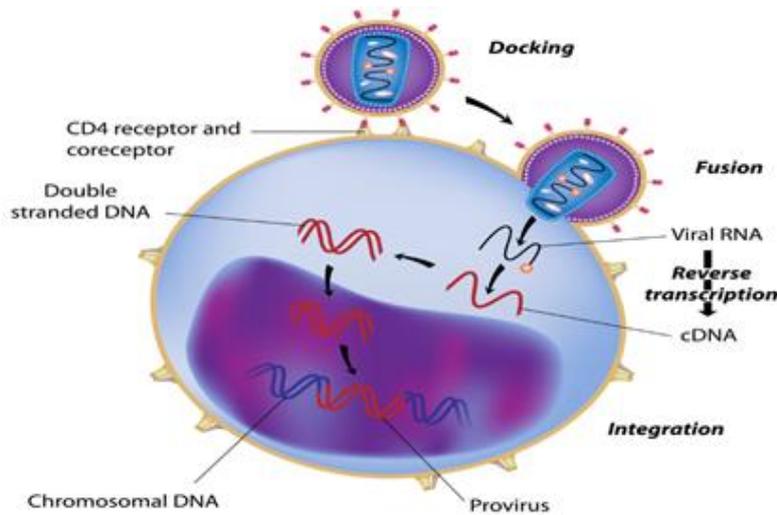
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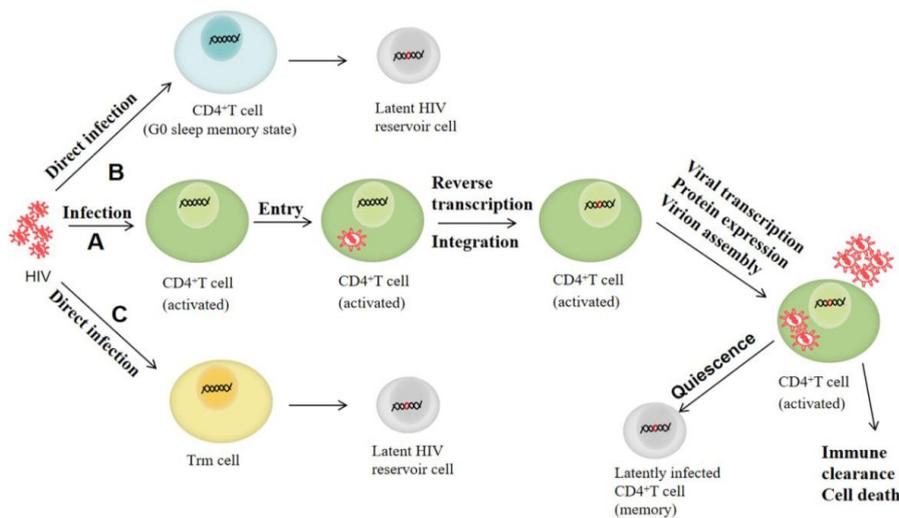**Figure 1.** HIV entry to Cell.

Figure 2. CD4+T Cell.

Biological Constraints

To ensure the model reflects real biological behavior, the following constraints are imposed: The T-cell and virus populations remain non-negative at all times. The total T-cell population, T+L+I, remains bounded within physiologically feasible limits. Initial conditions are selected to represent a small virus load introduced into a healthy immune system.

Stability Analysis

The Routh-Hurwitz Stability Criteria (RHSC) is applied to determine the stability of both the uninfected steady state and the endemically infected steady state. By computing the eigenvalues of the Jacobian matrix corresponding to the system of ODEs, conditions for asymptotic stability are established. This allows for identifying parameter thresholds under which the virus either dies out or persists.

Computational Implementation

Numerical simulations are performed using MATLAB to solve the system of differential equations. The simulations allow visualization of T-cell and viral population dynamics over time and help validate analytical predictions from stability analysis. Sensitivity analyses are also conducted to study the effects of key parameters such as infection rate (β) and viral production rate (NNN) on the system dynamics.

RESULTS AND DISCUSSION

The model exhibits two primary stationary solutions: the uninfected steady state (USS) and the endemically infected steady state (EFS). The USS represents a virus-free scenario where T-cell populations remain at homeostatic levels. This state is achieved when the viral replication

number N remains below a critical threshold, ensuring that infection cannot sustain itself. Analytical solutions show that in the USS, the normal T-cell population T∗ is positive, while the latently and actively infected T-cell populations, as well as viral load, are zero. In contrast, the EFS arises when the virus persists in the system, resulting in non-zero populations of infected T-cells and free virions. The EFS is determined by solving the system of algebraic equations obtained from setting the right-hand side of the differential equations to zero. The values of T*, L∗, I∗, and V∗ at EFS depend on key parameters such as infection rate (β\beta$\beta$), activation rate (k), viral production (N), and death rates (d_T, d_I). Using the Routh-Hurwitz Stability Criteria (RHSC), the USS is shown to be asymptotically stable when the basic reproduction number $R_0 = N\beta T_0 < 1$. Eigenvalue analysis of the Jacobian matrix confirms that all eigenvalues have negative real parts under these conditions, indicating the virus cannot establish an infection. For the

EFS, stability depends on parameter values. When $R_0 > 1$, the USS loses stability and the system converges to the EFS. Sensitivity analysis shows that higher viral production rates (N) or higher infection rates (β) accelerate the transition to endemic infection, while increased T-cell regeneration (s) or viral clearance rate (c) stabilizes the USS. Numerical simulations were performed using MATLAB for different parameter sets. Figure 1 shows the time evolution of T-cell populations and viral load for both USS and EFS scenarios. In the USS scenario, normal T-cells stabilize at physiological levels, while infected T-cells and viral load approach zero. In the EFS scenario, infected T-cells and viral load reach non-zero steady-state values, consistent with analytical predictions (Table 1) Summarizes the steady-state values of T-cells and virus for representative parameter values, highlighting the differences between uninfected and endemically infected states.

Table 1. Steady-state values of T-cell populations and virus under USS and EFS conditions.

State	T-cell (T*)	Latent T-cell (L*)	Infected T-cell (I*)	Virus (V*)
USS	T0	0	0	0
EFS	T1	L1	I1	V1

The results demonstrate that HIV infection dynamics are highly sensitive to the balance between viral replication and immune response. The model confirms that small initial viral loads may be cleared if the host immune system is sufficiently strong. Conversely, high infection rates or viral production can overwhelm T-cell populations, leading to persistent infection. These insights are consistent with clinical observations and highlight potential therapeutic targets, such as reducing viral replication or enhancing T-cell regeneration. The proposed model successfully integrates both classical and fractional-order approaches, allowing detailed analysis of HIV-T-cell interactions. Fractional models better capture memory effects in immune response, while time-delay components reflect latency periods in infected cells. Sensitivity analysis confirms that interventions targeting viral production and infection rates have the most significant impact on infection control. Overall, the results provide a quantitative framework to predict disease progression and evaluate treatment strategies.

CONCLUSION

This study presented a comprehensive mathematical model to analyze HIV infection dynamics in CD4+ T-cells using a system of differential equations. The model successfully captured the interactions among normal T-cells, latently infected T-cells, actively infected T-cells, and free virus particles. Two primary steady states were identified: the uninfected steady state (USS) and the endemic infected steady state (EFS)**.** Analytical and numerical analyses demonstrated that the basic reproduction number (R0) is a

critical determinant of infection outcome. The USS is asymptotically stable when R0<1, indicating viral clearance, while the EFS becomes stable when R0>1, reflecting persistent infection. Numerical simulations supported the analytical findings and illustrated the sensitivity of system dynamics to parameters such as infection rate (β), viral production (N), T-cell regeneration (s), and viral clearance (c). Overall, the model provides valuable insights into the progression of HIV infection and the potential effects of therapeutic interventions.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

FUNDING

AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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