

MATHEMATICAL MODELLING AND SIMULATION OF HIV DYNAMICS

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Abstract

Three ordinary differential equation formulations of within-host HIV dynamics are examined: an untreated target-cell model, a model with separate infection-blocking and viral-production controls, and a model with a single viral-production control. The study revisits an undergraduate thesis based on established HIV models and presents a reproducible analytical and numerical reassessment. A discrepancy between the thesis parameter table and its computational implementation is resolved by using the source rate supported by the implementation and reported equilibrium. For this parameter set, the untreated infected equilibrium is approximately (240,21.6667,902.7778), and the infected-cell reproduction number is 2.0833. Linearization gives one negative real eigenvalue and a complex-conjugate pair with negative real parts, identifying a locally asymptotically stable equilibrium with damped oscillatory modes. Constant treatment changes the reproduction number through the product of residual infection and production rates. Equal two-input efficacies must exceed approximately 0.3072 to stabilize the infection-free equilibrium, whereas a single production efficacy must exceed 0.52. Simulations with fourth-order Runge-Kutta integration illustrate suppression during treatment and rebound following withdrawal. Step refinement and comparison with an independent adaptive solver support numerical consistency. Matching the reproduction numbers of the two treatment formulations does not make their state trajectories equivalent. The results describe the behavior of an illustrative deterministic model rather than patient-specific outcomes or drug dosages.

INTRODUCTION

Mathematical models of within-host infection describe how susceptible target cells, infected cells, and free virus interact over time. In HIV modelling, these variables provide a compact framework for studying infection growth, viral production, and treatment-induced suppression. Perelson et al. [1] demonstrated the use of mathematical modelling to analyse viral-load measurements following treatment. Their work

illustrates the distinction between a model fitted to clinical observations and an illustrative system used to explore dynamical mechanisms.

The three-state model considered here belongs to an established class of target-cell models. Craig and Xia [2] discussed its use in control engineering, while Moysis, Kafetzis, and Politis [3] examined untreated dynamics, separate treatment inputs, a single-input formulation, and local linearization. The present work derives from the author's BS

Mathematics thesis [4], which reviewed the latter study and implemented numerical simulations. The model equations and basic treatment mechanisms are therefore credited to the existing literature; this article does not propose a new biological model.

The purpose of this reassessment is to connect the thesis simulations with an explicit analytical threshold and a reproducible computation. Three issues require particular care. First, the source rate printed in the thesis differs from the value in its computational appendix. Second, a complex-conjugate pair of stable eigenvalues requires an oscillatory stability classification. Third, replacing two treatment inputs by a single input needs a stated comparison criterion. Equality of a reproduction number is weaker than equality of the governing equations or observed trajectories. Recent work by Sardar et al. [5] considers a fractional-order HIV model with additional biological mechanisms, patient-data analysis, and optimized controls. The present study retains the

$$\frac{dT}{dt} = s - dT - \beta TV, \quad \frac{dI}{dt} = \beta TV - \delta I, \quad \frac{dV}{dt} = kI - cV. \quad (1)$$

Here s is the target-cell source rate, d and δ are the loss rates of uninfected and infected cells, β is the infection coefficient, k is the viral production coefficient, and c is the viral clearance rate. The thesis uses $m_2 = \delta$ and $m_1 = c$. Infection follows a bilinear mass-action term. The system does not explicitly include cytotoxic immune cells, latent

$$\begin{aligned} \frac{dT}{dt} &= s - dT - (1 - u_1)\beta TV, \\ \frac{dI}{dt} &= (1 - u_1)\beta TV - \delta I, \\ \frac{dV}{dt} &= (1 - u_2)kI - cV. \end{aligned} \quad (2)$$

These controls phenomenologically represent reduced infection and reduced production of infectious virus. In this simplified formulation, the production control does not distinguish infectious from noninfectious particles. An efficacy of zero leaves the corresponding process untreated;

$$\frac{dT}{dt} = s - dT - \beta TV, \quad \frac{dI}{dt} = \beta TV - \delta I, \quad \frac{dV}{dt} = (1 - u)kI - cV. \quad (3)$$

Equation (3) is the special case of equation (2) with $u_1 = 0$ and $u_2 = u$. It may serve as an effective

simpler integer-order system and does not claim those capabilities. Its contribution is a transparent reassessment of the thesis formulation, including consistent parameters, local stability calculations, treatment thresholds, regenerated trajectories, and numerical verification. Treatment interruption is examined only as a mathematical switching experiment.

2 Mathematical model and computational parameters

2.1 State variables and untreated dynamics

Let $T(t)$ denote uninfected CD4-positive target cells, $I(t)$ infected cells, and $V(t)$ free infectious virus. The notation I replaces T^* in the thesis to distinguish infected-cell density from an equilibrium superscript. Time is measured in days. The state variables are expressed in the illustrative model units used for the numerical comparison. No conversion to a clinical viral-load assay is assumed.

The untreated system is [2-4]

infection, drug concentrations, or drug resistance.

2.2 Treatment formulations

The two-input model assigns an infection-blocking efficacy $u_1(t)$ and a production-blocking efficacy $u_2(t)$, each in $[0,1]$:

increasing efficacy reduces that process. The residual factors are $1 - u_1$ and $1 - u_2$, not the efficacy values themselves. These dimensionless inputs are not prescribed doses in milligrams.

The single-input formulation retained from the thesis is

production-control model, but it is not automatically an exact representation of arbitrary

combined controls acting on both infection and production.

2.3 Consistent parameter selection

Table 1 lists the values used throughout the main computation. The thesis parameter table gives $s = 100$, whereas its MATLAB appendix sets

$s = 10$. The reported infected equilibrium also corresponds to $s = 10$. The latter value is therefore used to reproduce the implemented model. Section 4.5 separately examines the consequences of taking the printed value literally

Table 1. Parameters used in the reproduced computation. Cell and viral units refer to the numerical model scales, not calibrated clinical measurements.

Symbol	Meaning	Value	Dimensional role
s	Target-cell source	10	cell units per day
d	Target-cell loss	0.02	per day
β	Infection coefficient	2.4×10^{-5}	per viral unit per day
k	Viral production	100	viral units per cell unit per day
δ	Infected-cell loss	0.24	per day
c	Viral clearance	2.4	per day

The four untreated initial states are $(500, 10^{-6}, 60)$, $(800, 10, 70)$, $(1000, 50, 30)$, and $(1200, 0, 100)$, reproducing the combinations

in the thesis appendix. Treatment experiments use $(1200, 0, 100)$. These are illustrative initial conditions rather than observations from four patients.

3 Analytical and numerical methods

3.1 Positivity and boundedness

Write $b = (1 - u_1)\beta$ and $p = (1 - u_2)k$ on an interval with constant controls. The common form is

$$\dot{T} = s - dT - bTV, \quad \dot{I} = bTV - \delta I, \quad \dot{V} = pI - cV. \quad (4)$$

On the boundary $T = 0$, $\dot{T} = s \geq 0$; on $I = 0$, $\dot{I} = bTV \geq 0$; and on $V = 0$, $\dot{V} = pI \geq 0$. Thus nonnegative initial data remain nonnegative. The same property holds across the prescribed control switches because the state is continuous at each switch.

Let $N = T + I$ and $\mu = \min(d, \delta)$. Infection cancels from the total-cell balance, giving $\dot{N} = s - dT - \delta I \leq s - \mu N$. Hence $N(t) \leq M$, where $M = \max\{N(0), s/\mu\}$. Since $p \leq k$, comparison with $\dot{V} \leq kM - cV$ gives

$$V(t) \leq V(0)e^{-ct} + \frac{kM}{c}(1 - e^{-ct}). \quad (5)$$

The vector field is locally Lipschitz on each constant-control interval. Positivity and these bounds prevent finite-time escape, providing a unique nonnegative solution over the simulated time horizon.

3.2 Equilibria and reproduction number

For fixed controls, the infection-free equilibrium is $E_0 = (s/d, 0, 0)$. An infected cell survives for an average duration $1/\delta$ and produces infectious

virus at rate p ; virus survives for an average duration $1/c$ and infects target cells at rate $b(s/d)$. The resulting infected-cell reproduction number is

$$\mathcal{R} = \frac{bps}{d\delta c}, \quad \mathcal{R}_0 = \frac{\beta ks}{d\delta c}. \quad (6)$$

At E_0 , one eigenvalue is $-d$. The infected-cell and virus block has characteristic polynomial

$$\lambda^2 + (\delta + c)\lambda + \delta c(1 - \mathcal{R}). \quad (7)$$

Both roots have negative real parts when $\mathcal{R} < 1$. When $\mathcal{R} > 1$, the constant term is negative and one root is positive. Consequently E_0 is locally asymptotically stable below the threshold and If $b, p > 0$ and $\mathcal{R} > 1$, solving equation (4) at equilibrium gives

$$T_e = \frac{\delta c}{bp} = \frac{s/d}{\mathcal{R}}, \quad I_e = \frac{s - dT_e}{\delta}, \quad V_e = \frac{pI_e}{c}. \quad (8)$$

The infected equilibrium is biologically feasible only when $\mathcal{R} > 1$. For the untreated parameters in Table 1, $E_0 = (500, 0, 0)$, $\mathcal{R}_0 = 25/12 \approx$

unstable above it. At $\mathcal{R} = 1$, a zero eigenvalue occurs, so the linearization criterion alone does not determine the nonlinear behavior at the threshold.

2.083333, and $E_e \approx (240, 21.666667, 902.777778)$.

3.3 Local stability of the infected equilibrium

The Jacobian of equation (4) is

$$J(T, I, V) = \begin{pmatrix} -d - bV & 0 & -bT \\ bV & -\delta & bT \\ 0 & p & -c \end{pmatrix}. \quad (9)$$

At the infected equilibrium, $bT_e p = \delta c$. Set $a = d + bV_e = d\mathcal{R}$. The characteristic polynomial becomes

$$\lambda^3 + (a + \delta + c)\lambda^2 + a(\delta + c)\lambda + \delta c(a - d). \quad (10)$$

For $\mathcal{R} > 1$, all coefficients are positive. The remaining cubic Routh-Hurwitz inequality holds because

$$(a + \delta + c)a(\delta + c) - \delta c(a - d) = a^2(\delta + c) + a[(\delta + c)^2 - \delta c] + \delta cd > 0. \quad (11)$$

Thus the infected equilibrium is locally asymptotically stable whenever it is feasible in this model. This local result is not a proof that every admissible initial state converges to it.

Using the full parameter precision, the untreated Jacobian is

$$J(E_e) = \begin{pmatrix} -0.041666667 & 0 & -0.00576 \\ 0.021666667 & -0.24 & 0.00576 \\ 0 & 100 & -2.4 \end{pmatrix}, \quad (12)$$

with eigenvalues -2.64181683 and $-0.01992492 \pm 0.06578008i$. The equilibrium has stable damped oscillatory modes, often described as a stable focus or spiral-type equilibrium, rather than a stable node. For a perturbation $\xi = x - E_e$, the local

approximation is $\xi(t) = \exp[J(E_e)t]\xi(0)$.

Hartman-Grobman gives local qualitative equivalence near this hyperbolic equilibrium; it does not make the linearized solution globally accurate.

3.4 Treatment thresholds and model comparison

For constant two-input efficacy,

$$\mathcal{R}_{\text{two}} = (1 - u_1)(1 - u_2)\mathcal{R}_0. \quad (13)$$

For the single-input formulation, $\mathcal{R}_{\text{single}} = (1 - u)\mathcal{R}_0$. The infection-free equilibrium is locally stable when the relevant reproduction number is below one. Under equal two-input efficacies $u_1 = u_2 = q$, the strict threshold is $q > 1 - \mathcal{R}_0^{-1/2} \approx 0.307180$. For a single production input, it is $u > 1 - \mathcal{R}_0^{-1} = 0.52$.

Matching the reproduction numbers requires

$$u = 1 - (1 - u_1)(1 - u_2). \quad (14)$$

This relation matches the product bp , but equation (2) still changes infection whereas equation (3) does not. For a positive infected equilibrium with matched $\mathcal{R}$, T_e and I_e agree, but $V_{e,\text{single}} = (1 - u_1)V_{e,\text{two}}$. Transient trajectories can also differ. The threshold comparison therefore measures model behavior under efficacy parameters, not comparative clinical potency of drug regimens.

3.5 Numerical integration and verification

The classical fourth-order Runge-Kutta method [6] is applied to the vector field f with step $h = 0.1$ day:

$$\begin{aligned} K_1 &= f(t_n, x_n), \\ K_2 &= f(t_n + h/2, x_n + hK_1/2), \\ K_3 &= f(t_n + h/2, x_n + hK_2/2), \\ K_4 &= f(t_n + h, x_n + hK_3), \\ x_{n+1} &= x_n + \frac{h}{6}(K_1 + 2K_2 + 2K_3 + K_4). \end{aligned} \quad (15)$$

Untreated trajectories are computed to day 400. Treatment starts at day 150 and either ends at day 400 or continues to day 800. In interrupted runs, $u_1 = u_2 = 0$ after day 400. Each constant-control interval is integrated separately and the endpoint state initializes the next interval. This avoids sampling different control values within a Runge-Kutta step at a discontinuity. The final step before a switch uses the preceding interval's controls; the first step after it uses the subsequent controls. Verification uses $h = 0.05$ and 0.025 day and an independent DOP853 integration with relative tolerance 10^{-11} and absolute tolerance 10^{-13} .

Let x^{ref} denote the adaptive reference and $S_j = \max\{1, \max_n |x_j^{\text{ref}}(t_n)|\}$. The maximum normalized discrepancy is $\max_{n,j} |x_j(t_n) - x_j^{\text{ref}}(t_n)|/S_j$. Step differences use the same component scales at common grid points. An empirical order is estimated as $\log_2(E_{h,h/2}/E_{h/2,h/4})$. These measures test numerical consistency; the adaptive reference is not an exact solution. Finite values and nonnegative states are checked in every generated RK4 run. RK4 is not generally positivity-preserving for arbitrary step sizes.

4 Results

4.1

Untreated trajectories

All four simulated initial states approach the infected equilibrium over the 400-day window (Figure 1). The trajectory from $(1200, 0, 100)$ has state $(239.994964, 21.702297, 904.262992)$ at

day 400 and $(239.999958, 21.666674, 902.778110)$ at day 800. The infected-cell and viral components remain positive after infection begins.

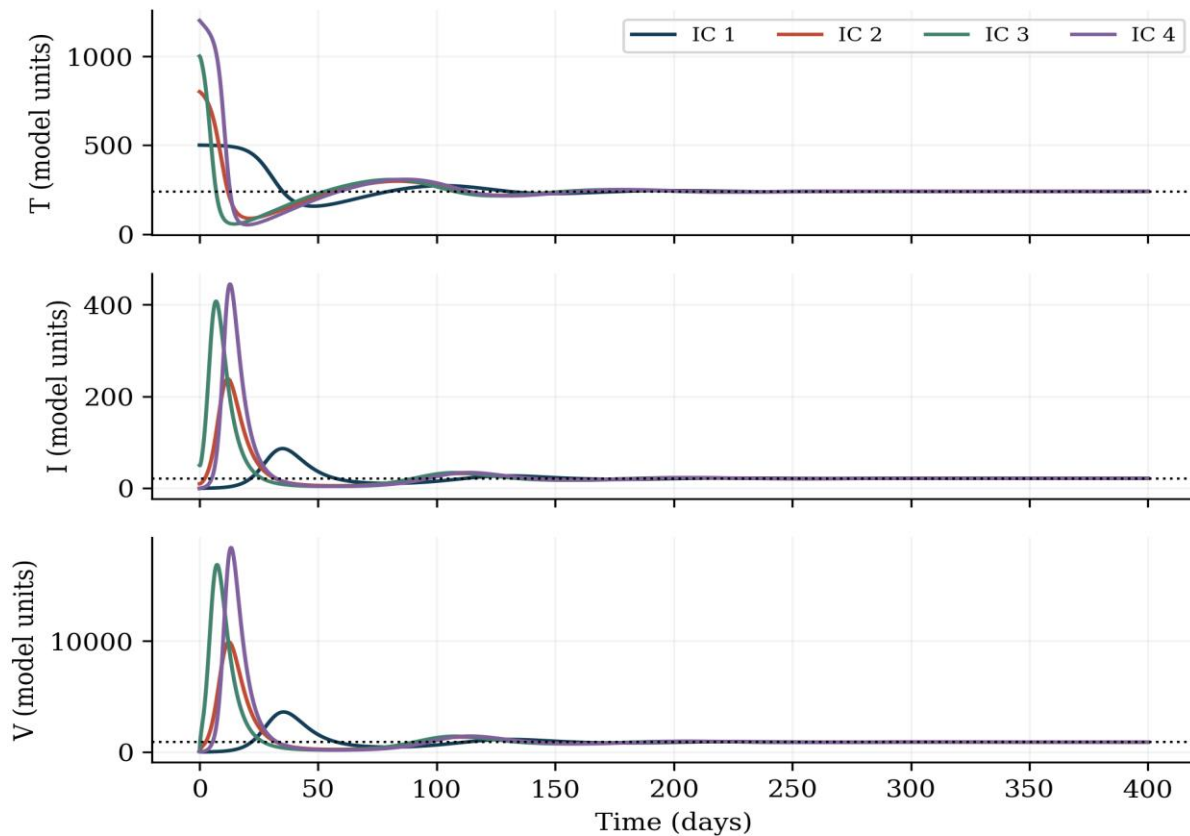


Figure 1. Untreated trajectories for the four initial conditions in Section 2.3. Dotted horizontal lines indicate the infected equilibrium; IC 1 to IC 4 follow the listed order.

The damped oscillations are consistent with the computed complex eigenvalues. They arise from feedback between target-cell availability, infection, and viral production. The model contains no explicit immune-response compartment; the decline from a viral peak should therefore not be

described as a directly simulated immune-cell response. Similarly, convergence to a mathematical equilibrium does not establish a clinical latency period or predict progression to AIDS.

4.2 Two treatment inputs

For equal efficacies $q = 0.2$, 0.3 , and 0.5 , the reproduction numbers are 1.333333 , 1.020833 , and 0.520833 , respectively. The first two settings remain above the infection-free stability threshold. Their infected equilibria are approximately $(375, 10.416667, 347.222222)$ and $(489.795918, 0.850340, 24.801587)$. The $q = 0.5$ setting is below threshold and stabilizes the infection-free equilibrium locally.

Figure 2 compares interruption at day 400 with continuous treatment. At day 400, the viral states for $q = 0.2$, 0.3 , and 0.5 are approximately 311.297704 , 2.012754 , and 1.859404×10^{-11} . In the $q = 0.3$ continuous run, V rises from its day-400 value to 8.786335 by day 800. This is compatible with an above-threshold infected equilibrium and shows why an initially strong decline does not establish asymptotic elimination.

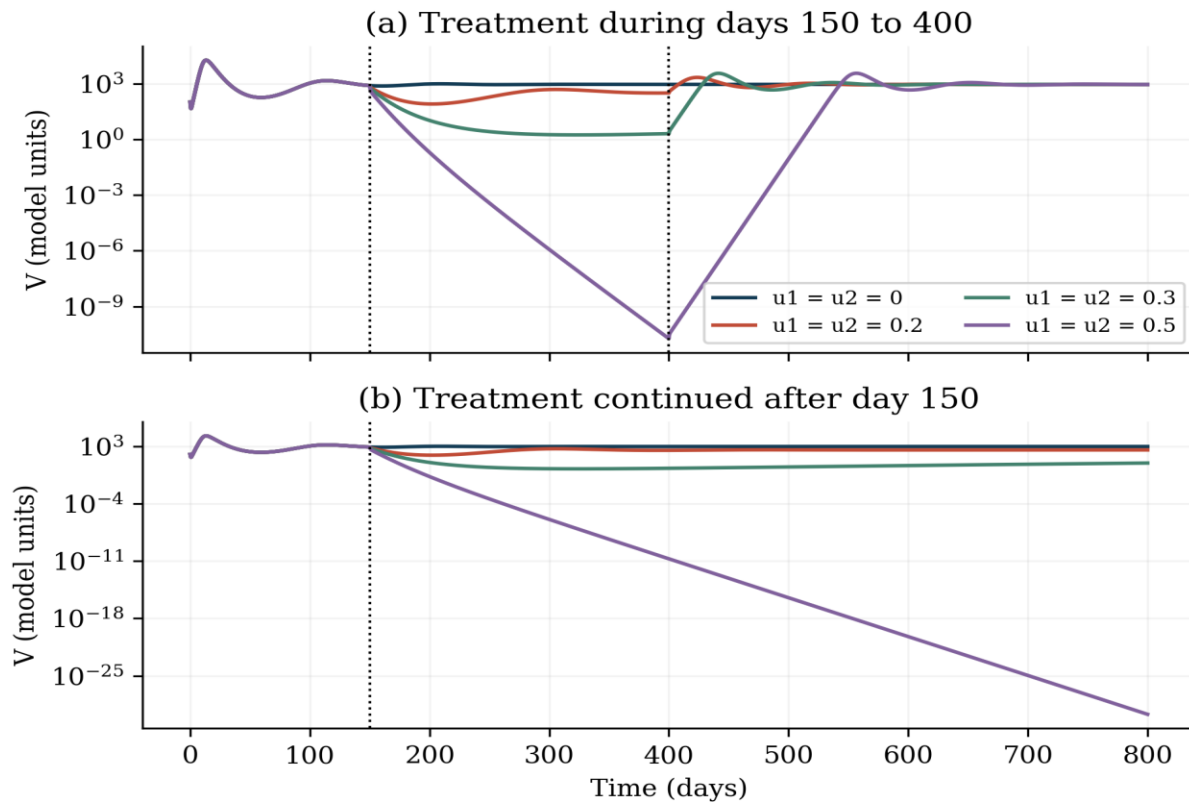


Figure 2. Viral trajectories under equal two-input efficacies. Panel a withdraws treatment at day 400; panel b continues treatment after day 150. The logarithmic scale displays very small positive deterministic states.

After withdrawal, all interrupted runs return toward the untreated infected equilibrium. For $q = 0.5$, the viral state is approximately 891.087103 at day 800, while continued treatment gives about 2.066476×10^{-30} . Such extremely small deterministic concentrations must not be interpreted as biologically meaningful fractional virions or a clinical cure. Their subsequent regrowth reflects the continuous-state equations, which preserve a positive residual infection.

4.3 Single production input

The single-input efficacy values $u = 0.4, 0.6$, and 0.7 give reproduction numbers 1.25, 0.833333, and 0.625. At $u = 0.4$, the infected equilibrium remains feasible and is (400, 8.333333, 208.333333). Its day-400 numerical state is (390.346091, 8.306620, 208.127428), indicating proximity to that equilibrium during the treatment interval. The larger efficacy values are below the reproduction threshold and drive infection to much smaller model states before withdrawal (Figure 3).

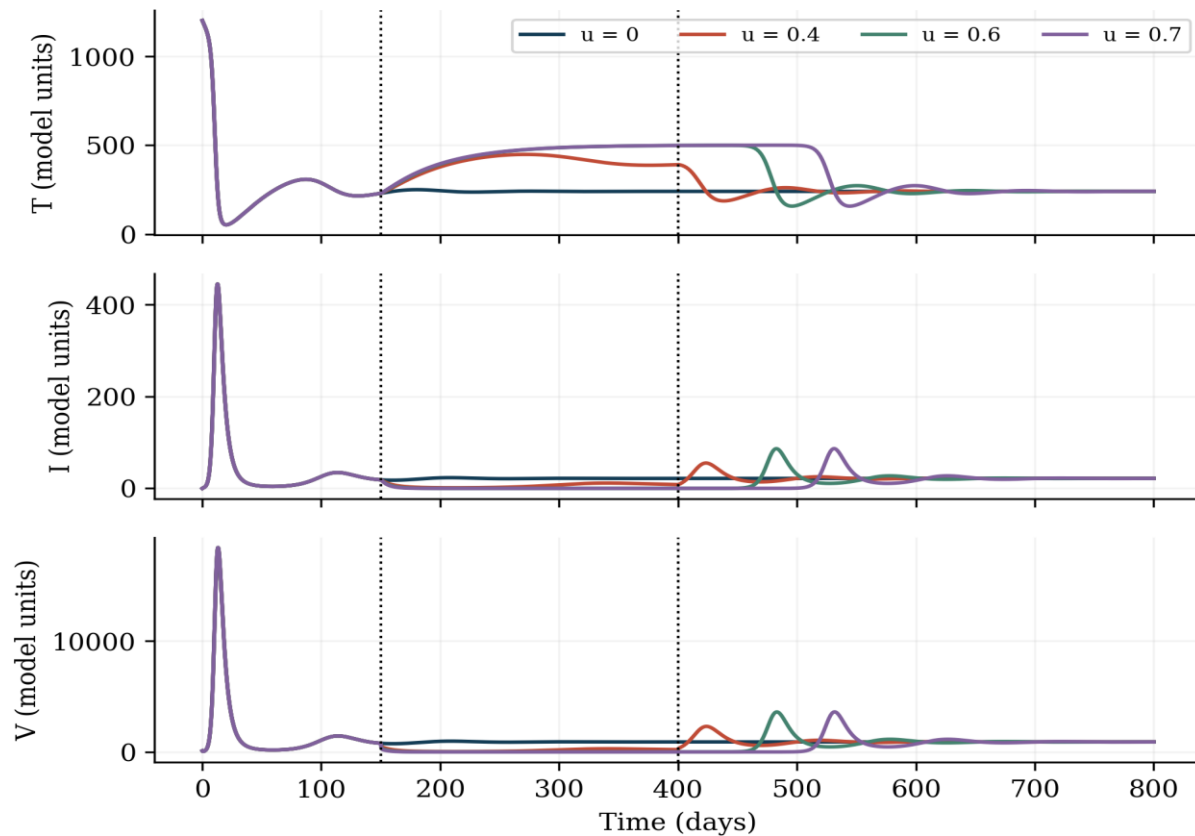


Figure 3. Single-input trajectories with production efficacies 0, 0.4, 0.6, and 0.7. Treatment is active only during days 150 to 400.

At day 400, viral states for $u = 0.6$ and 0.7 are approximately 1.388545×10^{-4} and 2.701804×10^{-9} . After interruption, both regrow toward the untreated equilibrium, reaching approximately 902.278483 and 903.691514 at day 800. The timing depends on efficacy, duration, and the residual state at withdrawal. These runs do not support a universal

claim that the single-input model always rebounds faster than the two-input model.

4.4 Matching the reproduction number

To make the comparison explicit, Figure 4 uses $u_1 = u_2 = 0.5$ in equation (2) and $u = 0.75$ in equation (3). Both settings give $\mathcal{R} = 0.520833$. Nevertheless, their trajectories differ because infection is reduced directly only in the two-input formulation

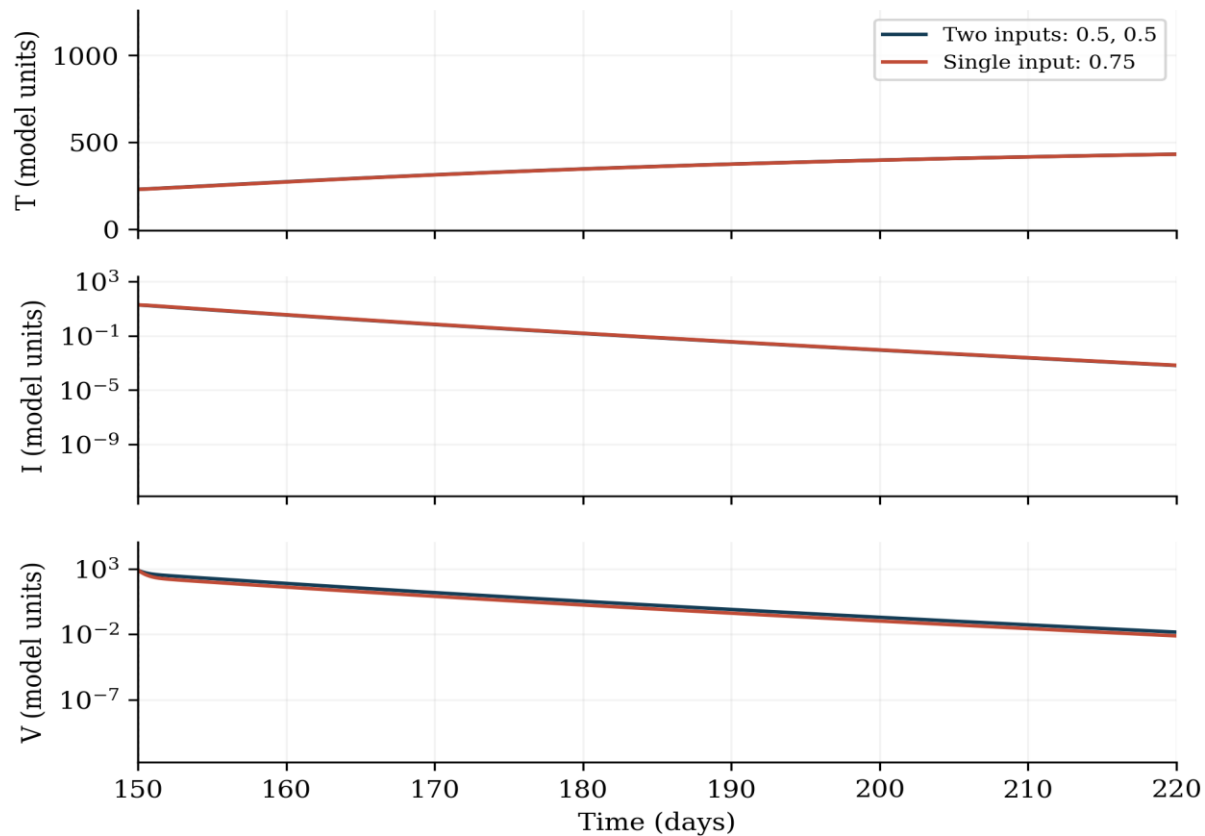


Figure 4. Comparison during the first 70 days of treatment: two-input efficacy 0.5 in each process and single-input efficacy 0.75. The reproduction numbers agree, but the transient states do not. Infected-cell and viral axes are logarithmic.

At treatment initiation, both formulations share approximately $T = 229.400514$, $I = 18.645199$, and $V = 780.153955$. Their instantaneous infected-cell derivatives differ by $0.5\beta TV$ because of the infection control. Thus equality of the reproduction number cannot imply equality of the state evolution. If the formulations are to be used interchangeably for a particular application, that replacement needs an additional output-based approximation criterion or data-based assessment.

4.5 Consequences of the printed source rate

Taking the thesis table value $s = 100$ gives $\mathcal{R}_0 = 20.833333$ and the untreated infected equilibrium $(240, 396.666667, 16527.777778)$. The target-cell equilibrium remains 240 because its formula is independent of s , whereas infected

cells and virus change substantially. Equal two-input efficacy would then need to exceed approximately 0.780911 , and a single production efficacy would need to exceed 0.952 for local infection-free stability.

These values follow from the same equilibrium and threshold formulas. They are an analytical parameter comparison, not an additional patient-data analysis. The difference demonstrates why identifying the source rate is essential: the printed and implemented values imply very different control requirements. It also prevents the article from combining an $s = 100$ table with $s = 10$ trajectories.

4.6 Numerical consistency

Table 2 summarizes verification over the complete 800-day trajectories. All maximum normalized

discrepancies from the adaptive reference are below 10^{-6} , and the empirical orders are close to four. The results support the selected step size for

the stated state scales and time windows. They do not provide an uncertainty interval for biological parameters or a reliable pointwise relative error for near-zero viral states.

Table 2. RK4 verification at common time points. Errors are normalized by the component scales defined in Section 3.5.

Scenario	$E_{0.1,0.05}$	$E_{0.05,0.025}$	Empirical order	Reference discrepancy
Untreated	2.199×10^{-7}	1.428×10^{-8}	3.945	2.351×10^{-7}
Two inputs 0.5 and 0.5	2.496×10^{-7}	1.428×10^{-8}	4.127	8.059×10^{-7}
Single input 0.7	3.724×10^{-7}	2.092×10^{-8}	4.154	3.946×10^{-7}
Matched single input 0.75	3.947×10^{-7}	2.219×10^{-8}	4.153	9.386×10^{-7}

5 Discussion

The analytical and numerical results explain several features of the thesis model. Above the reproduction threshold, an infected equilibrium exists and is locally stable. Below the threshold, the infection-free equilibrium becomes locally stable. Treatment changes the effective infection and production parameters, and withdrawing treatment restores the untreated threshold. These relationships give a precise model interpretation of suppression and rebound.

The two-input and single-input thresholds must be read alongside their mechanisms. Equal numerical efficacies in two separate processes multiply their residual effects, whereas a single production input changes only one process. A lower numerical threshold for equal two-input controls does not establish that a particular clinical combination requires a lower administered dose. The model has no pharmacokinetic or pharmacodynamic relation between the input parameters and medication amounts.

The source-rate correction is substantive. It changes the reproduction number by a factor of ten and alters infected-cell and viral equilibria. Recalculation from the full parameter values also produces eigenvalues different from the rounded values reported in the thesis. The agreement between the analytical equilibrium, the

implemented parameter set, and the regenerated long-time states is therefore more informative than retaining the original numbers without checking them.

Several limitations constrain biological interpretation. The model omits latent reservoirs, immune effector cells, resistance, stochastic extinction, and treatment absorption or decay. It assumes constant rates and immediate efficacy changes at the prescribed switch times. No patient data are fitted, and the numerical state scales are not calibrated to assay units. Viral suppression below an arbitrary plotted value consequently cannot be translated into a clinical detection threshold. In particular, tiny positive deterministic states can later regrow, while an exactly infection-free state cannot spontaneously generate infection in these equations.

The result is a reproducible computational reassessment of an established model. A patient-specific study would require consistently scaled observations, parameter estimation, identifiability analysis, and validation on data not used for fitting. A mechanistic extension could introduce latent infection or drug concentration dynamics, but its additional parameters would need independent justification. The current results provide a baseline against which such extensions could be evaluated.

6 Conclusion

The thesis has been recast as a focused analytical and numerical study of three established HIV formulations. Using the source rate supported by the thesis code gives an untreated reproduction number of 2.083333 and an infected equilibrium of approximately (240,21.666667,902.777778). The equilibrium is locally asymptotically stable with damped oscillatory modes. Constant controls yield explicit thresholds, and regenerated RK4 simulations agree closely with refined computations and an independent solver. Treatment withdrawal produces rebound in the tested positive-state trajectories. Matching the reproduction numbers of the one-input and two-input formulations preserves the threshold but does not preserve their trajectories. These conclusions concern the stated model and parameter set; clinical validation remains a separate requirement.

Data and code availability

The supplementary computational package contains the Python implementation, parameter values, initial conditions, regenerated figures, trajectory files, and numerical verification summary. It generates illustrative model data and contains no patient records.

Acknowledgements

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REFERENCES

- [1] A. S. Perelson, A. U. Neumann, M. Markowitz, J. M. Leonard, and D. D. Ho, "HIV-1 dynamics in vivo: virion clearance rate, infected cell life-span, and viral generation time," *Science*, vol. 271, no. 5255, pp. 1582-1586, 1996. <https://doi.org/10.1126/science.271.5255.1582>
- [2] I. K. Craig and X. Xia, "Can HIV/AIDS be controlled? Applying control engineering concepts outside traditional fields," *IEEE Control Systems Magazine*, vol. 25, no. 1, pp. 80-83, 2005. <https://doi.org/10.1109/MCS.2005.1388805>
- [3] L. Moysis, I. Kafetzis, and M. Politis, "A dynamic model for HIV infection," in *1st Panhellenic Conference of M.Sc. and Ph.D. New Holders in Mathematics*, University of Ioannina, Greece, May 27-28, 2016, special volume, pp. 50-58. https://www.researchgate.net/publication/303684537_A_dynamic_model_for_HIV_infection
- [4] A. Rab, *Mathematical modelling and simulation of HIV dynamics*, BS Mathematics thesis, Department of Mathematics and Social Science, Sukkur IBA University, Pakistan, 2019. Source: author-supplied thesis.
- [5] P. Sardar, B. Ranjit, S. Biswas, S. M. Boulaaras, K. Allali, B. Pal, and K. P. Das, "Modeling NRTIs and PIs class drug therapy on the dynamics of HIV infection with real patient data analysis and optimized control strategy," *Scientific Reports*, vol. 16, article 4580, 2026. <https://doi.org/10.1038/s41598-025-34601-3>
- [6] R. L. Burden and J. D. Faires, *Numerical Analysis*, 9th ed. Brooks/Cole, Cengage Learning, 2011. ISBN 978-0-538-73351-9.