Exploring Parameter Estimation Techniques for HIV Modeling: From Simulation Data to Real-world Applications

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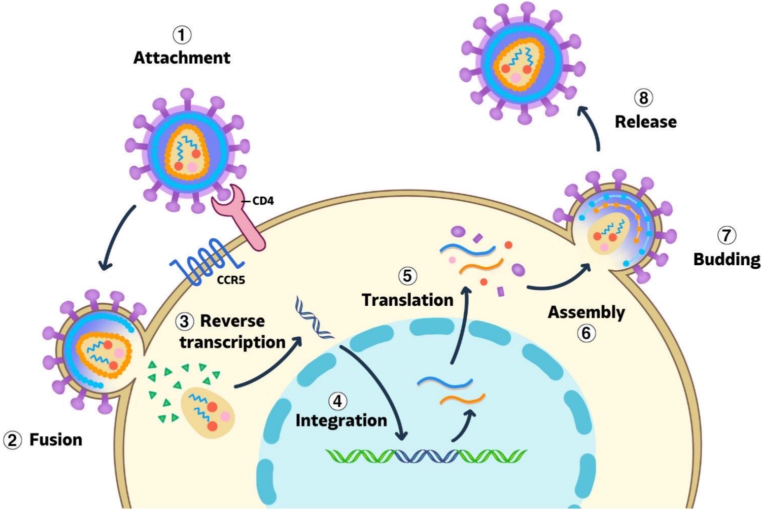
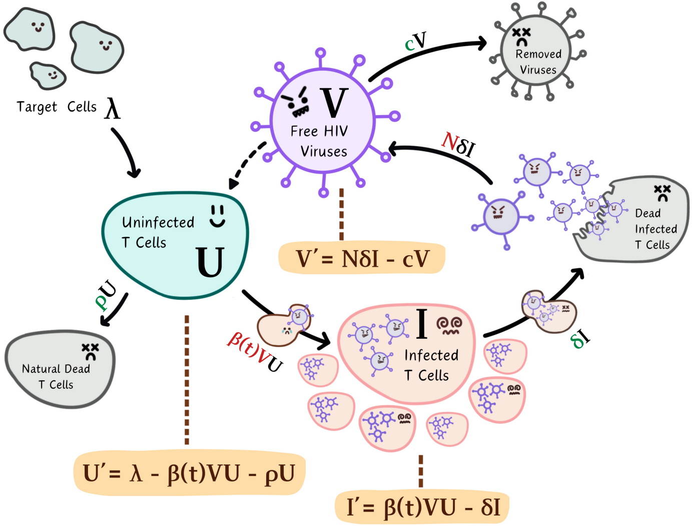
Introduction

- The role of CD4+T cells is to activate immune cells.
- HIV replicates in CD4+T and continually infects others.
- We evaluate the activity status of virus by monitoring the quantity of CD4+T.

Action Process



Schematic



Target Cells λ
cV
Removed Viruses
V
Free HIV Viruses
NδI
Uninfected T Cells
U
V′= NδI - cV
Dead Infected T Cells
ρU
β(t)VU
I
Infected T Cells
δI
Natural Dead T Cells
U′= λ - β(t)VU - ρU
I′= β(t)VU - δI

Basic model

$$\frac{dU}{dt} = \lambda - \beta(t)VU - \rho U,$$
$$\frac{dI}{dt} = \beta(t)VU - \delta I,$$
$$\frac{dV}{dt} = N\delta I - cV.$$

Symbol	Description	Initial Value
U	Density of susceptible target cells	$U_0 = 600$ cells $\cdot\mu L^{-1}$
I	Density of cells infected by the virus	$I_0 = 30$ cells $\cdot\mu L^{-1}$
V	Density of free viruses	$V_0 = 10^5$ copies $\cdot mL^{-1}$
β	Infection rate of target cells by free viruses	$\beta_0 = 9 \times 10^{-6} mL \cdot copies^{-1} \cdot day^{-1}$
λ	Production rate of target cells	36 cells $\cdot\mu L^{-1} \cdot day^{-1}$
ρ	Death rate of uninfected target cells	0.108 day^{-1}
δ	Death rate of target cells	0.5 day^{-1}
N	Number of virions produced from each infected cell	10^3 copies $\cdot\mu L \cdot cell^{-1} \cdot mL^{-1}$
c	Clearance rate of virus	3 day^{-1}

[Liang et al., 2010]

HIV MODELS

Nonautonomous system

$$\frac{dU}{dt} = \lambda - \beta(t)VU - \rho U,$$
$$\frac{dI}{dt} = \beta(t)VU - \delta I,$$
$$\frac{dV}{dt} = N\delta I - cV.$$

Equilibria

$$E^* = (U^*, I^*, V^*) = \left(\frac{c}{\beta N}, (\mathcal{R}_0 - 1)\frac{\rho c}{\beta\delta N}, (\mathcal{R}_0 - 1)\frac{\rho}{\beta}\right), \text{ where } \mathcal{R}_0 = \frac{\beta\lambda N}{\rho c}$$

[Perelson et al., 1996]

HIV MODELS

β system

$$\beta(t) = a(1 - d\cos(bt)), \quad a = 9 \times 10^{-5}, \quad b = \frac{\pi}{1000}, \quad d = 0.9$$

$$\beta'(t) = abd * \sin(bt)$$

$$\beta''(t) = ab^2d(\cos(bt)) = ab^2d(1 - \frac{\beta(t)}{a})$$

β system change to ω system

$\omega_1(t) = \beta(t) = a(1 - d * \cos(bt))$, $\qquad \omega_1(0) = 9 \times 10^{-6}$

$\omega_1' = \omega_2 = \beta'(t) = abd * \sin(bt)$, $\qquad \omega_2(0) = 0$

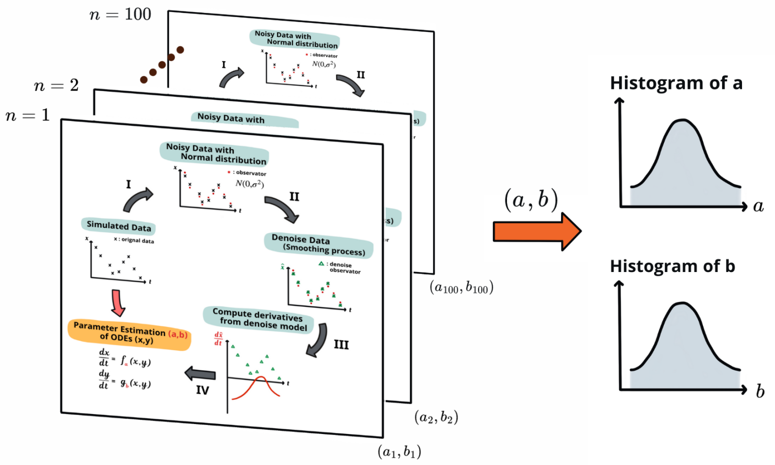
$\omega_2' = \beta''(t) = ab^2d(1 - \frac{\omega_1}{a})$

HIV MODELS

Autonomous system

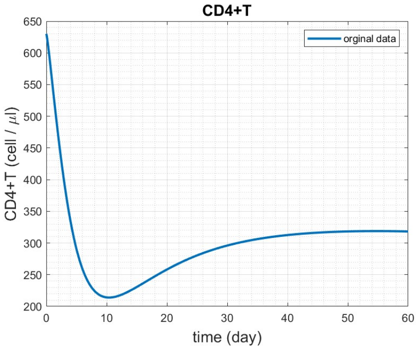
$$
\begin{aligned}
U' &= \lambda - \omega_1 VU - \rho U, & U(0) &= 600, \\
I' &= \omega_1 VU - \delta I, & I(0) &= 30, \\
V' &= N\delta I - cV, & V(0) &= 10^5, \\
\omega_1' &= \omega_2, & \omega_1(0) &= 9 \times 10^{-6}, \\
\omega_2' &= \omega_1'' = ab^2 d \left(1 - \frac{\omega_1}{a}\right), & \omega_2(0) &= 0.
\end{aligned}
$$

Flow Chart

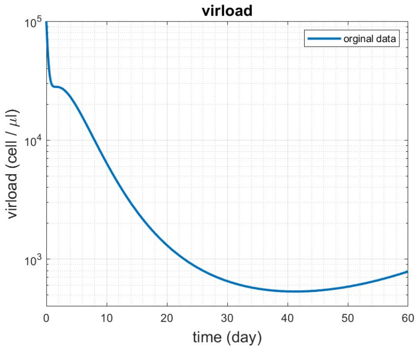


Flow chart with $\mathrm{N}(0, \sigma^2)$.

Simulation (original data)

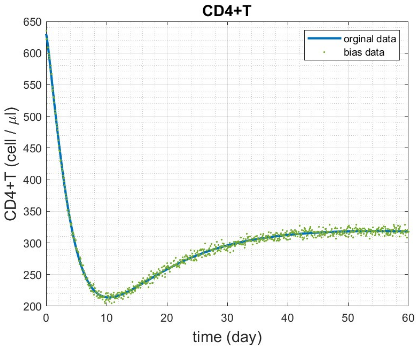


(a) CD4+T (U+I)

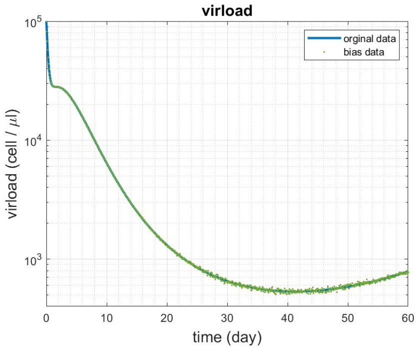


(b) viral load (V)

Simulation (bias data)

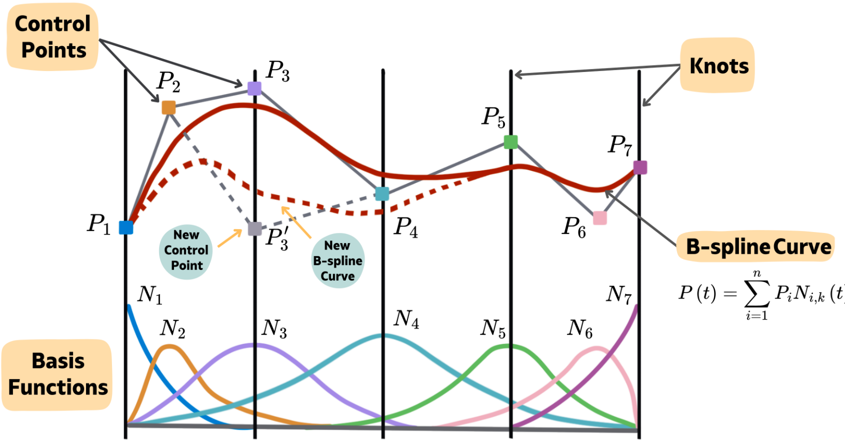


(c) CD4+T (U+I)



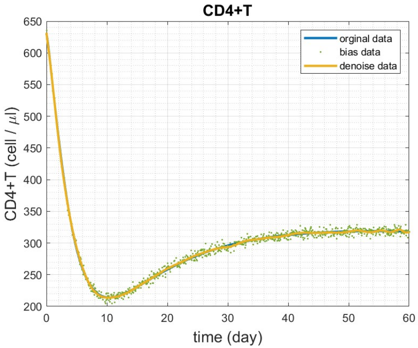
(d) viral load (V)

B-spline

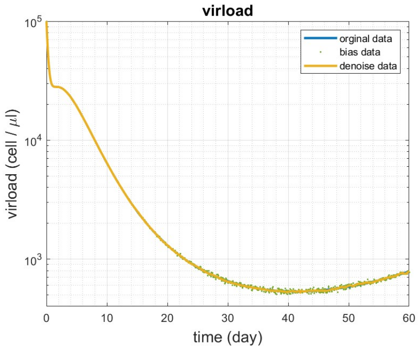


$$P(t) = \sum_{i=1}^{n} P_i N_{i,k}(t)$$

Simulation (denoise data)



(e) CD4+T (U+I)



(f) viral load (V)

Parameter Estimation

Least Square Method

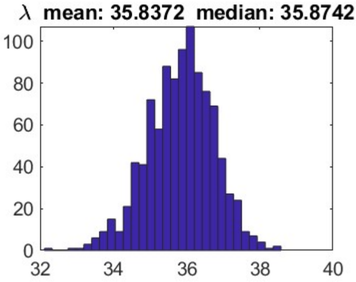
$$\frac{dT}{dt} = \lambda - \rho(T - I) - \delta I,$$
$$\frac{dV}{dt} = a_0 + a_1 T(t) + a_2 T'(t) - cV(t),$$

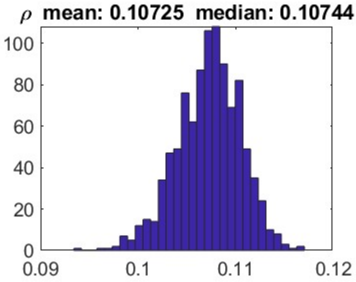
where $a_0 = -\frac{N\delta\lambda}{\rho-\delta}$, $a_1 = \frac{N\delta\rho}{\rho-\delta}$, $a_2 = \frac{N\delta}{\rho-\delta}$.

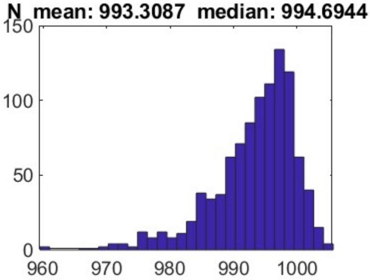
$$\frac{dU}{dt} = \lambda - \beta(t)VU - \rho U,\ \frac{dI}{dt} = \beta(t)VU - \delta,\ \frac{dV}{dt} = N\delta I - cV.$$

$$\begin{bmatrix} \vdots & \vdots & \vdots \\ 1 & T & T' \\ \vdots & \vdots & \vdots \end{bmatrix} \begin{bmatrix} a_0 \\ a_1 \\ a_2 \end{bmatrix} = \begin{bmatrix} \vdots \\ V' + CV \\ \vdots \end{bmatrix}$$

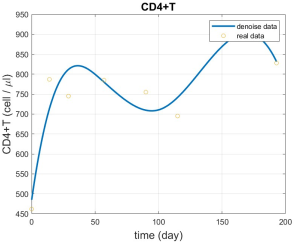
Histogram of Parameter Estimations



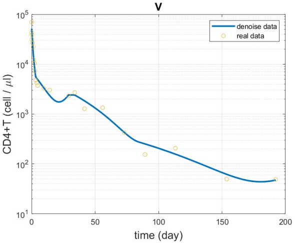




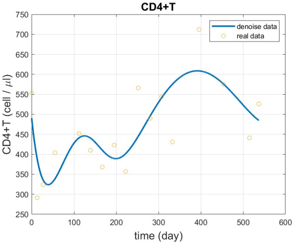
Real data



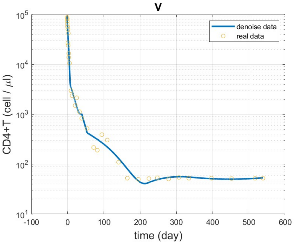
(g) CD4+T(patient1)



(h) viral load(patient1)



(i) CD4+T(patient2)



(j) viral load(patient2)

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Thank you for listening!