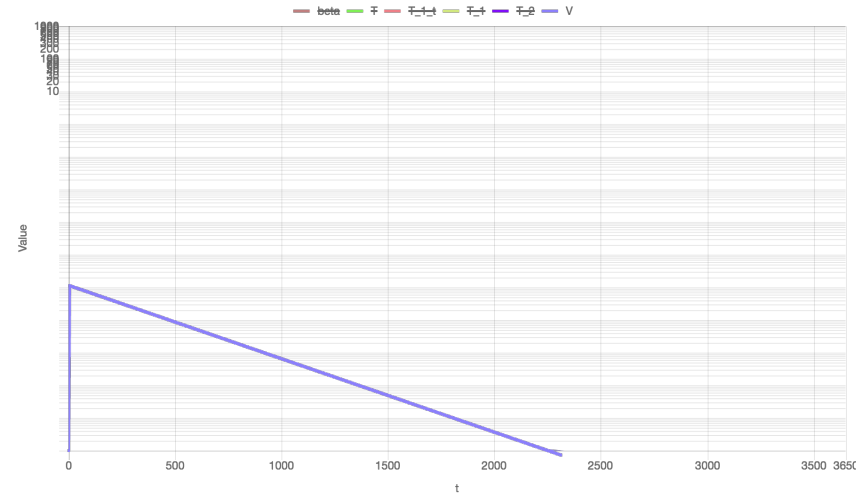


Replication of Figure 2 in simulation of population changes of T cells (T), latently infected T cells (T\*), actively infected T cells (T\*\*) and free viruses (V) performed by Perelson, Alan S. et al. Mathematical biosciences 114.1 (1993): 81-125. From these simulation results, it was confirmed that the population change was qualitatively the same as that of Figure 2 in the paper. The parameters of the model in the simulation were the same as in Table 1 of the paper, and only N was simulated at 1000, 1200, and 1400 as described in the paper. The simulation engine used was COPASI, with an end time of 3650 (10 years), a number of time points of 1000, and an absolute tolerance of 1.0e-12.

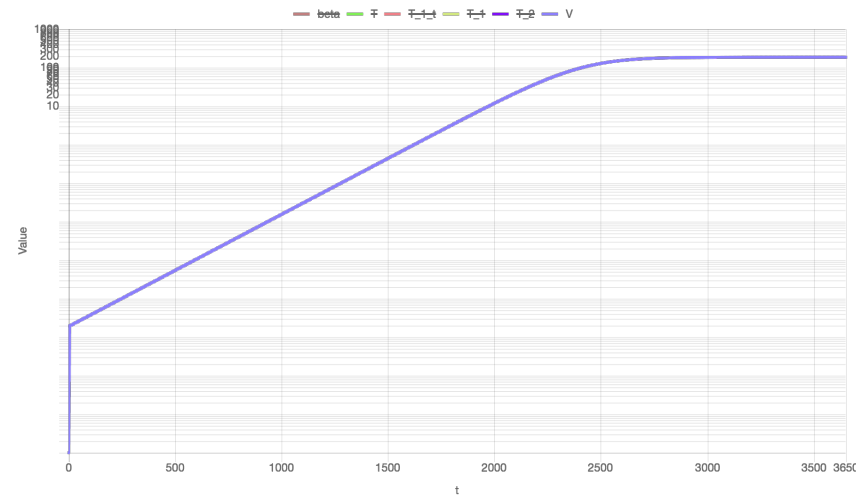
S2

V

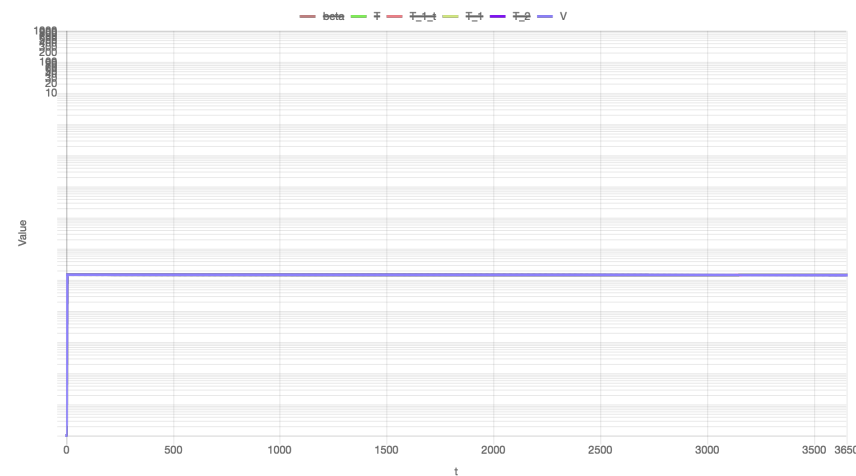
N = 600



N = 1000



N = 774



Replication of Figure 4 in simulation of population changes of free viruses (V) performed by Perelson, Alan S. et al. Mathematical biosciences 114.1 (1993): 81-125. From these simulation results, it was confirmed that the population change was qualitatively the same as that of Figure 4 in the paper. The parameters of the model in the simulation were the same as in Table 1 of the paper, and only N was simulated at 600, 774, and 1000 as described in the paper. The simulation engine used was COPASI, with an end time of 3650 (10 years), a number of time points of 1000, and an absolute tolerance of  $1.0e^{-12}$ .

S3

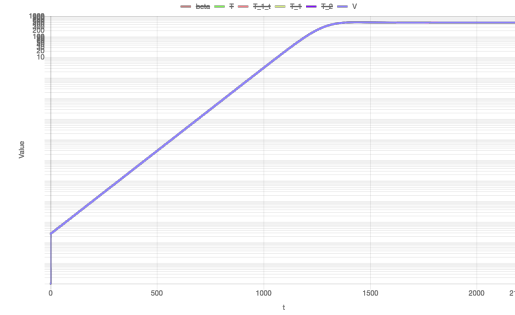
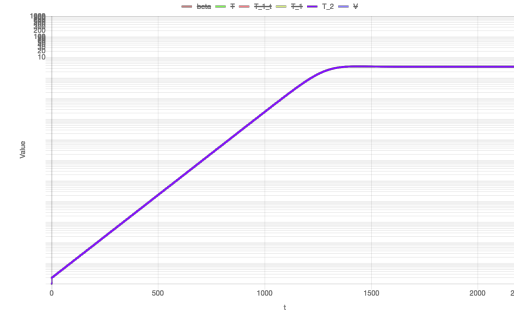
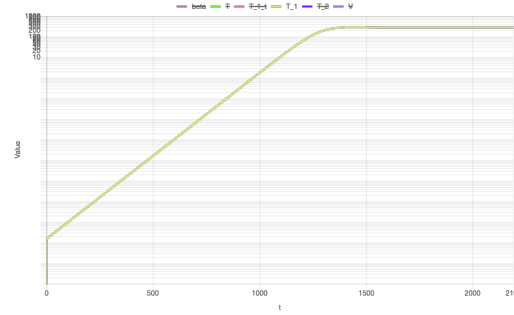
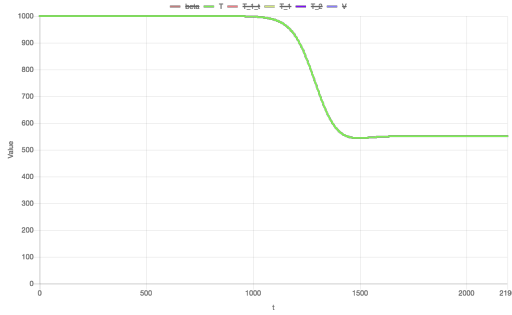
T

T\*

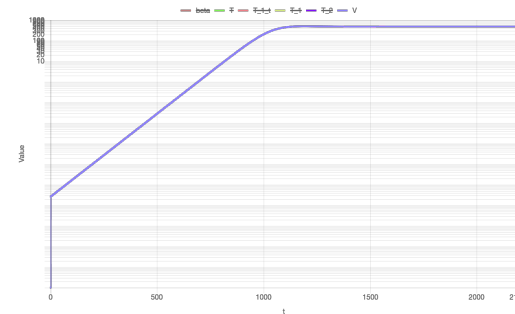
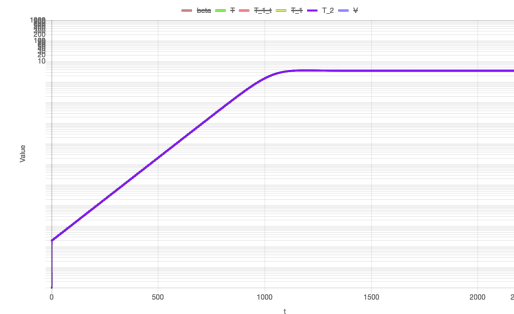
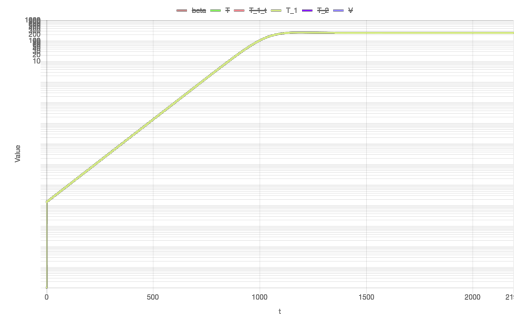
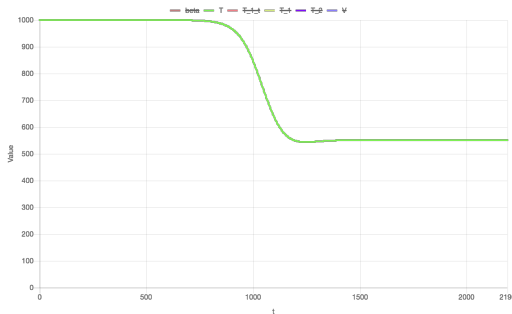
T\*\*

V

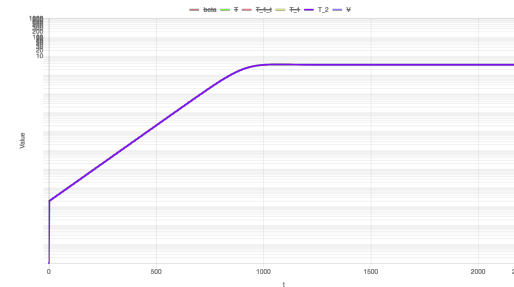
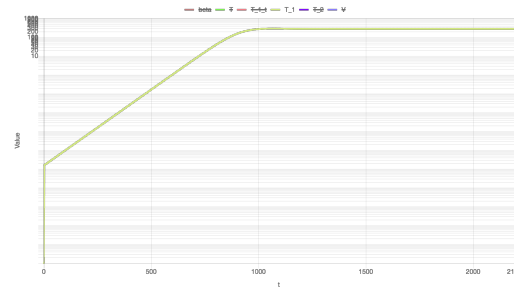
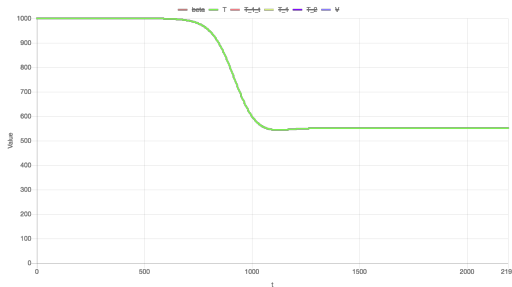
$V_0 = 10^{-6}$



$V_0 = 10^{-4}$

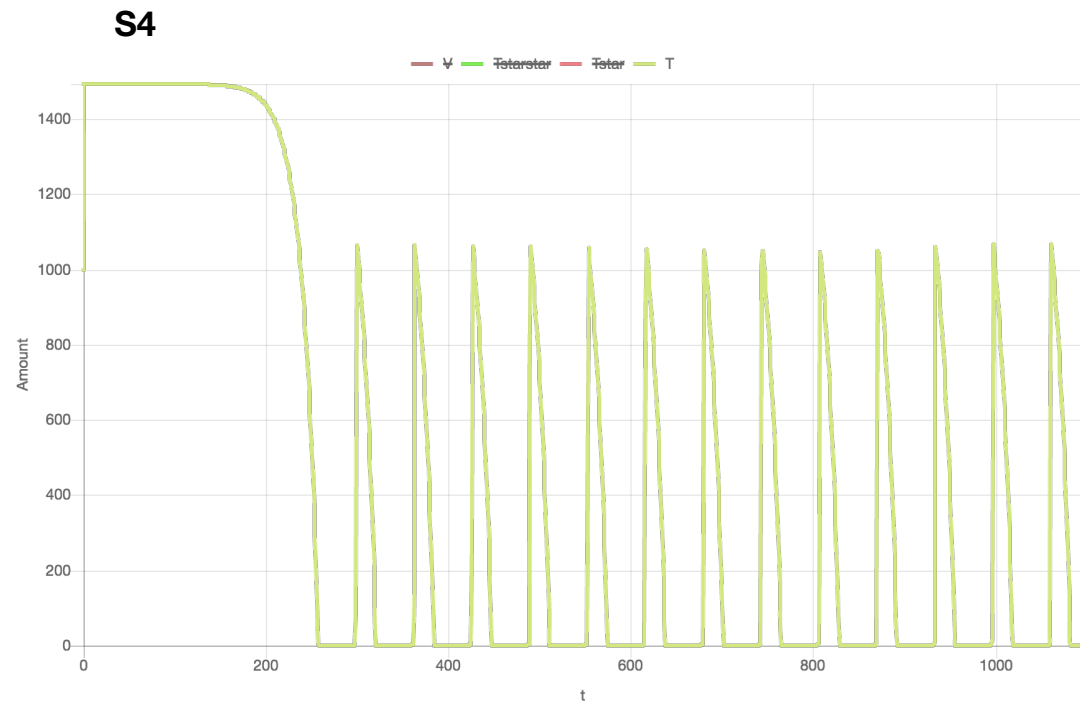


$V_0 = 10^{-2}$

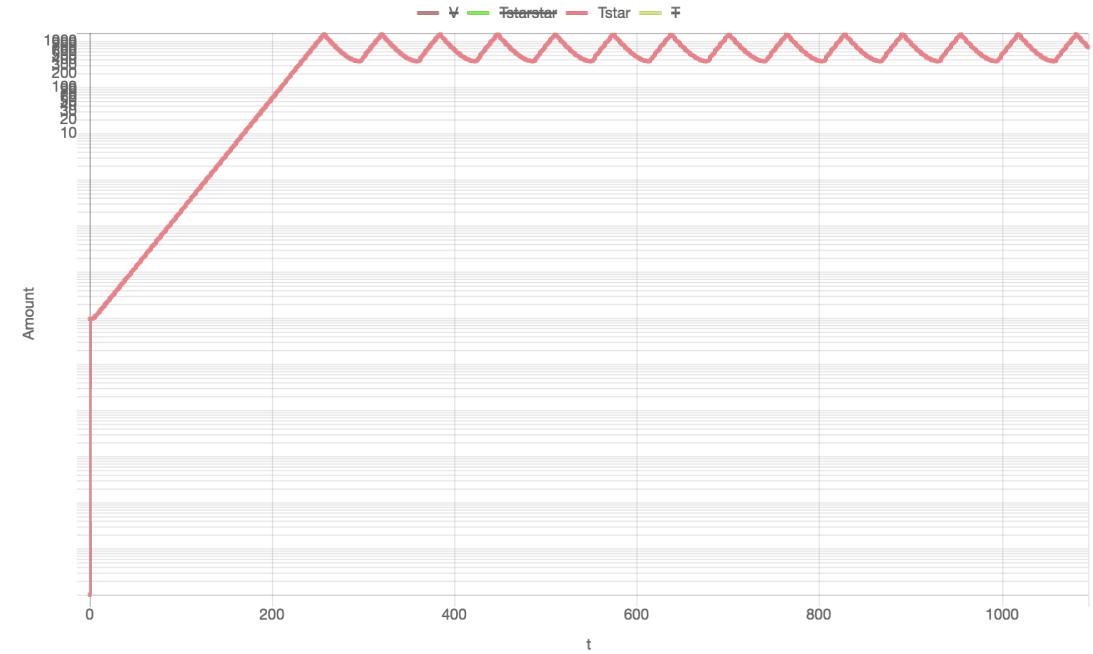


Replication of Figure 7 in simulation of population changes of free viruses (V) performed by Perelson, Alan S. et al. Mathematical biosciences 114.1 (1993): 81-125. From these simulation results, it was confirmed that the population change was qualitatively the same as that of Figure 7 in the paper. The parameters of the model in the simulation were the same as in Table 1 of the paper, and only  $V_0$  was simulated at  $10^{-6}$ ,  $10^{-4}$ , and  $10^{-2}$  as described in the paper. The simulation engine used was COPASI, with an end time of 2190 (6 years), a number of time points of 1000, and an absolute tolerance of  $1.0e^{-12}$ .

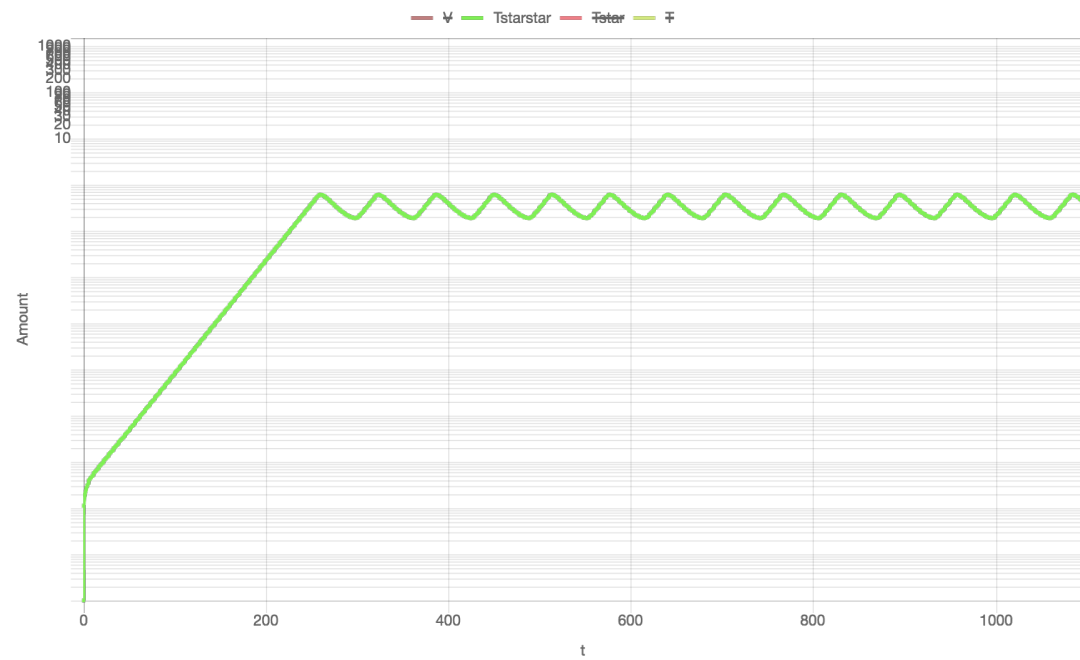
T



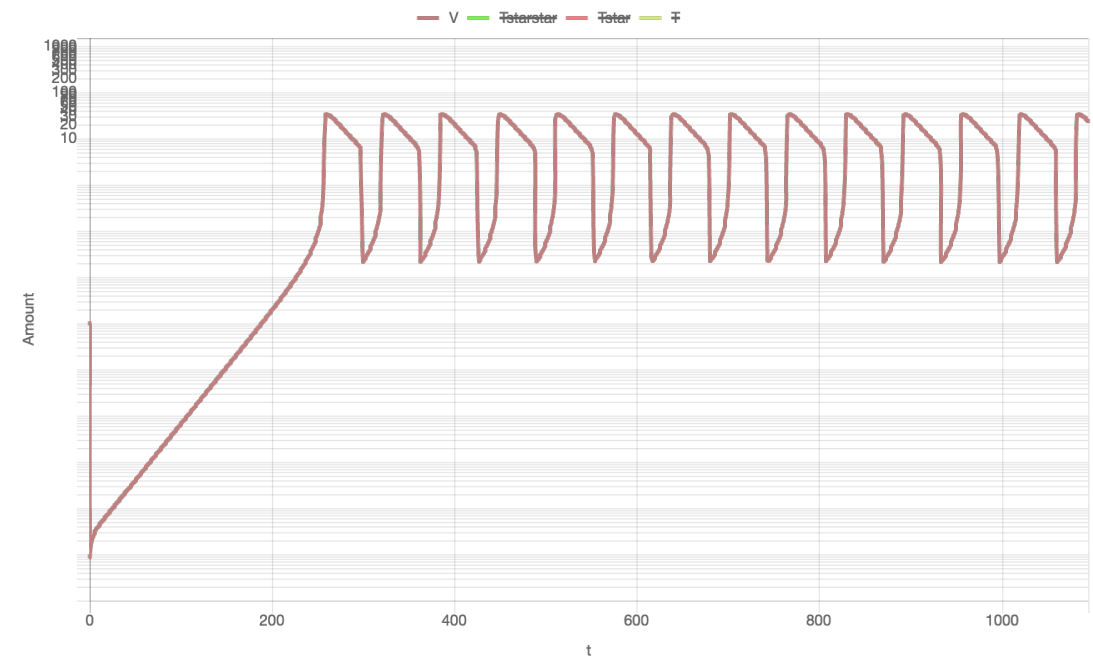
T\*



T\*\*



V



Replication of Figure 8 in simulation of population changes of free viruses (V) performed by Perelson, Alan S. et al. Mathematical biosciences 114.1 (1993): 81-125. From these simulation results, it was confirmed that the population change was qualitatively the same as that of Figure 8 in the paper. The parameters of the model in the simulation were the same as in Table 2 of the paper. The simulation engine used was COPASI, with an end time of 1095 (3 years), a number of time points of 1000, and an absolute tolerance of  $1.0e^{-12}$ .

Theoretical Unstable  
Fixed Point

=

$$\begin{cases} V = 0 \\ Tstarstar = 0 \\ Tstar = 0 \\ T = 1000 \end{cases}$$

Name	Type	Concentration (mol/l)	Rate (mol/l/s)	Transition Time (s)
V	REACTIONS	8.88696582051918E-23	-5.641328087473	0.1575332205948450
Tstarstar	REACTIONS	-1.45296982190835E-24	9.954254905636	4.166666666666670
Tstar	REACTIONS	-1.16237582434583E-22	4.8063361929200	24.18423883993120
T	REACTIONS	1000.0000000000000	3.5659804361829	50.00000000000000

KINETIC STABILITY ANALYSIS

The linear stability analysis based on the eigenvalues of the Jacobian matrix is only valid for steady states.

Summary:

This state is unstable.

Eigenvalue statistics:

Largest real part: 0.005917614529102015

Largest absolute imaginary part: 0

4 are purely real

0 are purely imaginary

0 are complex

0 are equal to zero

1 have positive real part

3 have negative real part

stiffness = 409.0660459649154

time hierarchy = 0.758277462876047

Replication of the results of steady-state analyses of the unstable fixed point of T cell (T), latently infected T cell (T\*), actively infected T cell (T\*\*), and free virus (V) populations performed by Perelson, Alan S. et al. Mathematical biosciences 114.1 (1993): 81-125. Almost the same number of unstable fixed point as the theoretically derived unstable fixed point was obtained by the SBMLWebApp. The parameters of the model were the same as in Table 1 of the paper. The steady-state analysis was performed with a resolution of 1.0e-9, a derivation factor of 1.0e-3, and an iteration limit of 50.

Theoretical Stable  
Fixed Point

=

$$\begin{cases} V = 185.7818 \\ Tstarstar = 1.872171 \\ Tstar = 149.7737 \\ T = 772.5899 \end{cases}$$

Name	Type	Concentration (mol/l)	Rate (mol/l/s)	Transition Time (s)
V	REACTIONS	185.7818104642200	0	0.4134722222222220
Tstarstar	REACTIONS	1.8721714188534100	0	4.1666666666666670
Tstar	REACTIONS	149.7737135082730	-4.45747554522868E-1	43.478260869565200
T	REACTIONS	772.5898555592880	0	40.88514131131750

KINETIC STABILITY ANALYSIS

The linear stability analysis based on the eigenvalues of the Jacobian matrix is only valid for steady states.

Summary:

This state is asymptotically stable.

Eigenvalue statistics:

Largest real part: -0.007580073808920534

Largest absolute imaginary part: 0

4 are purely real

0 are purely imaginary

0 are complex

0 are equal to zero

0 have positive real part

4 have negative real part

stiffness = 318.73143300999254

time hierarchy = 0.6165738196777563

Reproduction of the results of steady-state analyses of the stable fixed point of T cell (T), latently infected T cell (T\*), actively infected T cell (T\*\*), and free virus (V) populations performed by Perelson, Alan S. et al. Mathematical biosciences 114.1 (1993): 81-125. Almost the same number of stable fixed point as the theoretically derived stable fixed point was obtained by the SBMLWebApp. The parameters of the model were the same as in Table 1 of the paper. The steady-state analysis was performed with a resolution of 1.0e-9, a derivation factor of 1.0e-3, and an iteration limit of 50 with the initial condition of T, T\*, T\*\* and V were 700, 200, 200 and 0.001, respectively.

S7

Theoretical Unstable  
Fixed Point  
(With Oscillation)

$$= \begin{cases} V = 6.47353 \\ T_{starstar} = 0.1929402 \\ T_{star} = 385.8805 \\ T = 1.493205 \end{cases}$$

Name	Type	Concentration (mol/l)	Rate (mol/l/s)	Transition Time (s)
V	REACTIONS	6.473530498547430	7.13196087236589E-1	0.1165
Tstarstar	REACTIONS	0.1929402270668640	0	4.1666666666666670
Tstar	REACTIONS	385.88045413372900	-3.56598043618295E-1	16.633399866932800
T	REACTIONS	1.4932045779685300	3.56598043618295E-1	0.06411705950442200

KINETIC STABILITY ANALYSIS

The linear stability analysis based on the eigenvalues of the Jacobian matrix is only valid for steady states.

Summary:

This state is **unstable**.

Transient states in its vicinity have **oscillatory components**.

Eigenvalue statistics:

Largest real part: 0.055057250755708095

Largest absolute imaginary part: 0.3994090482034272

The complex eigenvalues with the largest real part are: 0.055057250755708095+I-0.3994090482034272 i

2 are purely real

0 are purely imaginary

2 are complex

0 are equal to zero

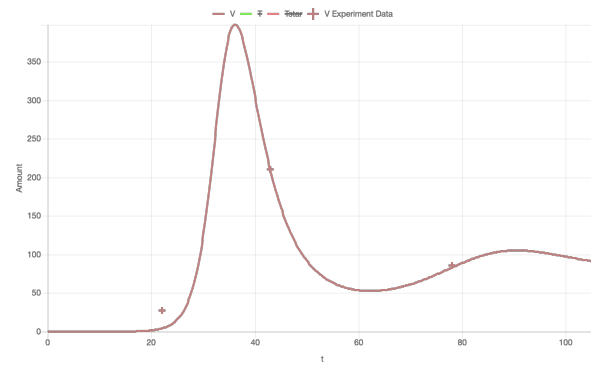
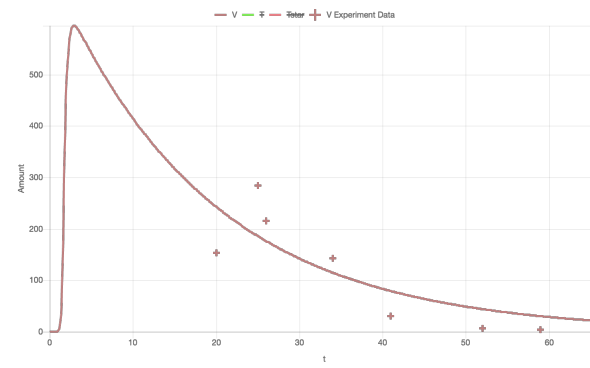
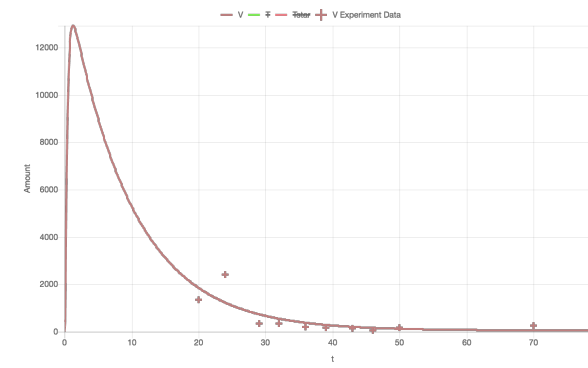
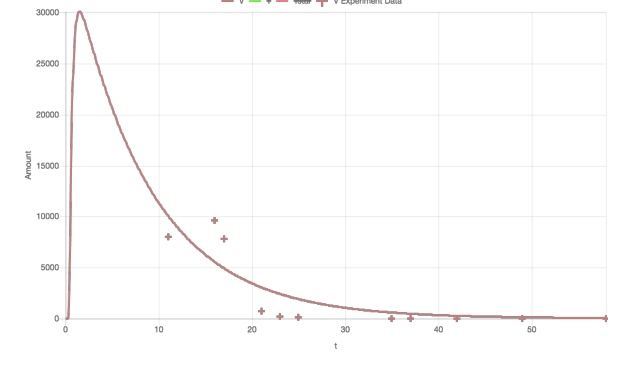
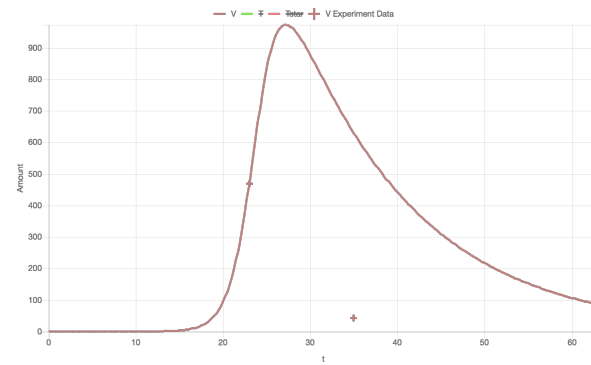
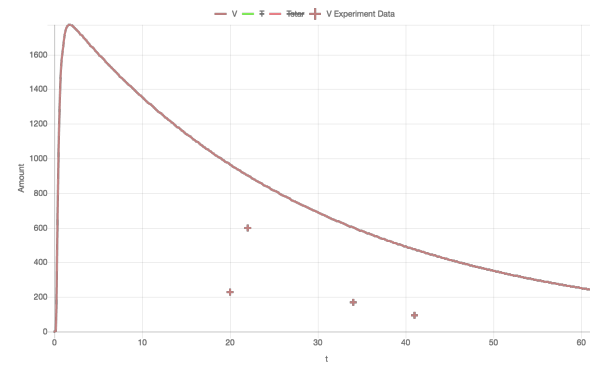
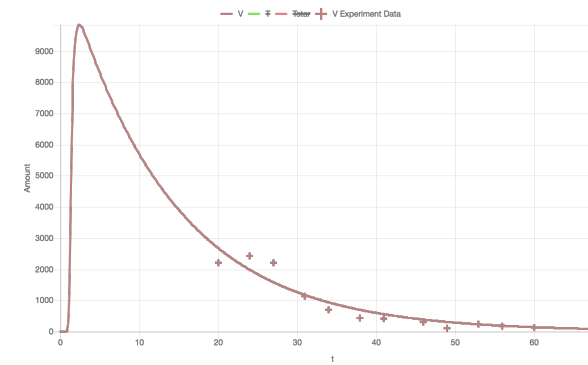
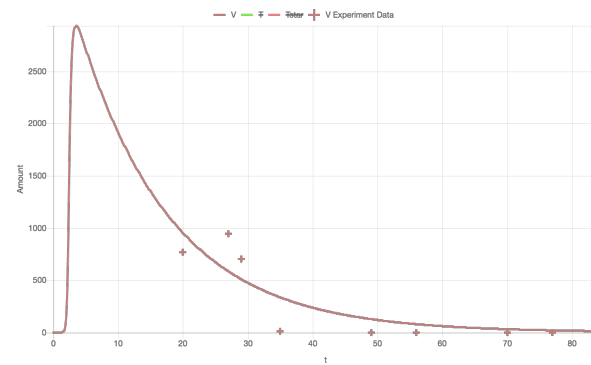
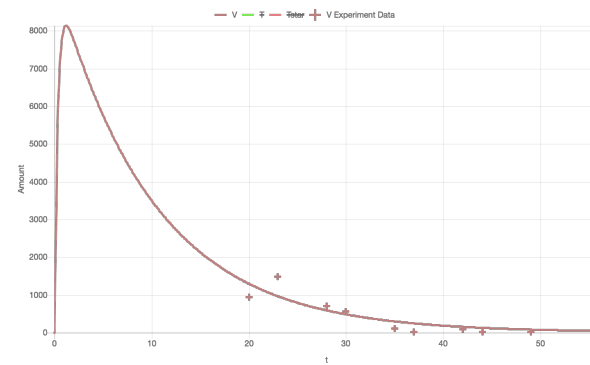
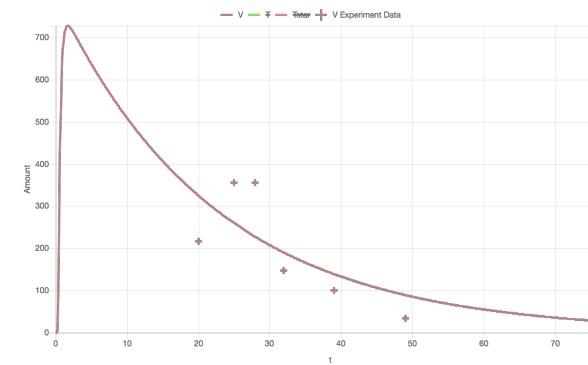
2 have positive real part

2 have negative real part

stiffness = 275.30517651142844

time hierarchy = 0.5719767225716659

Replication of the results of steady-state analyses of the oscillatory unstable fixed point of T cell (T), latently infected T cell (T\*), actively infected T cell (T\*\*), and free virus (V) populations performed by Perelson, Alan S. et al. Mathematical biosciences 114.1 (1993): 81-125. Almost the same number of oscillatory unstable fixed point as the theoretically derived oscillatory unstable fixed point was obtained by the SBMLWebApp. The parameters of the model were the same as in Table 2 of the paper. The steady-state analysis was performed with a resolution of 1.0e-9, a derivation factor of 1.0e-3, and an iteration limit of 50 with the initial condition of T, T\*, T\*\* and V were 10, 100, 100 and 100, respectively.

**S8****Patient 1****Patient 4****Patient 7****Patient 10****Patient 2****Patient 5****Patient 8****Patient 3****Patient 6****Patient 9**

Replication of the parameter estimation for the time series change in the number of free viruses in 10 patients performed by Stafford, Max A., et al. Journal of theoretical biology 203.3 (2000): 285-301. It can be seen that the simulation results (line) and the actual measurement results of the number of free viruses (plot) using the parameters estimated by the SBMLWebApp were in general agreement. The Levenberg-Marquardt method was used to estimate the parameters, with an iteration limit of 2000 and a tolerance of  $1.0e^{-6}$ .