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COVID-19: Modeling In-Host Viral and Innate Immune System Dynamics

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Abstract

Much of the success of the SARS-CoV-2 virus is due to its high rate of infectivity and ease of respiratory transmission. This has led to a pandemic spanning almost two years even with the introduction of vaccines and potential therapeutics to combat the virus. Key to research into the disease is the natural history of its viral load characteristics and how it might affect probability of transmission.

With a significant increase in vaccine rollout in recent months, many researchers have looked to understand the significance of antibodies, however new findings have revealed that CD4+ and CD8+ T cells may have significant implications on viral production, infectivity, and survival of the host.[23] The model presented here implements a target cell limited model incorporating both viral cellular dynamics and T cell immune response to get a representative picture of the importance of T cell induced protection via vaccination.

We find that by using a target cell model with immune system factors, we can model the number of virions produced and present in the body at a certain disease time. Based on our model, we see a peak viral load in patients with severe cases at 10 days post exposure.[1] The immune system has a delayed peak, which is supported by other studies.

Introduction

COVID-19's main pathway of infection is through respiratory droplets. Recently, there has been much investigation into the impact of this viral load and its relationship with viral transmission. Manski et al found that current data can widely underestimate the amount of infectious people with the presence of error in testing.[2] Additionally, this error impacts the perceived fatality rate of the diseases as well.

As such, most COVID-19 modelling has focused on the larger epidemiological studies. Some studies have been performed to model in-host kinetics and infection characteristics of COVID-19. Ejima et al used a two ODE system to estimate initial infection time and its impact on secondary infections.[3] Their model was further elaborated on by Kim et al to investigate potential treatments. Additionally, papers from Hernandez-Vargas and Valesco Hernandez have tried to model virion dynamics in-vivo.[4,5] Their findings concluded that by accounting for immune system dynamics, the model is able to better fit existing data.

Modelling the immune system is an important, yet difficult task due to both innate and adaptive responses. Du and Yuan applied mathematical modelling techniques to look at how incubation and pathogen behavior is affected by the immune system. They found that in severe COVD-19 cases, it is likely that the peak virus load in exhalation isn't proportional to systemic viral load. Rather, the peak systemic viral load occurs after the peak air viral load.[6]

Our approach is to combine two existing models from published literature to more accurately model in-host viral load from disease exposure.

Models

A standard model of in-human viral load kinetics often follows a target cell limited model with three compartments, seen in papers such as Hernandez-Vargas et al. These compartments are comprised of the target cell population, the infected cell population, and the virions. The following equations govern the rate of change with respect to time for each of these populations.

$$\frac{dU}{dt} = -\ \beta UV$$

$$\frac{dI}{dt} = \beta UV\ -\ \delta I$$

$$\frac{dV}{dt} = pI\ -\ cV$$

U is the amount of target cells that are susceptible to infection, I is the amount of infected cells, and V is the amount of virions. For the constants, β is the infection rate of the virions on target cells, while δ is the death/clearance rate of infected cells. Virions are produced at a rate of *p* per infected cell and get cleared at a rate of *c*.

Viral Load Model 1

Blanco-Rodríguez et al[7] adjust the conventional three-compartment model in a couple ways. First, they introduce a new compartment to describe the immune response of T-cells. Second, they reduce the number of compartments to two by ignoring target cells and infected cells. By doing so, the viral load kinetics are solely dependent on the number of virions and T-cells which are described by,

$$\frac{dV}{dt} = pV\left(1 - \frac{V}{K}\right)\ -\ c_t VT\ -\ cV$$

$$\frac{dT}{dt} = s_T + rT\frac{V^2}{V^2 + k_t^{\ 2}}\ -\ \delta T$$

where V is the viral load, T is the total number of T-cells, p is the viral production rate with maximum carrying capacity K, and c is the clearance rate of the virus. $c_T VT$ represents the rate of death of infected cells by the immune response.

Viral Load Model 2

The second viral model of interest is used in Marc et al[8]. This model differs from the standard target cell limited model by incorporating an eclipse phase, where the cell is yet to begin producing virions, but has been infected. Additionally, the model contains another group of virions that are non-infecting. This model, however, does not incorporate any type of immune response. Specifically, U is the target cells, E is the infected cells in the eclipsed phase, and I represents the infected and producing cells. V_I stands for the amount of infecting virions and V_{NI} stands for the number of non-infecting virions. In this model, k represents the rate of eclipsed cells moving to productive cells. The value of μ is the portion of virions that go on to infect more cells.

$$\frac{dU}{dt} = \quad - \beta T V_I$$

$$\frac{dE}{dt} = \beta T V_I - kE$$

$$\frac{dI}{dt} = kE - \delta I$$

$$\frac{dV_I}{dt} = p\mu I - cV_I$$

$$\frac{dV_{NI}}{dt} = p(1 - \mu)I - cV_{NI}$$

Novel Model Equations

$$\frac{dU}{dt} = nU(1 - U/U_0) - \beta U V_I$$

$$\frac{dE}{dt} = \beta U V_I - kE$$

$$\frac{dI}{dt} = kE - \delta I$$

$$\frac{dV_I}{dt} = p\mu I + p_t V_I(1 - \frac{V_I}{K}) - c_t V_I T - cV_I$$

$$\frac{dV_{NI}}{dt} = p(1 - \mu)I + p_t V_{NI}(1 - \frac{V_{NI}}{K}) - c_t V_{NI} T - cV_I$$

$$\frac{dT}{dt} = s_T + rT\frac{(V_I + V_{NI})^2}{(V_I + V_{NI})^2 + k_t^2} - \delta_t T$$

such that $s_T = \delta_t T_0$

In this paper, we propose combining the target-cell model (Model 2) with T-cell kinetics (Model 1). This system of ODEs can be broken down to explain different phenomena that we hope to capture and predict. Two factors control the rate of change in target cell population, U. The first factor models the replication rate with a carrying capacity of U_0 while the second factor models the infecting of target cells by COVID-19 virions. These cells move into the eclipsed phase, which is identical to the equation in Model 2.

Pulling from Model 1, we adapt the infecting virions equation to the above. In this case, we add two new terms, one to limit the carrying capacity of virions and another to account for virions cleared specifically by T-cells. Additionally, we include the T-cell ODE in our system, substituting V with $V_I + V_{NI}$ as we expect T-cells to attack all virions. This model will hopefully capture the impact and influence of the immune response in a more complex target cell model.

Presented in the following Tables 1 and 2 are the selected parameters and initial conditions used to create the model which are all pulled from current literature. The resulting graphical trends were compared to existing model outputs as a form of model validation.

Table 1: *The parameters used in our model (Novel Model) pulled from various sources.*

Parameters	**Value**
Lung Cell Turnover Rate (n)	0.003 cell/day[9]
Rate of Viral Infection (β)	1.58e-8 day·copies/mL[5]
Rate of Eclipsed to Productive Phase (k)	3 1/day[1]
Maximum Viral Load in Sputum (δ)	0.84 1/day[8]
Cellular Viral Replication Rate (p)	2.8e5 1/cell·day[8]
Viral Replication Rate with Carrying Capacity (p_t)	5.36[5]
Ratio of Infecting Virions (μ)	1e-4[1]
Virion Carrying Capacity (K)	2.35e9 copies/mL[10]
Clearance Rate Associated with T-Cells (c_t)	1.89e-6 copies/cell·day[5]
Clearance Rate Outside of T-Cells (c)	10 copies/day[5]
Replication Rate of T-Cells (δ_t)	0.1 1/day[5]
Half Saturation Constant (k_t)	1.26e5 copies/m[5]
T-Cell Proliferation Rate (r)	0.194 1/day[5]

Table 2: Initial conditions of target cells, latent cells, infected cells, infectious virions, non-infectious virions, and T-cells.

Variable Initial Conditions	**Value**
Target Cells, U_o	1.0E8 cells/mL[22]
Latent Cells, E_o	0 cells/mL[8]
Infected Cells, I_o	1/30 cells/mL[8]
Infectious Virions, $V_{I,o}$	0.31 virions/mL[5]
Non-Infectious Virions, $V_{NI,o}$	0 virions/mL[1]
T cells, T_o	1.0E6 cells/mL[8]

Results

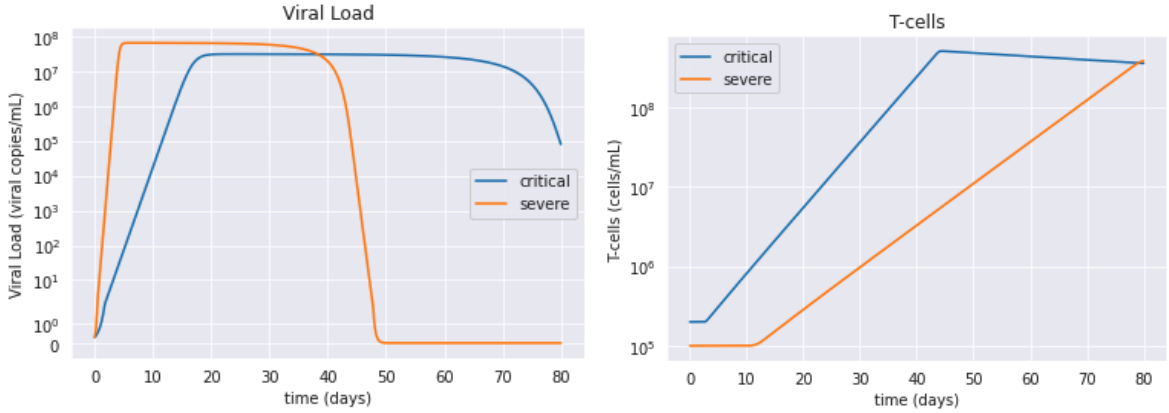


Figure 1: ***Model 1*** *- Left:* Virion counts in both severe and critical cases, with parameters and models from Blanco-Rodríguez et al. *Right:* T-cell counts in both severe and critical cases

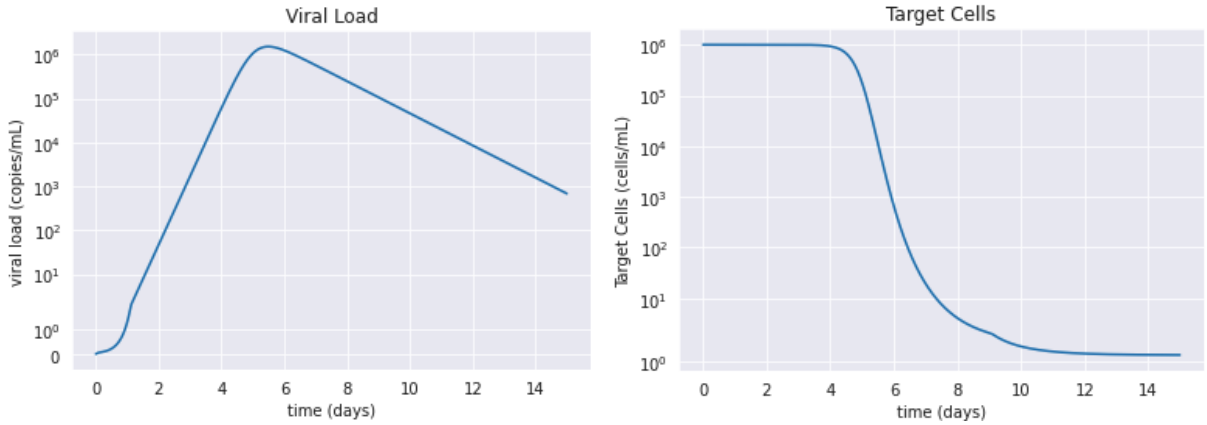


Figure 2: ***Model 2*** **-** *Left:* Target cell population with parameters and models from Marc et al from symptom onset. *Right:* Virion population counts from symptom onset

The above figures show results taken from Models 1 and 2. Figure 1 represents Model 1 where only the viral count and T cell counts are considered. In critical patients, the *rapid* increase in T-cell count to combat the viral load was effective in slowing the infection. However, this hyperactivation of T-cell response is often what causes death for these patients as it causes critical inflammation in the lungs[7]. Figure 2 represents Model 2 where the resulting transience of target cells and viral load are shown. This viral load trend is consistent with the results from Wang et al which were fitted to patient experimental data.[11] Below, Figure 3 highlights the results of the novel proposed model accounting for the effects of both T-cells as well as cellular dynamics. Note that as viral load increases, the T-cell population follows suit which causes the viral load to decrease. The target population decreases in accordance with the viral load.

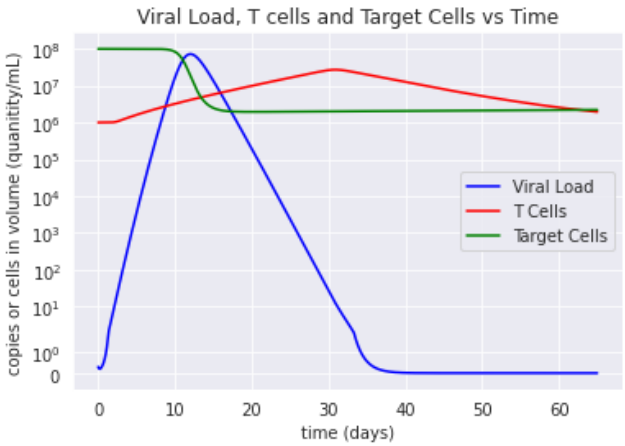
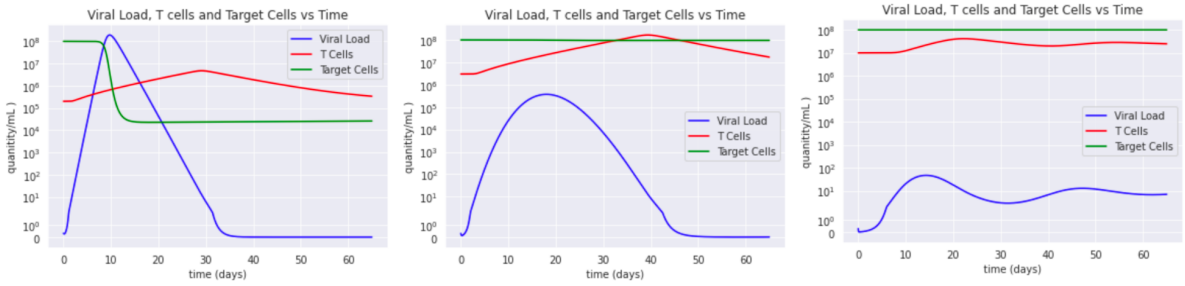


Figure 3: ***Novel Model*** *-* A comparison of the viral load, T-cell population, and target cells from the moment of infection.



(a) (b) (c)

Figure 4: ***Varying T_0*** *- (a):* $T_0 = 2 \times 10^5$*, (b):* $T_0 = 3 \times 10^6$*, (c):* $T_0 = 1 \times 10^7$*;* The effect of varying initial concentration of T cells. Increased concentration of T cells is shown to reduce the viral load in the system more quickly and effectively.

Comparing results in Figure 3 a clear trend emerges dependent on the initial concentration of T cells in the body. An increased concentration of T cells results in a more quick and effective reduction in viral load. Note that in figure 3, the viral load seems to approach an equilibrium concentration later discussed in the discussion section.

Discussion

Any virus or pathogen is notoriously difficult to model in the human body due to the complexity of the different interacting systems as well as variability of parameters. Our model captures the affected target cell populations and incorporates aspects of the adaptive immune response to a COVID-19 infection.

Our model shows several key characteristics of the natural history of COVID-19 in the body. Firstly, is a peak viral load approximately 10 days after initial exposure to the virus. The immune response peak occurs at approximately 30 days post exposure. This delayed immune response is well detailed in existing literature.[6,11]

The primary benefit of our model is apparent in comparison to the two other models. When examining Model 1, we observe similar peaks in time of T-cell responses. Model 1, however, does give a slower decrease post-peak than our model. This does make sense due to the differing in behavior of the virion population. While Model 1 has a fairly sustained presence of virions in the body, our model is more similar to Model 2's viral load response. We believe that Model 2 is the more accurate of the two since it takes into account the mechanisms of virion cellular production. So, with the sustained viral response in Model 1, it makes sense that the T-cell population would decline less rapidly than its rise.

Our model also has a faster decline in viral load than Model 2. Again, this can be explained by the presence of an additional clearing factor and ensures that our model/code is working as intended.

When looking at a variety of initial values for T cell concentration a threshold value begins to become apparent near $T_0 = 8x10^6$ cells/mL at which point the initial concentration of T cells is extremely high in comparison to the initial viral load ($VI_0 = 0.31$ copies/ml). This results in an unstable state where virions are never fully cleared from the body and thus the viral load takes the shape of a sinusoid with decreasing amplitude. We predict that this unsteady state is due to incredibly low concentrations of virions that are able to go "undetected" in the body, this concentration of virions is incredibly small on the scale of 10 copies/ml. Any concentration of virions higher than this threshold seems to invoke a T cell response and the concentration of virions is cleared back to equilibrium state near 10 copies/ml.

This model can inform decision-making at both the individual, and population level. For physicians, better modelling of viral dynamics in patients gives the doctor more discriminatory power on when aggressive and invasive treatments are necessary. Additionally, more effective timings of therapeutics and interventions can be optimally implemented.

From the larger perspective, guidelines that affect transmission and spread fundamentally use disease characteristics to be most effective. Our model would inform policymakers that from the time of exposure, days 5 to 13 are associated with the most infectiousness assuming a proportional relation with viral load. Additionally, we might warn that T-cell response will likely wane after 3 months and potentially allow for reinfection of the host.

If our model were to proceed to publication, we would expect our main limitations to be justification of parameter selection and model validation. For the former, we do source all our parameters from existing literature. However, these parameters are often found through the fitting to a specific dataset and have been shown to have high variance among cases. This makes it difficult to capture the trend of a specific patient if their parameters are not known. We also do not model other aspects of the immune system such as memory B-cells.

We validate our model by comparing it to existing published models and investigate key points and trends such as peaks and relative rate of changes. This is certainly a weakness as ideally we would want to compare our results to collected data. Given more resources as well as access to a respective dataset, it would be an essential step to complete.

Conclusion

Our combination of a target cell model and an immune response model shows promise in the modeling of in-host viral dynamics, as it accurately illustrates peak viral loads and immune response decay. While simple ODE models lack the complete complexity of the in-vivo response, they can be useful for estimating disease progression for therapeutics and transmission mitigation therapy. Additionally, our model hypothesizes the benefit of increasing concentrations of T cells on reduction in viral load and subsequent infectiousness as well as survival. The sensitivity of the model to the value of T_0 shows the importance of vaccinations. Future work will seek to find threshold values for the required initial concentration of T cells required to ensure survival and sufficient reduction in infectivity as a means of categorizing vaccine and future treatment efficacy.

In order for further conclusions to be drawn, the model must be further validated on clinical data sets that are not readily available. Parameters for models used in many similar papers are obtained and validated based on limited and small datasets and thus there is a need for larger and more complete data sets in order to accurately validate the model in this paper.

Software and Tools

All models were run with Python in a Google Colab environment. Packages include numpy, matplotlib, pylab, scipy, and seaborn.

Team Member Contribution

Kento Abeywardane

Contributions include literature review and selection of various models. Kento mainly created the scripts which were used to recreate the models found in selected papers. Further, Kento helped work on the combination of models to develop the novel model. He also contributed to the methods and results sections of the paper.

Benjamin Homer

Contributions include mainly background research and model selection/creation, as well as write up of the abstract, introduction, models, discussion, and conclusion sections. Ben also helped with parameter selection and novel model development.

Adam Spooner

Main contributions include working on creating the novel model script as well as finding the parameters and doing hand calculations to ensure accuracy as well as model validation. Additionally, Adam contributed to the results, discussion and conclusions sections and was responsible for the details relating to initial concentrations of T cells.

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Appendix

The code compiled for each of the models are shown below. They can also be found on Google Colab with the attached link. (https://colab.research.google.com/drive/1Xz7htZmX-OBk0Ul4bZmzb1eCoYQSdqMH?usp=sharing)

Import Packages

```
import numpy as np
import matplotlib.pyplot as plt
import pylab
from matplotlib import gridspec
from scipy.integrate import odeint, ode
import seaborn as sns
sns.set_style("darkgrid")
```

Viral Load Model 1

```
# Viral Load Model 1
# In-host model with T-cell response
```

```
# With reference to:
https://www.sciencedirect.com/science/article/pii/S1367578820300638?via%3D
ihub
## and https://www.sciencedirect.com/science/article/pii/S0169260721004867

class withimmune:
 def __init__(self, severity_params, T0):
   """severity_params = [p, ct, r]\n
   T0 = intial # of T cells """
   self.p, self.ct, self.r = severity_params
   self.T0 = T0

 def diffeqs(self, y, t):
   """Solver for COVID-19 in host model with immune response"""
   # variables
   V, T = y
   # fixed params
   K = 1e8       # copies/mL
   c = 2.4       # 1/day
   kt = 1.26e5   # copies/mL
   deltat = 0.01 # 1/day

   # ODEs
   dVdt = self.p*V*(1 - V/K) - self.ct*V*T - c*V # virions
   st = deltat * self.T0
   dTdt = st + self.r*T*(V**2/(V**2 + kt**2)) - deltat*T # T cells
   dydt = [dVdt, dTdt] # pack ODEs
   return dydt

 # runs the integrator
 def simulate(self, init_cond, tspan):
   """init_cond = [V0, T0]"""
   answer = odeint(self.diffeqs, init_cond, tspan) # solve ODEs
   V = answer[:, 0] # virions
   T = answer[:, 1] # T cells
   return V, T

# initial conditions
V0 = 0.31     # viral copies/mL
T0 = 1e6      # T cells/mL
```

```
y0 = [V0, T0]

# critical cases
p = 3.50      # 1/day
ct = 0.596e-8 # 1/day-cell
r = 0.131     # 1/day
severity_params_crit = [p,ct,r]
critical_T0 = 1e5

# severe cases
p = 6.99
ct = 1.47e-8
r = 0.2
severity_params_severe = [p,ct,r]
severe_T0 = 2e5

# time
t_start = 0.0
t_end = 80.0
N = 1000001
tspan = np.linspace(t_start, t_end, N)

# get the variables using parameters severeness=critical
critical = withimmune(severity_params_crit, critical_T0)
Vc, Tc = critical.simulate([V0, critical_T0], tspan)

# get the variables using parameters severeness=severe
severe = withimmune(severity_params_severe, severe_T0)
Vs, Ts = severe.simulate([V0, severe_T0], tspan)

plt.yscale('symlog')
plt.plot(tspan, Vc, label='critical')
plt.plot(tspan, Vs, label='severe')
plt.xlabel('time (days)')
plt.ylabel('Viral Load (viral copies/mL)')
plt.legend()
plt.title('Viral Load')
plt.show()

plt.yscale('symlog')
```

```
plt.plot(tspan, Ts, label='critical')
plt.plot(tspan, Tc, label='severe')
plt.legend()
plt.title('T-cells')
plt.ylabel('T-cells (cells/mL)')
plt.xlabel('time (days)')
plt.show()
```

Viral Load Model 2

```
# Viral Load Model 2
# With Reference to: https://elifesciences.org/articles/69302#content

def dydt(y, t, params):
 """System of ODEs to get in-human model without immune response.\n
 params = [b, k, d, p, mu, c]\n
 y = [T, E, I, VI, VNI]"""
 b, k, d, p, mu, c = params
 T, E, I, VI, VNI = y

 dTdt = - b*T*VI # Target Cells
 dEdt = b*T*VI - k*E # Latent Cells
 dIdt = k*E - d*I # Infected Cells
 dVIdt = p*mu*I - c*VI # Infectious Virions
 dVNIdt = p*(1-mu)*I - c*VNI # Noninfectious Virions
 dydt = [dTdt, dEdt, dIdt, dVIdt, dVNIdt]  # Pack the answer.
 return dydt

# time scale
t_start = 0.0
t_end = 15.0
N_time = 10001
times = np.linspace(t_start, t_end, N_time)

# logit-linear (M2) parameters
d = 0.84    # 1/day
c = 10      # 1/day
k = 4       # 1/day
mu = 1e-4
p = 2.8e5   # 1/cell/day
R0 = 13.6
```

```
U0 = 1.33e5 # target cells/mL
I0 = 1/30   # infected cells/mL
T0 = 1e6
b = R0*c*d/p/T0/mu

params = [b,k,d,p,mu,c] # pack parameters
y0 = [T0, 0, I0, 0, 0]  # intial conditions

# get the solution to the system of ODEs
answer = odeint(func=dydt, y0=y0, t=times, args=(params,))
T = answer[:, 0]    # Target Cells
E = answer[:, 1]    # Latent Cells
I = answer[:, 2]    # Infected Cells
VI = answer[:, 3]   # Infectious Virions
VNI = answer[:, 4]  # Non-infectious Virions

# plot Viral Load vs time (log scale)
plt.plot(times, VI)
plt.yscale('symlog')
plt.title('Viral Load')
plt.xlabel('time (days)')
plt.ylabel('viral load (copies/mL)')
plt.show()

# plot Target Cells vs time (log scale)
plt.plot(times, T)
plt.yscale('symlog')
plt.title('Target Cells')
plt.xlabel('time (days)')
plt.ylabel('Target Cells (cells/mL)')
plt.show()

# plot Viral Load vs time
plt.plot(times, VI)
plt.title('Viral Load')
plt.xlabel('time (days)')
plt.ylabel('viral load (copies/mL)')
plt.show()
```

Novel Model

```
# Our Novel Model
# combination of techniques from:
https://elifesciences.org/articles/69302#content
## and
https://www.sciencedirect.com/science/article/pii/S1367578820300638?via%3D
ihub#bib0004

def dydt(y, t, params):
 """System of ODEs to produce a total in-body model of COVID-19 with
immune response.\n
 y = [U, E, I, VI, VNI, T]\n
 params = [b, k, d, p, mu, c, ct, r]"""
 U, E, I, VI, VNI, T = y
 b, k, d, p, mu, c, ct, r = params
  dUdt =  (n*U*(1-U/U0)) - (b*U*VI) # target cells
 dEdt = (b*U*VI) - (k*E) # latent cells
 dIdt = (k*E) - (d*I) # infected cells
 dVIdt = ((p*mu*I) + (pt*VI*(1 - VI/K))) - (ct*VI*T) - (c*VI) # infectious
virions
 dVNIdt = (p*(1-mu)*I) + (pt*VNI*(1 - VNI/K)) - (ct*VNI*T) - (c*VNI) #
noninfectious virions
 st = deltat * T0
 dTdt = st + (r*T*((VI+VNI)**2/(((VI+VNI)**2) + (kt**2)))) - deltat*T #
T-cells

 dydt = [dUdt, dEdt, dIdt, dVIdt, dVNIdt, dTdt]  # Pack the odes
 return dydt

# time scale
t_start = 0.0
t_end = 80.0 # days
N_time = 10001
times = np.linspace(t_start, t_end, N_time)

# Parameters
n = 0.003    # cell/day, lung cell turnover rate:
https://link.springer.com/chapter/10.1007/978-3-642-69521-6_11
K =  2.35e9  # copies/ml, maximum viral load in sputum:
https://www.nature.com/articles/s41586-020-2196-x
```

```
d = 0.84     # 1/day, loss rate of productively infected cells:
https://elifesciences.org/articles/69302#content
c = 10       # 1/day, clearance rate:
https://elifesciences.org/articles/69302#content
k = 3        # 1/day, eclipse phase to infected rate:
journal.pcbi.1008785.pdf eclipse phase
mu = 1e-4    # unitless, proportion of infectious virus:
journal.pcbi.1008785.pdf
p = 2.8e5    # 1/cell-day, rate of viral production:
https://elifesciences.org/articles/69302#content; pT (copies/cell/d)
            # 2.2×10^4  or pN (copies/cell/d) 4.8×10^4 from
journal.pcbi.1008785%20(1).pdf
pt = 5.36    # copies*day*cell/mL, replication rate
https://www.sciencedirect.com/science/article/pii/S1367578820300638?via%3D
ihub#bib0078
            # pt just a variation for units taken from a second model as
opposed to above p
b = 1.58e-8  # day*copies/ml
https://www.sciencedirect.com/science/article/pii/S1367578820300638?via%3D
ihub#bib0078
deltat = 0.1 # 1/day
kt = 1.26e5  # copies/mL

# parameters characterizing severe cases (nonlethal)
ct = 1.89e-6 #
https://www.sciencedirect.com/science/article/pii/S1367578820300638?via%3D
ihub#bib0078
r = 0.194    #
https://www.sciencedirect.com/science/article/pii/S1367578820300638?via%3D
ihub#bib0078

#initial conds
U0 = 1.e8    # target cells/mL
I0 = 1/30    # infected cells/mL
T0 = 1e6     # T cells/mL
V0 = .31     # copies/ml
Ro = b*p*U0*mu /(c*d) # just calculated as a test to see if R0 is in
expected range (2-15)

# pack parameters and initial conditions for ode solver
```

```
params = [b,k,d,p,mu,c,ct,r]
y1 = [U0, 0, I0, V0, 0, T0]

# solve ode
answer = odeint(func=dydt, y0=y1, t=times, args=(params,))

#unpack
U = answer[:, 0]   # target cells vs time
E = answer[:, 1]   # latent cells vs time
I = answer[:, 2]   # infected cells vs time
VI = answer[:, 3]  # infectious virions vs time
VNI = answer[:, 4] # non-infectious virions vs time
T = answer[:, 5]   # T cells vs time

# graphs
# viral load vs time
VLoad = plt.plot(times, VI, "-b", label="Viral Load")
plt.title('Viral Load vs Time')
plt.xlabel('time (days)')
plt.ylabel('viral load (copies/mL)')
plt.yscale('symlog')
plt.show()

# T cells vs time
Tcells = plt.plot(times, T, "-r", label="T Cells")
plt.title('T-Cells vs Time')
plt.xlabel('time (days)')
plt.ylabel('T-cells (cells/mL)')
plt.yscale('symlog')
plt.show()

# target cells vs time
UCells = plt.plot(times, U, "-g", label="Target Cells")
plt.title('Target Cells vs Time')
plt.xlabel('time (days)')
plt.ylabel('Target cells (cells/mL)')
plt.yscale('symlog')
plt.show()

# all three graphs combined - log scale
```

```
VLoad = plt.plot(times, VI, "-b", label="Viral Load")
Tcells = plt.plot(times, T, "-r", label="T Cells")
UCells = plt.plot(times, U, "-g", label="Target Cells")
plt.title('Viral Load, T cells and Target Cells vs Time')
plt.xlabel('time (days)')
plt.ylabel('copies or cells in volume (quanitity/mL)')
plt.legend()
plt.yscale('symlog')
plt.show()

# all three graphs combined - normal scale
VLoad = plt.plot(times, VI, "-b", label="Viral Load")
Tcells = plt.plot(times, T, "-r", label="T Cells")
UCells = plt.plot(times, U, "-g", label="Target Cells")
plt.title('Viral Load, T cells and Target Cells vs Time')
plt.xlabel('time (days)')
plt.ylabel('copies or cells in volume(quanitity/mL)')
plt.legend()
plt.show()
```