

# Modeling Rhinovirus Using Real-World Data

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### Background

- Rhinovirus is the cause of what we consider to be an everyday cold and other minor ailments.
- There are no set treatments, but symptoms can however be managed and the body usually resolves the virus.
- Rhinovirus has a typical incubation period of about 12-72 hours and can last from about a week to two weeks.
- Little is known about how the virus spreads from cell to cell.
- We use a mathematical model to help us understand in-host spread of the virus.

### Mathematical models

To model rhinovirus we used an ODE model with 4 equations. Each equation represents different elements of the virus.

$$\frac{dT}{dt} = -\beta TV$$
$$\frac{dE}{dt} = \beta TV - (KE)$$
$$\frac{dI}{dt} = KE - \delta I$$
$$\frac{dV}{dt} = pI - cV$$

The first equation represents the change in target cells (T) as a function of time which depends on the amount of virus (V) and the infection rate  $(\beta)$ . The second equation represents cells in the eclipse phase (E), which are cells that are infected but not yet producing virus. The third equation relates to how many cells are in the infectious phase wherein they produce virus. The final equation corresponds to how much virus there is in the system.

We also used a simpler function to characterize the viral load.

$$V(t) = \frac{2V_p}{e^{(-\lambda_g(t-t_p))} + e^{(\lambda_d(t-t_p))}},$$

where  $V_p$  is the peak viral load,  $t_p$  is the time of viral peak,  $\lambda_a$  is the viral growth rate, and  $\lambda_d$  is the viral decay rate.

### **Parameter and Variables**

In our model there are several key parameters and variables that need to be established.

Parameter	Meaning
K	duration of eclipse phase
β	infection rate
δ	Lifetime of cells
р	virus production rate
с	clearance rate

In addition, there are also four variables that we measure: V, T, E, and I which represent the number of virus, target cells, eclipse cells, and infectious cells respectively.

## **Curve Fitting Rhinovirus**

The next step was to curve fit our model to a small set of data.



Curve fitting our model allows us to estimate the values of the parameters in our model so we can understand how rhinovirus spreads between cells. We used data collected from humans infected with rhinovirus. The data were collected by the Laboratory for the Study of Stress, Immunity, and Disease at Carnegie Mellon University under the directorship of Sheldon Cohen, PhD; and were accessed via the Common Cold Project website (www.commoncoldproject.com).

### **MCMC**

Markov Chain Monte Carlo, better known as MCMC, is a method that creates posterior distributions based on data and initial guesses. MCMC works by taking initial guesses and bounds of your parameters and takes steps away from you initial guess and towards a parameter that best fits the data.



MCMC returns distributions of possible values for each of the parameters. Since all the clouds of points are roughly circular, there are no correlations between any of the parameters. All the distributions also have a distinct peak, so there is a clear most likely value for each parameter.

We also found the median values for the parameters in the triangle function.

• We used rhinovirus data and MCMC to find parameter values for two models.

### Parameter estimates for **ODE** model

We used the median function in python to get estimates for each of the parameters in the ODE model.

Parameter	Median Value
K	0.9991
$\beta$	0.000516
δ	3.2399
p	0.9370
с	7.05006

The eclipse phase for rhinovirus lasts for about 1 day while the infectious lifespan is about 7.5 hours. Virus is cleared in about 3.5 hours.





### Parameter estimates for triangle function

Parameter	Median Value
$\lambda_g$	0.500010
$\lambda_d$	0.000511
Tp	2.99
Vp	99.9

### Conclusions

• We found that rhinovirus viral load peaks at about 3 days.

• The viral load of rhinovirus increases about 100 times faster than it decreases.

• The eclipse phase of rhinovirus infected cells lasts about 24 hours while the infectious phase lasts about 7.5 hours.

• A rhinovirus particle is cleared in about 3.5 hours.



Rhinovirus is the most prevalent virus in humans and is often the cause of the common cold. Modeling the dynamics of rhinovirus can allow us to observe important parts of the virus including the general growth of the virus. Following that, we can estimate parameters of the model by fitting the model to data using a method called MCMC to try and gain more accurate estimates of those parameters based on observed data. Modeling rhinovirus gives us insight into the workings of rhinovirus and helps us to try and create more accurate models.