Applications of Mathematical Models of Virus to Mpox

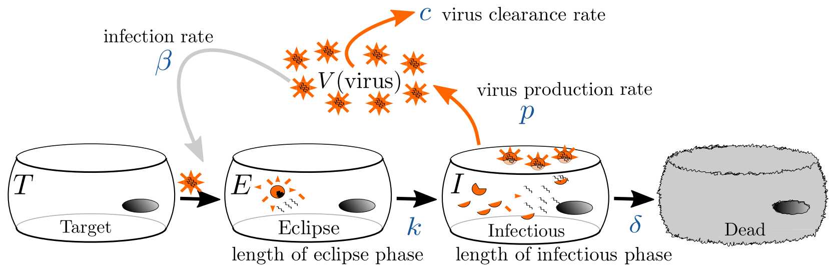
Gabriel McCarthy and Hana M. Dobrovolny

Department of Physics and Astronomy, Texas Christian University, Fort Worth, TX, USA

Background

- Mpox is a virus that is similar to smallpox and can cause disease in humans.
- Mpox can cause severe illness and may even result in death in humans.
- Viruses like Mpox can be represent by within-host viral infections are commonly represented by ordinary differential equation (ODE) models that track the amount of virus and the number of various cell types.
- Several clinical studies have been conducted to collect data on Mpox that may allow us to gain insight into Mpox characteristics via fitting our ODE models.
- Mathematical understanding of Mpox characteristics may allow for the development of better treatment regimens.

Basic model of viral infection



Target cells are infected by virus at infection rate β. Once infected, cells enter the eclipse phase where they are undergoing internal replication. After a time $1/k$, the cells become productively infectious, producing virus at rate p. After a time $1/\delta$, the cells die. Virus is cleared at rate c. This is described by the set of differential equations,

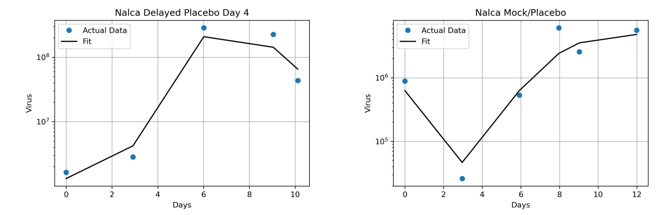
$$\begin{aligned}\frac{dT}{dt} &= -\beta VT\\ \frac{dE}{dt} &= \beta VT - kE\\ \frac{dI}{dt} &= kE - \delta I\\ \frac{dV}{dt} &= pI - cV.\end{aligned}$$

Data and Fitting

- The model was fit to several datasets collected from 3 papers (Berhanu et al., Jordan et al., Nalca et al.).
- Each paper contained time course data on mpox infection within either cynomolgus macaques.
- Data from these papers was fit in python using SSR to obtain best fit parameters for each dataset which could then be analyzed.

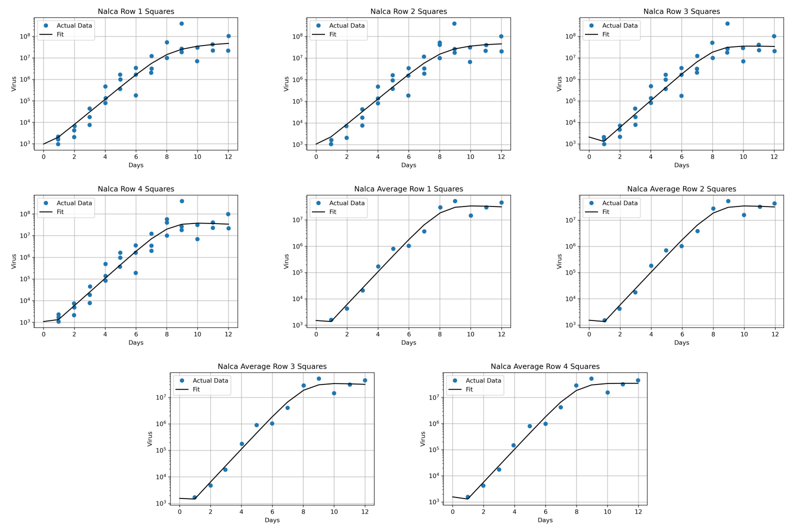
Berhanu

The experimental data and model best fits for the Berhanu paper can be seen below.



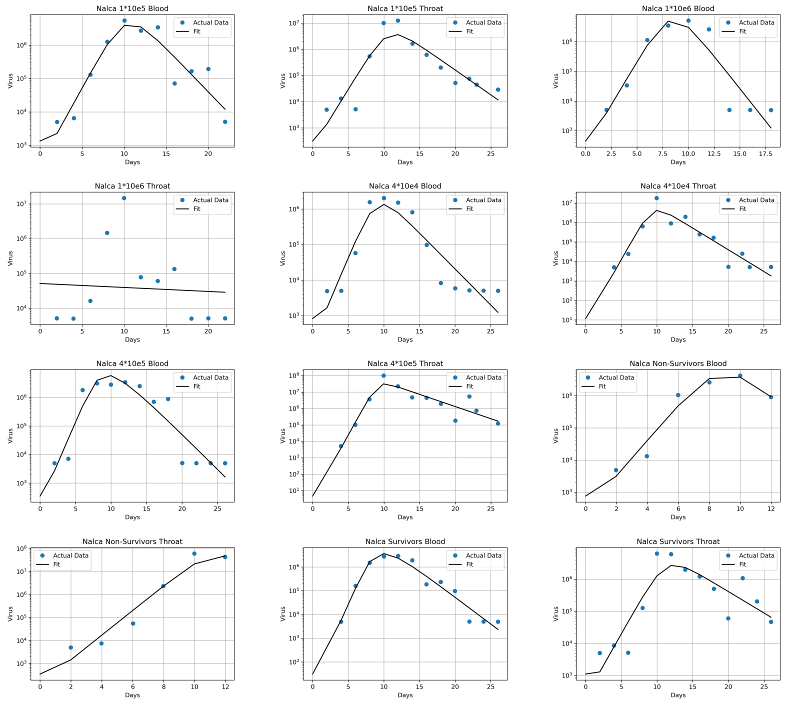
Jordan

The experimental data and model best fits for the Jordan paper can be seen below.



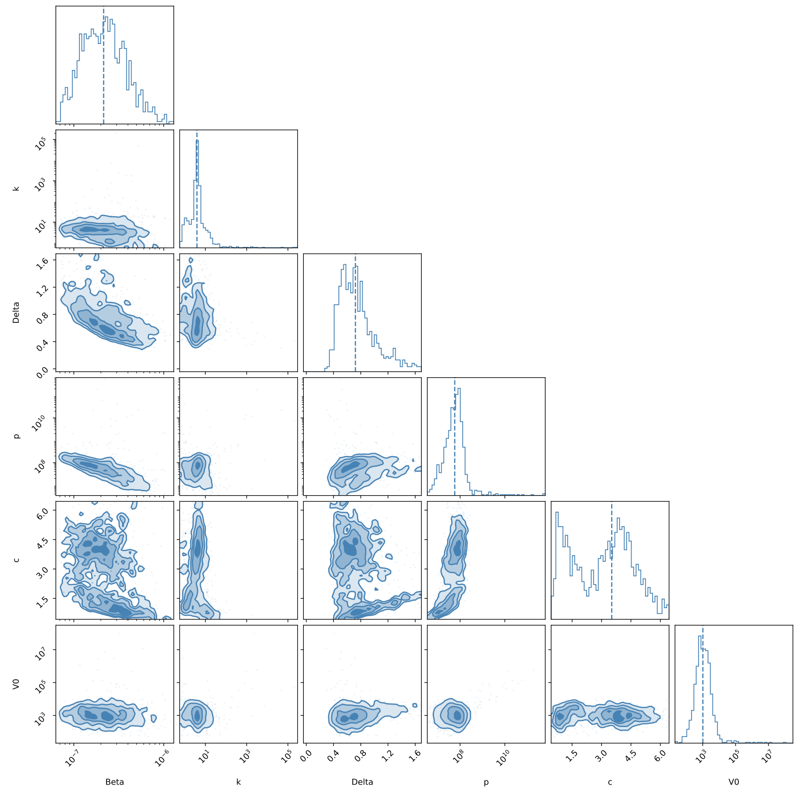
Nalca

The experimental data and model best fits for the Nalca paper can be seen below.



Bootstrapping

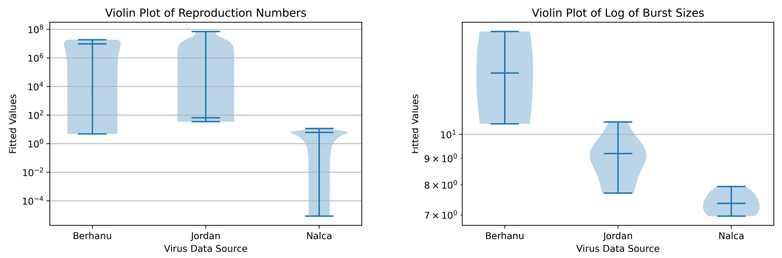
Using the best fits for each dataset, bootstrapping was conducted to obtain possible parameter distributions that were used to examine possible correlation between parameters and to determine confidence intervals. One such plot is seen below.



R_0 and Burst Size

$$R_0 = \frac{p\beta}{c\delta},\ Burst\ Size = \frac{p}{\delta}$$

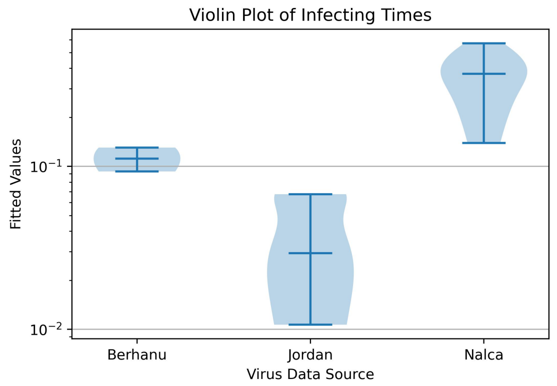
From our parameterizations, we can calculate the reproduction number (R_0) and the infecting time t_i using the equation above, which represents the average number of secondary infections caused by each infection and the average infecting time, respectively. Below, we have created Violin plots to visualize the difference between papers.



Infecting Time

$$t_i = \sqrt{\frac{2}{p\beta}}$$

Using our parameterization, we can calculate the infecting time for each dataset using the equation above. A violin plot comparing the distributions of this can be seen in the graph below.



Conclusions

- ODE models for the virus can be applied to Mpox data to better understand important characteristics of Mpox infection.
- We can compare the distributions of these characteristics across different experiments.
- We can create histograms to see where possible values of the reproduction number, burst size, and infecting time may lie for Mpox.
- We can create confidence intervals for the actual values of the parameters for the Mpox virus.

References

1. Nalca et al. Experimental infection of cynomolgus macaques (macaca fascicularis) with aerosolized monkeypox virus. PLOS ONE, 2010.
2. Jordan et al. ST-246 antiviral efficacy in a nonhuman primate monkeypox model: Determination of the minimal effective dose and human dose justification. Antimicrobial Agents and Chemotherapy, 2009.
3. Berhanu et al. Treatment with the smallpox antiviral tecovirimat (ST-246) alone or in combination with ACAM2000 vaccination is effective as a postsymptomatic therapy for monkeypox virus infection. Antimicrobial Agents and Chemotherapy, 2015.