A Novel Mathematical Model of Oropouche Virus Transmission Dynamics

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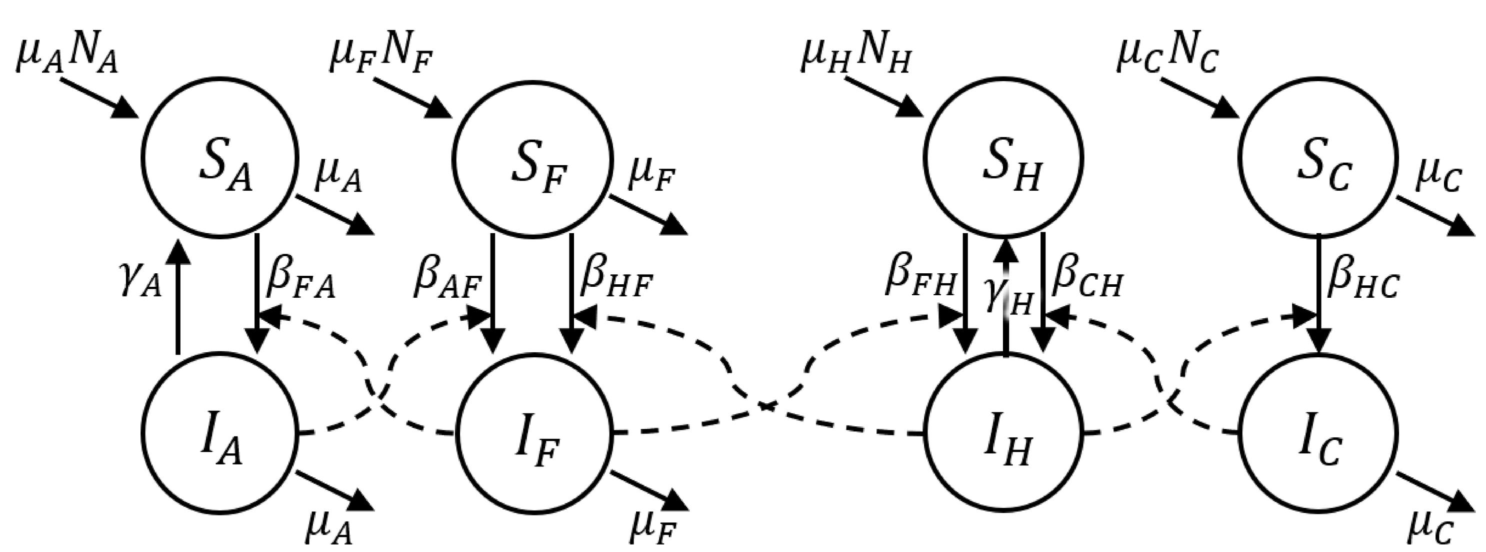
Background

- Oropouche virus (OROV) is a vector-borne disease originating from the Amazon basin.
- The current outbreak has more than 10,000 confirmed cases in the Americas.
- The disease presents as a febrile illness characterized by severe headaches, myalgia, and arthralgia.
- It is theorized that the disease circulates in two distinct cycles; a sylvatic and an urban cycle.
- Climate change and urbanization are exacerbating the public health challenges that OROV presents.

Research Question: What relationship, if any, can be inferred between seasonality and midge biting activity based on the weekly incidence of human OROV infections in the state of Amazonas, Brazil?

Disease Dynamics



Here, sloths (A) are taken to be the representative host in the sylvatic region. Forest midges (F) infect humans (H) who travel or work in the forest. The humans in turn infect city midges (C) who propagate the epidemic.

Reduced System of ODEs

By assuming constant populations, we can reduce the system from 8 equations to only 4.

$$
\begin{aligned}
\frac{\mathrm{d}I_A}{\mathrm{d}t} &= \underbrace{\beta_{FA} I_F \frac{N_A - I_A}{N_A}}_{\text{infection}} - \underbrace{\gamma_A I_A}_{\text{recovery}} - \underbrace{\mu_A I_A}_{\text{death}},\\
\frac{\mathrm{d}I_F}{\mathrm{d}t} &= \underbrace{\left(\beta_{AF}\frac{I_A}{N_A} + \beta_{HF}\frac{I_H}{N_H}\right)(N_F - I_F)}_{\text{infection}} - \underbrace{\mu_V I_F}_{\text{death}},\\
\frac{\mathrm{d}I_H}{\mathrm{d}t} &= \underbrace{(\beta_{FH} I_F + \beta_{CH} I_C)\frac{(N_H - I_H)}{N_H}}_{\text{infection}} - \underbrace{\gamma_H I_H}_{\text{recovery}} - \underbrace{\mu_H I_H}_{\text{death}},\\
\frac{\mathrm{d}I_C}{\mathrm{d}t} &= \underbrace{\beta_{HC}\frac{I_H}{N_H}(N_C - I_C)}_{\text{infection}} - \underbrace{\mu_V I_C}_{\text{death}}
\end{aligned}
\tag{1}
$$

Qualitative Analysis of the Autonomous System

Assuming all infection parameters are constant by taking $t = t^*$, the system has two equilibria: a disease free equilibrium (DFE) at $(0,0,0,0)$ and an endemic equilibrium (EE) at $(I_A^*, I_F^*, I_H^*, I_C^*)$.

Next-generation operator method proposed by van den Driessche and Watmough yields basic reproductive number:

$$\mathcal{R}_0 = \frac{1}{\sqrt{2}}\sqrt{R_{CH} + R_{FA} + R_{FH} + \sqrt{(R_{CH} + R_{FA} + R_{FH})^2 - 4R_{FA}R_{CH}}},$$

where:

- $R_{CH} = \frac{\beta_{CH}}{\mu_H + \gamma_H}\frac{\beta_{HC}}{\mu_V}\frac{N_C}{N_H}$ denotes transmission between vector and human in the urban area,
- $R_{FH} = \frac{\beta_{HF}}{\mu_V}\frac{\beta_{FH}}{(\mu_H + \gamma_H)}\frac{N_F}{N_H}$ denotes transmission between vector and human in the sylvatic patch and
- $R_{FA} = \frac{\beta_{AF}}{\mu_V}\frac{\beta_{FA}}{\mu_A + \gamma_A}\frac{N_F}{N_A}$ denotes transmission between vector and sloths.

We can bound $\mathcal{R}_0$ above and below as follows:

$$\sqrt{R_{FA} + R_{FH} + R_{CH} - \sqrt{R_{FA}R_{CH}}} < \mathcal{R}_0 < \sqrt{R_{FA} + R_{FH} + R_{CH}}.$$

The next generation operator method tells us that the DFE is locally asymptotically stable when $\mathcal{R}_0 < 1$.

Infection Rates

To explore the relationship between seasonality and the biting behavior of midges, we define each infection rate β as follows:

$$
\begin{aligned}
\beta_{FA}(t) &= b\pi_{VH}\frac{kN_A}{kN_A + (1-p)N_H}e^{-\left(\frac{t-t^*}{a}\right)^2},\\
\beta_{FH}(t) &= b\pi_{VH}\frac{(1-p)N_H}{kN_A + (1-p)N_H}e^{-\left(\frac{t-t^*}{a}\right)^2},\\
\beta_{CH}(t) &= b\pi_{VH}e^{-\left(\frac{t-t^*}{a}\right)^2},\\
\beta_{AF}(t) &= b\pi_{HV}\frac{kN_A}{kN_A + (1-p)N_H}e^{-\left(\frac{t-t^*}{a}\right)^2},\\
\beta_{HF}(t) &= b\pi_{HV}\frac{(1-p)N_H}{kN_A + (1-p)N_H}e^{-\left(\frac{t-t^*}{a}\right)^2},\\
\beta_{HC}(t) &= b\pi_{HV}e^{-\left(\frac{t-t^*}{a}\right)^2}.
\end{aligned}
$$

Parameter Estimation

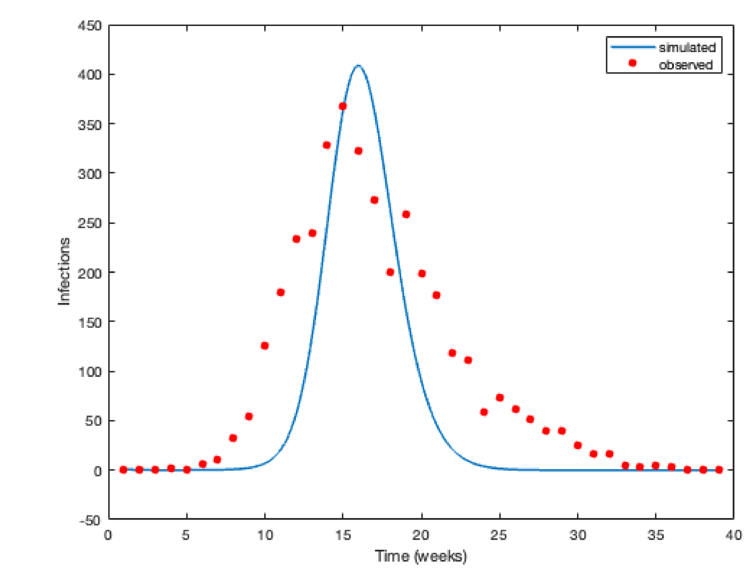
The data fitting problem is formulated as the following constrained optimization problem:

$$\min_{\theta \in T_{ad}} J(I_{HC}, \theta) := \frac{\omega}{2}\sum_{i=1}^{N_t}(I_{HC}(t^i) - X^i)^2 + \frac{\nu}{2}\|\theta\|_2^2, \text{ subject to model (1).}$$

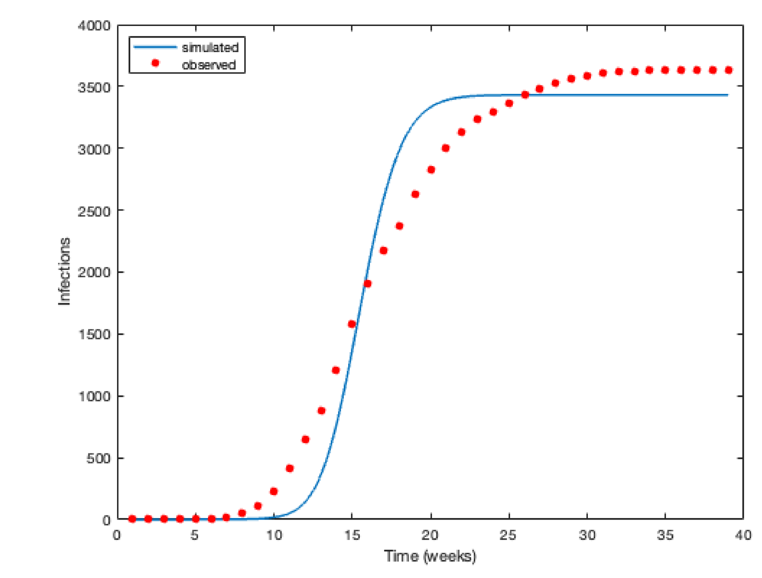
We employ the relative l^2 error percentage which is calculated as

$$EP = \sqrt{\frac{\sum_{i=1}^{N_t}(I_H(t^i) - X^i)^2}{\sum_{i=1}^{N_t}(X^i)^2}} \times 100.$$

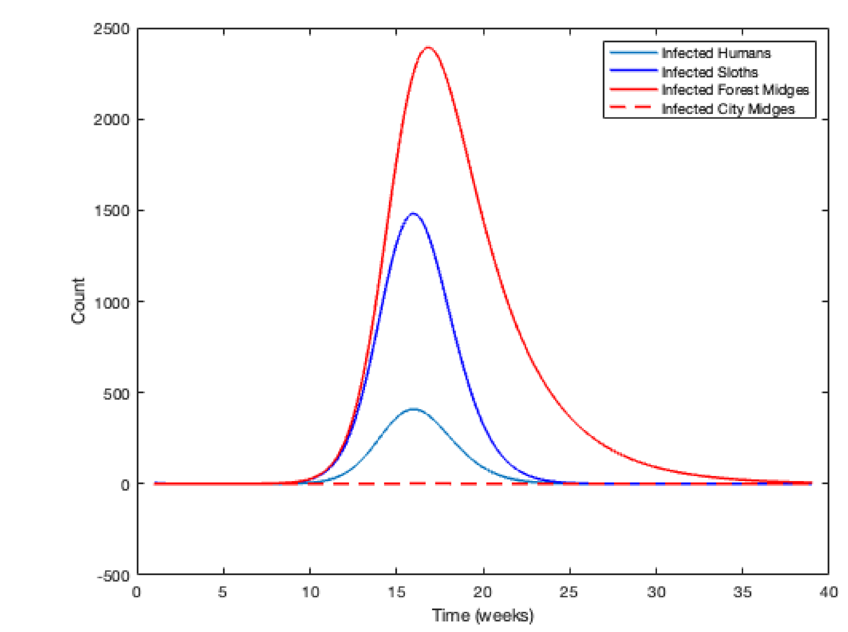
Numerical Results



(a)



(b)



(c)

Using the best fit parameter set, we plot simulated infection counts alongside confirmed weekly (a) and cumulative (b) OROV cases in Amazonas, Brazil from October 2023 to July 2024. While the cumulative infections were fit closely, this parameter set does not capture the temporal spread of the disease. In (c), we see that the viral presence peaks at roughly the same time.

Discussion and Future Work

- OROV is becoming a major public health threat as outbreaks worsen due to climate change and urbanization.
- Our novel mathematical model describes the dynamics of OROV transmission between the sylvatic and urban cycles.
- We computed the basic reproductive number, $\mathcal{R}_0$, found lower and upper bounds for it and confirmed that the DFE was LAS when $\mathcal{R}_0 < 1$.
- Incorporating seasonality in the infection terms, we accurately reproduced the shape of the data and found a relative l^2 error percentage of 9.223%.
- Future works include investigating different functional representations of the infection rates, incorporating precipitation and temperature data and considering different sylvatic hosts.

References and Acknowledgements

References:

1. MA Files, *et al.* Baseline mapping of Oropouche virology, epidemiology, therapeutics, and vaccine research and development, *npj Vaccines (2022)*.
2. GC Scachetti, *et al.* Re-emergence of Oropouche virus between 2023 and 2024 in Brazil: an observational epidemiological study. *Lancet Infect Dis (2024)*.

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