Matrix and Graph-Theoretic Methods in Global Stability Analysis of Zika Virus (ZIKV) Dynamics

K. Bessey[1] M. Mavis[2] J. Zhang[3]

[1]Department of Mathematics, University of North Georgia, GA

[2]Rosenstiel School of Marine and Atmospheric Science, University of Miami, FL

[3]Department of Mathematics, Johns Hopkins University, MD

REU Final Presentation
August 2, 2018

Overview

- Background Information on the Zika Virus
- The Model from Agusto et al.
- Our Contributions
  - The Model of Agusto et al.
    - A More Rigorous Proof of Global Stability
  - The First Modified Model
    - Existence of a Disease Free Equilibrium
    - Construction of Lyapunov Functions
    - Global Stability Analysis
  - The Generalized Model of Zika Virus Dynamics
    - Existence of a Disease Free Equilibrium
    - Construction of Lyapunov Functions
    - Global Stability Analysis of the Disease Free Equilibrium
    - Existence of an Endemic Equilibrium
    - Global Stability Analysis of the Endemic Equilibrium

The Zika Virus (ZIKV)

- Spread in three ways:
  - Human $\rightarrow$ human (horizontal transmission)
  - Mother $\rightarrow$ fetus (vertical transmission)
  - Mosquito $\rightarrow$ human (vector transmission)
- The transmission from mother to fetus can cause certain birth defects, specifically microcephaly.
- In the past 10 years, there have been outbreaks in the Americas. Most research on the disease comes from Brazil.
- There is a lack of data on the transmission of Zika, so there are not a lot of mathematical models available for the disease.

Why Are We Studying These Models?

- Previous REU students researched and analyzed a model of the Zika virus that included vector transmission and horizontal transmission.
- Other models, including the one we studied, differ because they include only vector transmission and vertical transmission, but not horizontal transmission. We improved upon the model by combining all three types of transmission into a generalized model.

Model from Agusto et al.

The Variables

$$
\begin{aligned}
S_B(t), S_W(t) &= \text{Susceptible newly born babies and adults}\\
E_B(t), E_W(t) &= \text{Exposed newly born babies and adults}\\
A_B(t), A_W(t) &= \text{Asymptomatic newly born babies and adults}\\
I_B(t), I_W(t) &= \text{Infectious symptomatic newly born babies without microcephaly and adults}\\
I_{BM}(t), I_{WM}(t) &= \text{Microcephalic newly born babies and adults}\\
R_B(t), R_W(t) &= \text{Recovered newly born babies and adults}\\
S_V(t) &= \text{Susceptible female mosquitoes}\\
E_V(t) &= \text{Exposed female mosquitoes}\\
I_V(t) &= \text{Infected female mosquitoes}
\end{aligned}
$$

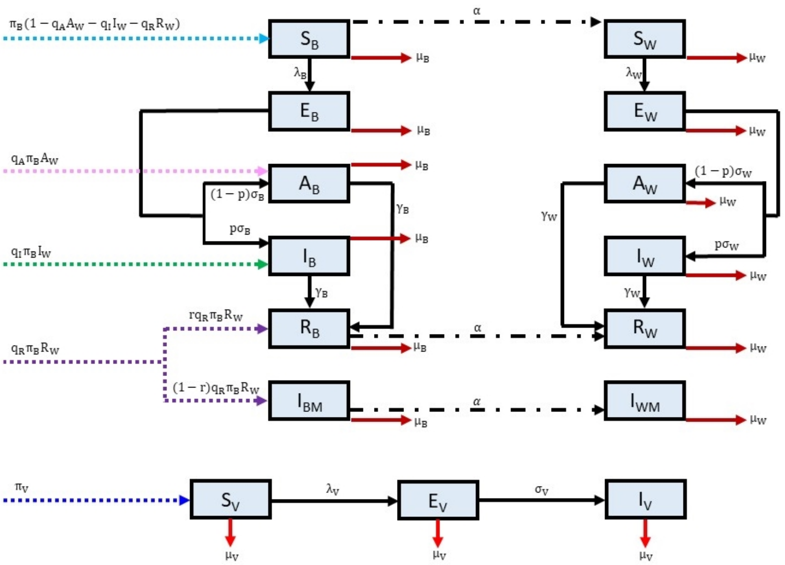
Model from Agusto et al.

The Parameters

$$
\begin{aligned}
\pi_B &= \text{Birth rate} \\
p &= \text{Fraction of adults and newly born babies who are asymptomatic} \\
1 - p &= \text{Remaining fraction of adults and newly born babies who are infectious} \\
\alpha &= \text{Maturation rate} \\
r, q_A, q_I, q_R &= \text{Fractions of newly born babies who are infected and have microcephaly} \\
1 - r &= \text{Remaining fraction of newly born babies who have microcephaly} \\
\eta &= \text{Modification parameter} \\
\beta_W, \beta_B &= \text{Transmission probability } \textit{per} \text{ contact of adults and newly born babies} \\
\rho_W, \rho_B &= \text{Infectivity modification parameters in asymptomatic adults and newly born babies} \\
\sigma_W, \sigma_B &= \text{Progression rate of exposed adults and newly born babies} \\
\gamma_W, \gamma_B &= \text{Recovery rate of asymptomatic and symptomatic adults and newly born babies} \\
\mu_w, \mu_B &= \text{Natural death rate of adults and newly born babies} \\
\pi_V &= \text{Recruitment rate of mosquitoes} \\
\beta_V &= \text{Transmission probability } \textit{per} \text{ contact of susceptible mosquitoes} \\
b_V &= \text{Mosquito biting rate} \\
\sigma_V &= \text{Progression rate of exposed mosquitoes} \\
\mu_V &= \text{Natural death rate of mosquitoes}
\end{aligned}
$$

Model from Agusto et al.

Flow Chart of the Model



$$
\begin{aligned}
S_B'(t) &= \pi_B - q_A\pi_B A_W(t) - q_I\pi_B I_W(t) - q_R\pi_B R_W(t) - \lambda_B(I_V, N_B)S_B(t) - (\alpha + \mu_B)S_B(t)\\
E_B'(t) &= \lambda_B(I_V, N_B)S_B(t) - (\alpha + \sigma_B + \mu_B)E_B(t)\\
A_B'(t) &= q_A\pi_B A_W(t) + (1-p)\sigma_B E_B(t) - (\alpha + \gamma_B + \mu_B)A_B(t)\\
I_B'(t) &= q_I\pi_B I_W(t) + p\sigma_B E_B(t) - (\alpha + \gamma_B + \mu_B)I_B(t)\\
I_{BM}'(t) &= rq_R\pi_B R_W(t) - (\alpha + \mu_B)I_{BM}(t)\\
R_B'(t) &= (1-r)q_R\pi_B R_W(t) + \gamma_B A_B(t) + \gamma_B I_B(t) - (\alpha + \mu_B)R_B(t)\\
S_W'(t) &= \alpha S_B(t) - \lambda_W(I_V, N_W)S_W(t) - \mu_W S_W(t)\\
E_W'(t) &= \lambda_W(I_V, N_W)S_W(t) - (\sigma_W + \mu_W)E_W(t)\\
A_W'(t) &= (1-p)\sigma_W E_W(t) - (\gamma_W + \mu_W)A_W(t)\\
I_W'(t) &= p\sigma_W E_W(t) - (\gamma_W + \mu_W)I_W(t)\\
I_{WM}'(t) &= \alpha I_{BM}(t) - \mu_W I_{WM}(t)\\
R_W'(t) &= \alpha R_B(t) + \gamma_W A_W(t) + \gamma_W I_W(t) - \mu_W R_W(t)\\
S_V'(t) &= \pi_V - \lambda_V(A_B, I_B, A_W, I_W, N_B, N_W)S_V(t) - \mu_v S_V(t)\\
E_V'(t) &= \lambda_V(A_B, I_B, A_W, I_W, N_B, N_W)S_V(t) - (\mu_V + \sigma_V)E_V(t)\\
I_V'(t) &= \sigma_V E_V(t) - \mu_V I_V(t)
\end{aligned}
$$

Model from Agusto et al.

The Model

With

$$\lambda_B(I_V, N_B) = \frac{\eta\beta_B b_V I_V}{N_B}$$
$$\lambda_W(I_V, N_W) = \frac{\beta_W b_V I_V}{N_W}$$
$$\lambda_V(A_B, I_B, A_W, I_W, N_B, N_W) = \beta_V b_V (\frac{I_W + \rho_W A_W + \eta(I_B + \rho_B A_B)}{N_W + \eta N_B})$$

$$N_B = S_B + E_B + A_B + I_B + I_{BM} + R_B$$
$$N_W = S_W + E_W + A_W + I_W + I_{WM} + R_W$$
$$N_V = S_V + E_V + I_V$$
$$N_H = N_B + N_W$$

where the total populations N_H and N_V are constant.

Dynamical Systems

Finding explicit solutions of this kind of system is impossible. The goal in dynamical systems is to understand the qualitative behavior of solutions even if they are not available, and to provide rigorous results on the main properties of the system, including:

- Existence of attracting sets
- Stability properties
- Bifurcations
- Chaos
- Asymptotic Analysis

Equilibrium Points and Stability

Definition

Consider the system $x' = f(x)$ ($f : \mathbb{R}^n \to \mathbb{R}^n$). There will exist an **equilibrium point** when $x' = 0$.

Local vs. Global Stability

- Local stability analyzes the stability in a neighborhood around the equilibrium point.
    - Linearization at the equilibrium point.
- Global stability describes the stability around a larger set containing the equilibrium point, and global stability implies local stability.
    - Lyapunov functions allow the proof of global stability at the equilibrium point.

Feasible Region

Definition

A set $S \subset R^n$ is said to be **positively invariant** with respect to $x' = f(x)$ if $x(0) \in S \Longrightarrow x(t) \in S$ for all $t \geq 0$.

We next prove that the feasible region, $\Gamma = \Gamma_H \times \Gamma_V \subset \mathbb{R}_+^{12} \times \mathbb{R}_+^3$ with

$$\Gamma_H = \{S_B, E_B, A_B, I_B, I_{BM}, R_B, S_W, E_W, A_W, I_W, I_{WM}, R_W : N_H \leq \frac{\pi_B}{\mu_H} + S_H(0)\}$$

$$\Gamma_V = \{S_V, E_V, I_V : N_V \leq \frac{\pi_V}{\mu_V} + N_V(0)\}$$

is positively invariant where we assume $S_V \leq S_V^o$.

Note: This region is less restrictive than the one given in Agusto et al.

Feasible Region

Adding the first twelve equations and the last three equations of the model, we obtain
$N'_H(t) = \pi_B - \mu_B N_B(t) - \mu_W N_W(t) - \alpha(E_B(t) + A_B(t) + I_B(t))$
and $N'_V(t) = \pi_V - \mu_V N_V(t)$, respectively.

Furthermore, to show that Γ is positively invariant, we use the following inequalities:

$$N'_H(t) \leq \pi_B - \mu_H N_H(t)$$
$$N'_V(t) = \pi_V - \mu_V N_V(t)$$

Where $\mu_H = min\{\mu_B, \mu_W\}$

Feasible Region

Now, consider:

$$\tilde{N}'_H(t) = \pi_B - \mu_H N_H(t)$$
$$\tilde{N}_H(t) = \frac{\pi_B}{\mu_H}\left[1 - e^{-\mu_H t}\right] + \tilde{N}_H(0)e^{-\mu_H t}$$

$$\tilde{N}_H(0) = N_H(0)$$

Using theorem 6.1 from Hale, we get the following differential inequality,

$$N_H(t) \leq \frac{\pi_B}{\mu_H}\left[1 - e^{-\mu_H t}\right] + \tilde{N}_H(0)e^{-\mu_H t}$$

$$N_H(t) \leq \frac{\pi_B}{\mu_H} + N_H(0), \quad \text{for } t \geq 0$$

Finding Equilibrium Points

To solve our system $f(x) = 0$, we begin with the equation $R'_W(t) = \alpha R_B(t) + \gamma_W A_W(t) + \gamma_W I_W(t) - \mu_W R_W(t)$.

It makes biological sense that $\gamma_W(A_W(t) + I_W(t)) > \mu_W R_W(t)$ for $t \geq 0$.

Considering $\gamma_W > 0$, $\mu_W > 0$, $A_W(t) \geq 0$, $I_W(t) \geq 0$, and $R_W(t) \geq 0$, we see that:

$$\gamma_W A_W + \gamma_W I_W - \mu_W R_W > 0.$$

Then setting the initial R'_W equation equal to zero shows that $\alpha R_B(t) = 0$, and therefore that $R_B^o = 0$.

Finding the Disease Free Equilibrium

Following the same procedure, we get the following:

From Equation	We See That
$R'_W(t) = 0$	$R^o_B = 0,\ R^o_W = 0,\ A^o_W = 0,\ I^o_W = 0$
$R'_B(t) = 0$	$A^o_B = 0,\ I^o_B = 0$
$A'_B(t) = 0$	$E^o_B = 0$
$I'_{BM}(t) = 0$	$I^o_{BM} = 0$
$I'_{WM}(t) = 0$	$I^o_{WM} = 0$
$E'_V(t) = 0$	$E^o_V = 0$
$I'_V(t) = 0$	$I^o_V = 0$
$A'_W(t) = 0$	$E^o_W = 0$
$S'_V(t) = 0$	$S^o_V = \frac{\pi_V}{\mu_V}$
$S'_B(t) = 0$	$S^o_B = \frac{\pi_B}{\alpha + \mu_B}$
$S'_W(t) = 0$	$S^o_W = \frac{\alpha \pi_B}{\mu_W(\alpha + \mu_B)}$

Finding the Disease Free Equilibrium

Therefore, the only equilibrium point of the original model is the disease free equilibrium (E_0) where

$$E_0 = (S_B^o, E_B^o, A_B^o, I_B^o, I_{BM}^o, R_B^o, S_W^o, E_W^o, A_W^o, I_W^o, I_{WM}^o, R_W^o, S_V^o, E_V^o, I_V^o)$$

Or, more specifically,

$$E_0 = \left(\frac{\pi_B}{\alpha + \mu_B}, 0, 0, 0, 0, 0, \frac{\alpha \pi_B}{\mu_W(\alpha + \mu_B)}, 0, 0, 0, 0, 0, \frac{\pi_V}{\mu_V}, 0, 0 \right)$$

Therefore, the disease free equilibrium (E_0) is the only equilibrium point of the system (unique), and no endemic equilibrium point exists.

Analyzing the global asymptotic stability (GAS) of the DFE

We approach the model as done by Shuai et al. We split the variables of the model into two compartments: a disease compartment $x \in \mathbb{R}^{10}$ and a disease free compartment $y \in \mathbb{R}^{5}$, in the form:

$$\mathrm{x} = \begin{bmatrix} E_B \\ A_B \\ I_B \\ I_{BM} \\ E_W \\ A_W \\ I_W \\ I_{WM} \\ E_V \\ I_V \end{bmatrix} \quad \text{and} \quad \mathrm{y} = \begin{bmatrix} S_B \\ R_B \\ S_W \\ R_W \\ S_V \end{bmatrix}$$

where

$$x' = \mathcal{F}(x, y) - \mathcal{V}(x, y) \qquad\qquad y' = g(x, y)$$

We define two vectors $\in \mathbb{R}^{10}$, $\mathcal{F}$ and $\mathcal{V}$, which will be created from the diseased compartment (the vector x) such that

$$\mathcal{F} = \begin{bmatrix} \frac{\eta\beta_B b_V I_V(t)}{N_B(t)} S_B(t) \\ 0 \\ 0 \\ r q_R \pi_B R_W(t) \\ \frac{\beta_W b_V I_V(t)}{N_W(t)} S_W(t) \\ 0 \\ 0 \\ 0 \\ \beta_V b_V (\frac{I_W + \rho_W A_W + \eta(I_B + \rho_B A_B)}{N_W + \eta N_B}) S_V(t) \\ 0 \end{bmatrix} \quad \mathcal{V} = \begin{bmatrix} (\alpha + \sigma_B + \mu_B) E_B(t) \\ (\alpha + \gamma_B + \mu_B) A_B(t) - q_A \pi_B A_W(t) - (1-p)\sigma_B E_B(t) \\ (\alpha + \gamma_B + \mu_B) I_B(t) - q_I \pi_B I_W(t) - p\sigma_B E_B(t) \\ (\alpha + \mu_B) I_{BM}(t) \\ (\sigma_W + \mu_W) E_W(t) \\ (\gamma_W + \mu_W) A_W(t) - (1-p)\sigma_W E_W(t) \\ (\gamma_W + \mu_W) I_W(t) - p\sigma_W E_W(t) \\ \mu_W I_{WM}(t) - \alpha I_{BM}(t) \\ (\mu_V + \sigma_V) E_V(t) \\ \mu_V I_V(t) - \sigma_V E_V(t) \end{bmatrix}$$

Where $\mathcal{F}$ contains the terms that contribute to new infection, and $\mathcal{V}$ contains the terms that contribute to recovery and death.

We then define two 10×10 matrices F and V, such that

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(0, y_0)(E_0)\right] \text{ and } V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(0, y_0)(E_0)\right]$$

Where E_0 is the DFE

$$E_0 = \left(\frac{\pi_B}{\alpha + \mu_B}, 0, 0, 0, 0, 0, \frac{\alpha \pi_B}{\mu_W(\alpha + \mu_B)}, 0, 0, 0, 0, 0, \frac{\pi_V}{\mu_V}, 0, 0\right)$$

and

$$y_0 = (S_B^o, R_B^o, S_W^o, R_W^o, S_V^o) = \left(\frac{\pi_B}{\alpha + \mu_B}, 0, \frac{\alpha \pi_B}{\mu_W(\alpha + \mu_B)}, 0, \frac{\pi_V}{\mu_V}\right)$$

Global Asymptotic Stability

The F Matrix

$$F = \begin{bmatrix}
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dfrac{\eta\beta_B b_V S_B^o}{N_B^o} \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dfrac{\beta_W b_V S_W^o}{N_W^o} \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & \dfrac{\eta\beta_V b_V \rho_B S_V^o}{S_W^o + \eta S_B^o} & \dfrac{\eta\beta_V b_V S_V^o}{S_W^o + \eta S_B^o} & 0 & 0 & \dfrac{\rho_W \beta_V b_V S_V^o}{S_W^o + \eta S_B^o} & \dfrac{\beta_V b_V S_V^o}{S_W^o + \eta S_B^o} & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix}$$

Global Asymptotic Stability

The V Matrix

$$V = \begin{bmatrix} \alpha+\sigma_B+\mu_B & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -(1-p)\sigma_B & \alpha+\gamma_B+\mu_B & 0 & 0 & 0 & -q_A\pi_B & 0 & 0 & 0 & 0 \\ -p\sigma_B & 0 & \alpha+\gamma_B+\mu_B & 0 & 0 & 0 & -q_I\pi_B & 0 & 0 & 0 \\ 0 & 0 & 0 & \alpha+\mu_B & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma_W+\mu_W & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (1-p)\sigma_W & \gamma_W+\mu_W & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -p\sigma_W & 0 & \gamma_W+\mu_W & 0 & 0 & 0 \\ 0 & 0 & 0 & -\alpha & 0 & 0 & 0 & \mu_W & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_V+\sigma_V & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\sigma_V & \mu_V \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix}
\frac{1}{k_1} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\frac{\sigma_B(1-p)}{k_1k_2} & \frac{1}{k_2} & 0 & 0 & \frac{\pi_B q_A \sigma_W(1-p)}{k_1k_4k_5} & \frac{\pi_B q_A}{k_2k_5} & 0 & 0 & 0 & 0 \\
\frac{\pi_B\sigma_B}{k_1k_2} & 0 & \frac{1}{k_2} & 0 & \frac{p\sigma_B q_I \sigma_W}{k_2k_4k_5} & 0 & \frac{\pi_B q_I}{k_2k_5} & 0 & 0 & 0 \\
0 & 0 & 0 & \frac{1}{k_3} & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \frac{1}{k_4} & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \frac{\sigma_W(1-p)}{k_4k_5} & \frac{1}{k_5} & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & \frac{p\sigma_W}{k_4k_5} & 0 & \frac{1}{k_5} & 0 & 0 & 0 \\
0 & 0 & 0 & \frac{\alpha}{\mu_W k_3} & 0 & 0 & 0 & \frac{1}{\mu_W} & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{k_6} & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\sigma_V}{\mu_V k_6} & \frac{1}{\mu_v}
\end{bmatrix}$$

where

$$k_1 = \alpha + \sigma_B + \mu_B,\ k_2 = \alpha + \gamma_B + \mu_B,\ k_3 = \alpha + \mu_B,\ k_4 = \sigma_W + \mu_W,\ k_5 = \gamma_W + \mu_W,\ k_6 = \mu_V + \sigma_V$$

Definition

Assume that $F \geq 0$ and $V^{-1} \geq 0$, which is biologically reasonable. Then the **next-generation matrix** is $A = FV^{-1}$, where entry A_{ij} represents the expected number of new infections in compartment i produced by infected individuals in compartment j.

Definition

Given a matrix A and eigenvalues λ_i, $(i = 1, \ldots, n)$, the **spectral radius** (ρ) of A is defined as $\rho(A) = \max_{\{1 \leq i \leq n\}} |\lambda_i|$.

Definition

Given matrices F and V, the **basic reproduction number** $(\mathcal{R}_0)$ is defined as $\rho(FV^{-1})$.

Notes:

- $\mathcal{R}_0$ is the average number of people infected by one infected person in a totally susceptible population.
- The spectral radius of A is not necessarily an eigenvalue of A.

Therefore, knowing F and V^{-1}, we can find our **Next Generation Matrix**, (FV^{-1}).

From this matrix, we found that

$$\mathcal{R}_0 = \rho(FV^{-1}) = \sqrt{AE + CI}$$

Where

$$A = \frac{\sigma_V \eta \beta_B b_V S_B^o}{(\mu_V + \sigma_V)\mu_V N_B^o}$$

$$C = \frac{\sigma_V \beta_W b_V S_W^o}{(\mu_V + \sigma_V)\mu_V N_W^o}$$

$$E = \frac{\sigma_B \eta \beta_V b_V S_V^o[(1-p)\rho_B + p]}{(\alpha + \sigma_B + \mu_B)(\alpha + \gamma_B + \mu_B)(S_W^o + \eta S_B^o)}$$

$$I = \frac{\sigma_W \beta_V b_V S_V^o[(1-p)\rho_W + p]}{(\sigma_W + \mu_W)(\gamma_W + \mu_W)(S_W^o + \eta S_B^o)} + \frac{\pi_B \sigma_W \eta \beta_V b_V S_V^o[q_I p + q_A(1-p)\rho_B]}{(\sigma_W + \mu_W)(\gamma_W + \mu_W)(\alpha + \mu_B + \gamma_B)(S_W^o + \eta S_B^o)}$$

Following the systematic method established by equation (2.1) in Shuai et al, we set

$$f(x, y) := (F - V)x - \mathcal{F}(x, y) + \mathcal{V}(x, y)$$

Then

$$f(x,y) = \begin{bmatrix} \eta\beta_B b_V I_V(\frac{S_B^o}{N_B^o} - \frac{S_B}{N_B}) \\ 0 \\ 0 \\ -rq_R\pi_B R_W \\ \beta_W b_V I_V(\frac{S_W^o}{N_W^o} - \frac{S_W}{N_W}) \\ 0 \\ 0 \\ 0 \\ \beta_V b_V(I_W + \rho_W A_W + \eta(I_B + \rho_B A_B))(\frac{S_V^o}{S_W^o + \eta S_B^o} - \frac{S_V}{N_W + \eta N_B}) \\ 0 \end{bmatrix}$$

*Note that not all terms are positive.

Definition

A function $Q : \mathbb{R}^n \to \mathbb{R} \in C^1(E)$, with E an open set containing the equilibrium point $x_0 \in \mathbb{R}^n$ is called a **Lyapunov function** if:

- $Q(x) > 0, Q(x_0) = 0$
- $\frac{d}{dt}Q(x(t)) \leq 0$

Disclaimer: Finding a Lyapunov function is difficult if not impossible.

To construct a Lyapunov function of the system under certain conditions:

Theorem (Shuai et al)

*Let F, V, and $f(x, y)$ be defined as before, and let $\omega^T \geq 0$ be a left eigenvector of the nonnegative matrix $V^{-1}F$ corresponding to the eigenvalue *$\rho(V^{-1}F) = \rho(FV^{-1}) = \mathcal{R}_0$. If $f(x, y) \geq 0$* in $\Gamma \subset \mathbb{R}_+^{n+m}$, $F \geq 0$, $V \geq 0$, and $\mathcal{R}_0 \leq 1$, then the function*

$$Q = \omega^T V^{-1} x$$

is a Lyapunov function for the model on Γ.

Note: We were not able to directly apply this theorem to the model because several of the conditions failed.

We were not able to apply this theorem to the model because several of the conditions failed.

Even though the model does not satisfy all conditions of the theorem, we will prove that $\omega^T V^{-1} f(x, y)$ is non-negative, which eventually impies that Q' is non-positive.

Therefore, $Q = \omega^T V^{-1} x$ can still be used as a Lyapunov function for the original model.

Theorem (LaSalle's Invariance Principle)

Let $\Gamma \subset D \subset \mathbb{R}^n$ be a compact positively invariant set with respect to the system. Let $Q : D \to \mathbb{R}$ be a continuously differentiable function such that $Q'(x(t)) \leq 0$ in Γ (e. g. Q is a Lyapunov function). Let $S \subset \Gamma$ be the set of all points in Γ where $Q'(x(t)) = 0$. Let $M \subset S$ be the largest invariant set in S. Then every solution starting in Γ approaches M as $t \to \infty$, that is,

$$\lim_{t\to\infty} \left[\inf_{z\in M} ||x(t) - z|| \right] = 0$$

Theorem (BMZ)

The disease free equilibrium of the Agusto model system is globally asymptotically stable on Γ *if* $S_V \leq S_V^o$ *and* $\mathcal{R}_0 < 1$.

Note: This theorem only requires two sufficient conditions to hold. This is a more general form than the work that was done by previous researchers and REU students.

Proof.

Approach to prove global asymptotic stability of the DFE using LaSalle: (1) Find a Lyapunov function for the system, (2) Find the set S in Γ where $Q' = 0$, (3) Show that the largest invariant set in S is the DFE.

(1) Consider the function,

$$Q = \omega^T V^{-1} x$$

where ω^T is a left eigenvector of the matrix $V^{-1}F$corresponding to the eigenvalue $\mathcal{R}_0$. In general, $\mathcal{R}_0$ is not necessarily an eigenvalue of $V^{-1}F$. In our case, we confirmed that $\mathcal{R}_0$ is an eigenvalue and that there is a non-negative eigenvector ω^T corresponding to $\mathcal{R}_0$. In fact, ω^T has the form

$$\begin{bmatrix} 0 & A & B & 0 & 0 & C & D & 0 & 0 & E \end{bmatrix}$$

where A, B, C, D, and E are positive values. Note that $\dfrac{d}{dt}Q'(x(t)) =$ $\omega^T V^{-1} x' = \omega^T V^{-1}(F - V)x - \omega^T V^{-1} f(x,y) = (\mathcal{R}_0 - 1)\omega^T x - \omega^T V^{-1} f(x,y)$.

Also, computation in MatLab shows that $\omega^T V^{-1} f(x,y)$ is non-negative. x is also non-negative, so when $\mathcal{R}_0 \leq 1$, $\frac{d}{dt}Q'(x(t)) = (\mathcal{R}_0 - 1)\omega^T x - \omega^T V^{-1} f(x,y) \leq 0$. Also, one can observe that we have $Q \geq 0$, which implies that Q is indeed a Lyapunov function in Γ.

(2) We want to find the set $S = \{x \in \mathbb{R}_{15} : Q' = 0\}$. When $Q' = 0$, we must have that $(\mathcal{R}_0 - 1)\omega^T x = \omega^T V^{-1} f(x,y)$. And since $\mathcal{R}_0 < 1$, we have $(\mathcal{R}_0 - 1)\omega^T x$ non-positive and $\omega^T V^{-1} f(x,y)$ non-negative. Thus, $(\mathcal{R}_0 - 1)\omega^T x = 0$, so $\omega^T x = 0$. This only implies that $A_B = I_B = A_W = I_W = I_V = 0$. Thus, $S = \{x \in \mathbb{R}_{15} : A_B = I_B = A_W = I_W = I_V = 0\}$. On this set S, we are left with the following system:

Global Asymptotic Stability

Convergence to the Disease Free Equilibrium

$$
\begin{aligned}
S_B'(t) &= \pi_B - q_R\pi_B R_W(t) - (\alpha + \mu_B)S_B(t)\\
E_B'(t) &= -(\alpha + \sigma_B + \mu_B)E_B(t)\\
I_{BM}'(t) &= rq_R\pi_B R_W(t) - (\alpha + \mu_B)I_{BM}(t)\\
R_B'(t) &= (1-r)q_R\pi_B R_W(t) - (\alpha + \mu_B)R_B(t)\\
S_W'(t) &= \alpha S_B(t) - \mu_W S_W(t)\\
E_W'(t) &= -(\sigma_W + \mu_W)E_W(t)\\
I_{WM}'(t) &= \alpha I_{BM}(t) - \mu_W I_{WM}(t)\\
R_W'(t) &= \alpha R_B(t) - \mu_W R_W(t)\\
S_V'(t) &= \pi_V - \mu_v S_V(t)\\
E_V'(t) &= -(\mu_V + \sigma_V)E_V(t)
\end{aligned}
$$

We next prove that all trajectories of solutions to this system go to the DFE.

(3) To solve each of the differential equations, we will use the integrating factor for differential equations of the following form

$$y' + ay = f(t)$$
$$y(t) = e^{-at}\int_0^t e^{as}f(s)ds + Ce^{-at}$$

where $C = y(0)$.
After rearranging $S_B'(t)$, the integrating factor method can be applied.
(i)

$$S_B'(t) + (\alpha + \mu_B)S_B(t) = \pi_B - q_R\pi_B R_W(t)$$
$$S_B(t) = e^{-(\alpha+\mu_B)t}\int_0^t e^{(\alpha+\mu_B)s}[\pi_B - q_R\pi_B R_W(s)]ds + Ce^{-(\alpha+\mu_B)t}$$

Simplifying the expression gives

$$S_B(t) = e^{-(\alpha+\mu_B)t}\left[\frac{\pi_B}{\alpha+\mu_B}(e^{(\alpha+\mu_B)t}-1) - q_R\pi_B\int_0^t e^{(\alpha+\mu_B)s}R_W(s)ds\right] + Ce^{-(\alpha+\mu_B)t}$$

$$S_B(t) = \frac{\pi_B}{\alpha+\mu_B} - \frac{\pi_B}{\alpha+\mu_B}e^{-(\alpha+\mu_B)t} - q_R\pi_B e^{-(\alpha+\mu_B)t}\int_0^t e^{(\alpha+\mu_B)s}R_W(s)ds + Ce^{-(\alpha+\mu_B)t}$$

We can show that $e^{-(\alpha+\mu_B)t}\int_0^t e^{(\alpha+\mu_B)s}R_W(s)ds$ is bounded which allows us to conclude that

$$\lim_{t\to\infty} S_B(t) = \frac{\pi_B}{\alpha+\mu_B} = S_B^o(t)$$

Likewise, the integrating factor method can be implemented for the other differential equations.

(ii)

$$\lim_{t\to\infty} R_B(t) = 0 = R_B^o$$

(iii)

$$S'_W(t) + \mu_W S_W(t) = \alpha S_B(t)$$

$$S_W(t) = e^{-\mu_W t} \int_0^t e^{\mu_W s} \alpha S_B(s) ds + Ce^{-\mu_W t}$$

Substituting for $S_B(s)$ from (2.10) gives

$$S_W(t) = \alpha e^{-\mu_W t} \int_0^t e^{\mu_W s} \left[\frac{\pi_B}{z} - \frac{\pi_B}{z} e^{-(z)s} - q_R \pi_B e^{-(z)s} \int_0^s e^{(z)r} R_W(r) dr + Ce^{-(z)s} \right] ds + Ce^{-\mu_W t}$$

$$= \alpha e^{-\mu_W t} \int_0^t \frac{\pi_B e^{\mu_W s}}{z} - \frac{\pi_B e^{(\mu_W - (z))s}}{\alpha + \mu_B} - q_R \pi_B e^{(\mu_W - (z))s} \int_0^s e^{zr} R_W(r) dr + Ce^{(\mu_W - (z))s} ds + Ce^{-\mu_W t}$$

Where $z = \alpha + \mu_B$

Similarly from the previous result,

$$\lim_{t \to \infty} S_W(t) = \frac{\alpha \pi_B}{\mu_W(\alpha + \mu_B)} = S_W^o$$

Global Asymptotic Stability

Convergence to the Disease Free Equilibrium

(iv)

$$\lim_{t\to\infty} R_W(t) = 0 = R_W^o$$

(v)

$$\lim_{t\to\infty} S_V(t) = \frac{\pi_V}{\mu_V} = S_V^o$$

(vi)

$$\lim_{t\to\infty} E_B(t) = 0 = E_B^o$$

(vii)

$$\lim_{t\to\infty} I_{BM}(t) = 0 = I_{BM}^o$$

(viii)

$$\lim_{t\to\infty} E_W(t) = 0 = E_W^o$$

(ix)

$$\lim_{t\to\infty} I_{WM}(t) = 0 = I_{WM}^o$$

(x)

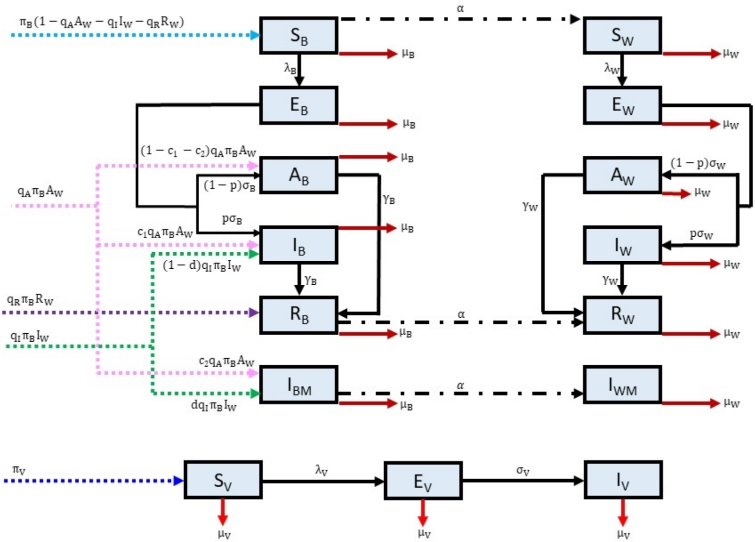
$$\lim_{t\to\infty} E_V(t) = 0 = E_V^o$$

By solving the system of differential equations, we were able to prove that as $t \to \infty$, all possible trajectories of the system approach the DFE. Thus, E_0 is the largest and only invariant set in S with respect to the system. Clearly, Γ is compact and we have shown that it is positively invariant with respect to the system. Applying LaSalle's Invariance Principle, we conclude that the disease free equilibrium point E_0 is globally asymptotically stable when $\mathcal{R}_0 < 1$.

□

The First Modified Model

Flow Chart of the First Modified Model



$$
\begin{aligned}
S_B'(t) &= \pi_B - q_A\pi_B A_W(t) - q_I\pi_B I_W(t) - q_R\pi_B R_W(t) - \lambda_B(I_V, N_B)S_B(t) - (\alpha + \mu_B)S_B(t)\\
E_B'(t) &= \lambda_B(I_V, N_B)S_B(t) - (\sigma_B + \mu_B)E_B(t)\\
A_B'(t) &= (1 - c_1 - c_2)q_A\pi_B A_W(t) + (1-p)\sigma_B E_B(t) - (\gamma_B + \mu_B)A_B(t)\\
I_B'(t) &= (1-d)q_I\pi_B I_W(t) + c_1 q_A\pi_B A_W(t) + p\sigma_B E_B(t) - (\gamma_B + \mu_B)I_B(t)\\
I_{BM}'(t) &= c_2 q_A\pi_B A_W(t) + d q_I\pi_B I_W(t) - (\alpha + \mu_B)I_{BM}(t)\\
R_B'(t) &= q_R\pi_B R_W(t) + \gamma_B A_B(t) + \gamma_B I_B(t) - (\alpha + \mu_B)R_B(t)\\
S_W'(t) &= \alpha S_B(t) - \lambda_W(I_V, N_W)S_W(t) - \mu_W S_W(t)\\
E_W'(t) &= \lambda_W(I_V, N_W)S_W(t) - (\sigma_W + \mu_W)E_W(t)\\
A_W'(t) &= (1-p)\sigma_W E_W(t) - (\gamma_W + \mu_W)A_W(t)\\
I_W'(t) &= p\sigma_W E_W(t) - (\gamma_W + \mu_W)I_W(t)\\
I_{WM}'(t) &= \alpha I_{BM}(t) - \mu_W I_{WM}(t)\\
R_W'(t) &= \alpha R_B(t) + \gamma_W A_W(t) + \gamma_W I_W(t) - \mu_W R_W(t)\\
S_V'(t) &= \pi_V - \lambda_V(I_B, I_W, N_B, N_W)S_V(t) - \mu_V S_V(t)\\
E_V'(t) &= \lambda_V(I_B, I_W, N_B, N_W)S_V(t) - (\mu_V + \sigma_V)E_V(t)\\
I_V'(t) &= \sigma_V E_V(t) - \mu_V I_V(t)
\end{aligned}
$$

Where

$$\lambda_B(I_V, N_B) = \frac{\eta\beta_B b_V I_V}{N_B}$$
$$\lambda_W(I_V, N_W) = \frac{\beta_W b_V I_V}{N_W}$$
$$\lambda_V(I_B, I_W, N_B, N_W) = \beta_V b_V(\frac{I_W + \eta I_B}{N_W + \eta N_B})$$

And

$$N_B(t) = S_B(t) + E_B(t) + A_B(t) + I_B(t) + I_{BM}(t) + R_B(t)$$
$$N_W(t) = S_W(t) + E_W(t) + A_W(t) + I_W(t) + I_{WM}(t) + R_W(t)$$
$$N_V(t) = S_V(t) + E_V(t) + I_V(t)$$

Conclusions from the First Modified Model

As we showed in the midterm presentations, we were able to prove the global asymptotic stability of the unique disease free equilibrium point for our first modified model. However, no endemic equilibrium exists for this system of equations.

Variables

$S_B(t), S_W(t)$ = Susceptible newly born babies and adults

$E_B(t), E_W(t)$ = Exposed newly born babies and adults

$A_B(t), A_W(t)$ = Asymptomatic newly born babies and adults

$I_B(t), I_W(t)$ = Infectious symptomatic newly born babies without microcephaly and adults

$I_{BM}(t), I_{WM}(t)$ = Microcephalic newly born babies and adults

$R_B(t), R_W(t)$ = Recovered newly born babies and adults

$S_V(t)$ = Susceptible female mosquitoes

$E_V(t)$ = Exposed female mosquitoes

$I_V(t)$ = Infected female mosquitoes

Constants

N_B = Number of newly born babies

N_W = Number of adults

N_V = Number of mosquitoes

K_V = Carrying capacity of mosquitoes

The Generalized Model of Zika Virus Dynamics

The Parameters

$\bigstar\mu_H$ = Birth rate and natural death rate of newly born babies and adults

p = Fraction of adults who are infected

$1 - p$ = Remaining fraction of adults who are asymptomatic

α = Maturation rate

$q_A, q_I, \bigstar q_E$ = Transmission rates from asymptomatic, infected, and exposed adults to susceptible babies, respectively

c = Fraction of newly born babies who are infected

d = Fraction of newly born babies who have microcephaly

$1 - c - d$ = Remaining fraction of newly born babies who are asymptomatic

η = Modification parameter

$\bigstar\theta$ = Relative mosquito-to-human transmission probability of exposed mosquitoes to susceptible humans

β_W, β_B = Transmission probability *per* contact of adults and newly born babies

σ_W, σ_B = Progression rate of exposed adults and newly born babies

γ_W, γ_B = Recovery rate of asymptomatic and symptomatic adults and newly born babies

$\bigstar\chi$ = Transmission rate from infected adults to susceptible adults

$\bigstar\kappa$ = Relative human-to-human transmission probability of exposed adults to susceptible adults

$\bigstar\psi$ = Relative human-to-human transmission probability of asymptomatic adults to susceptible adults

π_V = Recruitment rate of mosquitoes

β_V = Transmission probability *per* contact of susceptible mosquitoes

b_V = Mosquito biting rate

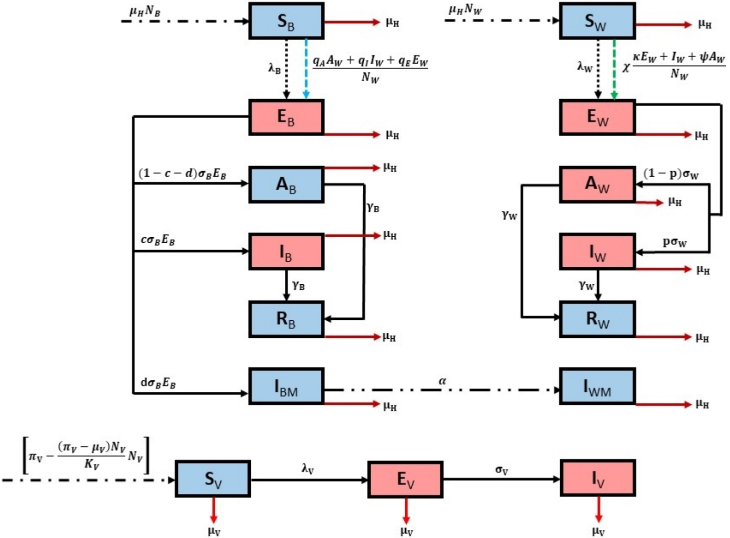
$\bigstar\phi$ = Relative human-to-mosquito transmission probability of exposed humans to susceptible mosquitoes

σ_V = Progression rate of exposed mosquitoes

μ_V = Natural death rate of mosquitoes

The Generalized Model of Zika Virus Dynamics

Flow Diagram of the Model



$$
\begin{aligned}
S_B'(t) &= \mu_H(N_B - S_B(t)) - \left(\frac{q_A A_W(t) + q_I I_W(t) + q_E E_W(t)}{N_W(t)}\right) S_B(t) - \lambda_B(E_V, I_V, N_B) S_B(t) \\
E_B'(t) &= \lambda_B(E_V, I_V, N_B) S_B(t) + \left(\frac{q_A A_W(t) + q_I I_W(t) + q_E E_W(t)}{N_W(t)}\right) S_B(t) - (\sigma_B + \mu_H) E_B(t) \\
A_B'(t) &= (1 - c - d)\sigma_B E_B(t) - (\gamma_B + \mu_H) A_B(t) \\
I_B'(t) &= c\sigma_B E_B(t) - (\gamma_B + \mu_H) I_B(t) \\
I_{BM}'(t) &= d\sigma_B E_B - (\alpha + \mu_H) I_{BM}(t) \\
R_B'(t) &= \gamma_B A_B(t) + \gamma_B I_B(t) - \mu_H R_B(t) \\
S_W'(t) &= \mu_H(N_W - S_W(t)) - \lambda_W(E_V, I_V, N_W) S_W(t) - \chi\left(\frac{\kappa E_W + I_W + \psi A_W}{N_W}\right) S_W(t) \\
E_W'(t) &= \lambda_W(E_V, I_V, N_W) S_W(t) + \chi\left(\frac{\kappa E_W + I_W + \psi A_W}{N_W}\right) S_W(t) - (\sigma_W + \mu_H) E_W(t) \\
A_W'(t) &= (1 - p)\sigma_W E_W(t) - (\gamma_W + \mu_H) A_W(t) \\
I_W'(t) &= p\sigma_W E_W(t) - (\gamma_W + \mu_H) I_W(t) \\
I_{WM}'(t) &= \alpha I_{BM}(t) - \mu_H I_{WM}(t) \\
R_W'(t) &= \gamma_W A_W(t) + \gamma_W I_W(t) - \mu_H R_W(t) \\
S_V'(t) &= \left(\pi_V - \frac{(\pi_V - \mu_V) N_V}{K_V}\right) N_V - \lambda_V(E_B, I_B, E_W, I_W, N_B, N_W) S_V(t) - \mu_V S_V(t) \\
E_V'(t) &= \lambda_V(E_B, I_B, E_W, I_W, N_B, N_W) S_V(t) - (\mu_V + \sigma_V) E_V(t) \\
I_V'(t) &= \sigma_V E_V(t) - \mu_V I_V(t)
\end{aligned}
$$

$$\lambda_B(E_V, I_V, N_B) = \frac{\eta\beta_B b_V(I_V + \theta E_V)}{N_B}$$

$$\lambda_W(E_V, I_V, N_W) = \frac{\beta_W b_V(I_V + \theta E_V)}{N_W}$$

$$\lambda_V(E_B, I_B, E_W, I_W, N_B, N_W) = \beta_V b_V(\frac{\phi E_W + \eta\phi E_B + I_W + \eta I_B}{N_W + \eta N_B})$$

The total population of adults (N_W), the total population of newly-born babies (N_B), and the total vector population (N_V) are given by:

$$N_B(t) = S_B(t) + E_B(t) + A_B(t) + I_B(t) + I_{BM}(t) + R_B(t)$$

$$N_W(t) = S_W(t) + E_W(t) + A_W(t) + I_W(t) + I_{WM}(t) + R_W(t)$$

$$N_V(t) = S_V(t) + E_V(t) + I_V(t)$$

$$N_H(t) = N_B(t) + N_W(t)$$

Where the total populations N_B, N_W, and N_V are constant.

The Feasible Region

The feasible region for the model is $\Gamma_3 = \Gamma_H \times \Gamma_V \subset \mathbb{R}^{12}_+ \times \mathbb{R}^3_+$ with

$$\Gamma_H = \{S_B, E_B, A_B, I_B, I_{BM}, R_B, S_W, E_W, A_W, I_W, I_{WM}, R_W : N_H \leq N_H(0)\}$$

$$\Gamma_V = \{S_V, E_V, I_V : N_V \leq K_V\}.$$

We now show that this region is positively invariant. Adding the first twelve equations and the last three equations of the model, we obtain that $N_H'(t) = 0$ and $N_V'(t) = N_V(t)(1 - \frac{N_V(t)}{K_V})(\pi_V - \mu_V)$, respectively. Then $N_H(t)$ is constant, so for all $t \geq 0$, $N_H(t) \leq N_H(0)$. Separating the other equation, we get $\frac{1}{N_V(t)(1 - \frac{N_V(t)}{K_V})} N_V'(t) = \pi_v - \mu_V$. Integrating and simplifying, we get $N_V(t) = \frac{K_V e^{(\pi_V - \mu_V)t}}{e^{(\pi_V - \mu_V)t} + c}$. This expression can be rewritten as $K_V - \frac{K_V c}{c + e^{(\pi_V - \mu_V)t}}$. Also, one can see that $c = \frac{K_V}{N_V(0)}$ is non-negative. Thus, for all $t \geq 0$, $N_V(t) \leq K_V$.

The Feasible Region

Now, we show that for non-negative initial points, solutions to the system stay non-negative for all $t > 0$. That is, for example, if $S_B(0) \geq 0$, then $S_B(t) \geq 0$ for $t \geq 0$. First, consider

$$S_B'(t) = \mu_H(N_B - S_B(t)) - \left(\frac{q_A A_W(t) + q_I I_W(t) + q_E E_W(t)}{N_W(t)}\right) S_B(t) - \lambda_B(E_V, I_V, N_B) S_B(t)$$

Rearranging terms and utilizing an integrating factor, we get

$$\frac{d}{dt} S_B(t) e^{\int_0^{t_1} \lambda_B(I_V N_B) + (\frac{q_A A_W(u) + q_I I_W(u) + q_E E_W(u)}{N_W(u)}) + \mu_H t} = \int_0^{t_1} [\mu_H N_B e^{\int_0^{t_1} \lambda_B(I_V, N_B) + (\frac{q_A A_W(u) + q_I I_W(u) + q_E E_W(u)}{N_W(u)}) + \mu_H u}] du$$

$$S_B(t_1) e^{\int_0^{t_1} \lambda_B(I_V N_B) + (\frac{q_A A_W(u) + q_I I_W(u) + q_E E_W(u)}{N_W(u)}) + \mu_H t} - S_B(0) = \int_0^{t_1} [\mu_H N_B e^{\int_0^{t_1} \lambda_B(I_V, N_B) + (\frac{q_A A_W(u) + q_I I_W(u) + q_E E_W(u)}{N_W(u)}) + \mu_H u}] du$$

$$S_B(t_1) = \frac{S_B(0) + \int_0^{t_1} [\mu_H N_B e^{\int_0^{t_1} \lambda_B(I_V, N_B) + (\frac{q_A A_W(u) + q_I I_W(u) + q_E E_W(u)}{N_W(u)}) + \mu_H u}] du}{e^{\int_0^{t_1} \lambda_B(I_V N_B) + (\frac{q_A A_W(u) + q_I I_W(u) + q_E E_W(u)}{N_W(u)}) + \mu_H t}}$$

Thus, when starting data is nonnegative, $S_B(t) \geq 0$ for all $t > 0$. Similarly, we can show that the other populations stay non-negative as well. Therefore, Γ_3 is positively invariant.

Finding the Disease Free Equilibrium

We found that the disease free equilibrium is given by:

$$E_0 = \{N_B, 0, 0, 0, 0, 0, N_W, 0, 0, 0, 0, 0, K_V, 0, 0\}$$

Theorem (AP)

If $\mathcal{R}_0 < 1$, then the disease-free equilibrium E_0 is globally asymptotically stable in Γ_3.

Proof.

As before, we compartmentalize the model into disease and non-disease.

$$x = \begin{bmatrix} E_B \\ I_B \\ E_W \\ A_W \\ I_W \\ E_V \\ I_V \end{bmatrix} \quad \text{and} \quad y = \begin{bmatrix} S_B \\ A_B \\ I_{BM} \\ R_B \\ S_W \\ I_{WM} \\ R_W \\ S_V \end{bmatrix}$$

$$\mathcal{F} = \begin{bmatrix} \lambda_B(E_V, I_V, N_B)S_B(t) + \left(\frac{q_A A_W(t) + q_I I_W(t) + q_E E_W(t)}{N_W(t)}\right) S_B(t) \\ 0 \\ \lambda_W(E_V, I_V, N_W)S_W(t) + \chi\left(\frac{\kappa E_W + I_W + \psi A_W}{N_W}\right) S_W(t) \\ 0 \\ 0 \\ \lambda_V(E_B, I_B, E_W, I_W, N_B, N_W)S_V(t) \\ 0 \end{bmatrix}$$

$$\mathcal{V} = \begin{bmatrix} (\sigma_B + \mu_H)E_B(t) \\ (\gamma_B + \mu_H)I_B(t) - c\sigma_B E_B(t) \\ (\sigma_W + \mu_H)E_W(t) \\ (\gamma_W + \mu_H)A_W(t) - (1-p)\sigma_W E_W(t) \\ (\gamma_W + \mu_H)I_W(t) - p\sigma_W E_W(t) \\ (\mu_V + \sigma_V)E_V(t) \\ \mu_V I_V(t) - \sigma_V E_V(t) \end{bmatrix}$$

Global Asymptotic Stability

The F Matrix

$$F = \begin{bmatrix} 0 & 0 & q_E \frac{N_B}{N_W} & q_A \frac{N_B}{N_W} & q_I \frac{N_B}{N_W} & \theta\eta\beta_B b_V & \eta\beta_B b_V \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \chi\kappa & \chi\psi & \chi & \theta\beta_W b_V & \beta_W b_V \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\eta\beta_V b_V \phi K_V}{N_W+\eta N_B} & \frac{\eta\beta_V b_V K_V}{N_W+\eta N_B} & \frac{\beta_V b_V \phi K_V}{N_W+\eta N_B} & 0 & \frac{\beta_V b_V K_V}{N_W+\eta N_B} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Global Asymptotic Stability

The V Matrix

$$V = \begin{bmatrix} \sigma_B + \mu_H & 0 & 0 & 0 & 0 & 0 & 0 \\ -c\sigma_B & \gamma_B + \mu_H & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \sigma_W + \mu_H & 0 & 0 & 0 & 0 \\ 0 & 0 & -(1-p)\sigma_W & \gamma_W + \mu_H & 0 & 0 & 0 \\ 0 & 0 & -p\sigma_W & 0 & \gamma_W + \mu_H & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \mu_V + \sigma_V & 0 \\ 0 & 0 & 0 & 0 & 0 & -\sigma_V & \mu_V \end{bmatrix}$$

Global Asymptotic Stability

The $f(x,y)$ Matrix

$$f(x,y) = \begin{bmatrix} \eta\beta_B b_V(I_V+\theta E_V)\left(1-\frac{S_B}{N_B}\right)+(q_E E_W+q_A A_W+q_I I_W)\left(\frac{N_B}{N_W}-\frac{S_B}{N_W}\right) \\ 0 \\ \left(\chi(\kappa E_W+I_W+\psi A_W)+\beta_W b_V(I_V+\theta E_V)\right)\left(1-\frac{S_W}{N_W}\right) \\ 0 \\ 0 \\ \beta_V b_V(I_W+\eta I_B+\phi E_W+\eta\phi E_B)\left(\frac{K_V}{N_W+\eta N_B}-\frac{S_V}{N_W+\eta N_B}\right) \\ 0 \end{bmatrix} \geq 0$$

Global Asymptotic Stability

The V^{-1} Matrix

$$V^{-1} = \begin{bmatrix} \frac{1}{\sigma_B+\mu_H} & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{c\sigma_B}{(\sigma_W+\mu_H)(\gamma_B+\mu_H)} & \frac{1}{\gamma_B+\mu_H} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{1}{\sigma_W+\mu_H} & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{\sigma_W(1-p)}{(\sigma_W+\mu_H)(\gamma_W+\mu_H)} & \frac{1}{\gamma_W+\mu_H} & 0 & 0 & 0 \\ 0 & 0 & \frac{\sigma_W p}{(\sigma_W+\mu_H)(\gamma_W+\mu_H)} & 0 & \frac{1}{\gamma_W+\mu_H} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{\sigma_V+\mu_V} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{\sigma_V}{\mu_V(\sigma_V+\mu_V)} & \frac{1}{\mu_V} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & 0 & A & B & C & D & E \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & P & G & H & I & J \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ K & L & M & 0 & N & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

The matrix $V^{-1}F$ has the form (it's irreducible!):

$$V^{-1}F = \begin{bmatrix} 0 & 0 & \mathcal{A}_1 & \mathcal{A}_2 & \mathcal{A}_3 & \mathcal{A}_4 & \mathcal{A}_5 \\ 0 & 0 & \mathcal{A}_6 & \mathcal{A}_7 & \mathcal{A}_8 & \mathcal{A}_9 & \mathcal{A}_{10} \\ 0 & 0 & \mathcal{A}_{11} & \mathcal{A}_{12} & \mathcal{A}_{13} & \mathcal{A}_{14} & \mathcal{A}_{15} \\ 0 & 0 & \mathcal{A}_{16} & \mathcal{A}_{17} & \mathcal{A}_{18} & \mathcal{A}_{19} & \mathcal{A}_{20} \\ 0 & 0 & \mathcal{A}_{21} & \mathcal{A}_{22} & \mathcal{A}_{23} & \mathcal{A}_{24} & \mathcal{A}_{25} \\ \mathcal{A}_{26} & \mathcal{A}_{27} & \mathcal{A}_{28} & 0 & \mathcal{A}_{29} & 0 & 0 \\ \mathcal{A}_{30} & \mathcal{A}_{31} & \mathcal{A}_{32} & 0 & \mathcal{A}_{33} & 0 & 0 \end{bmatrix}$$

Where each $\mathcal{A}_X$ denotes a strictly positive value.

Perron-Frobenius Theorem

Theorem (Perron-Frobenius)

Let A be an irreducible non-negative $n \times n$ matrix with spectral radius $\rho(A) = r$. Then the following statements hold:

- *r is a positive simple eigenvalue of the matrix A.*
- *A has a left eigenvector ω with eigenvalue r whose components are all positive.*

Here, we see that the directed graph associated with $V^{-1}F$ is strongly connected. This implies that $V^{-1}F$ is an irreducible matrix. Applying the Perron-Frobenius Theorem, we conclude that the spectral radius of $V^{-1}F$, $\rho(V^{-1}F)$, is in fact a simple positive eigenvalue and has an associated left eigenvector ω that is strictly positive. Also, note that $\rho(V^{-1}F) = \rho(FV^{-1})$. Thus, $\mathcal{R}_0 = \rho(FV^{-1})$ is an eigenvalue of $V^{-1}F$. Thus, by Shuai's Theorem 2.1, $Q = \omega^T V^{-1}x$ is a Lyapunov function . Again, $Q' = (\mathcal{R}_0 - 1)\omega^T x - \omega^T V^{-1} f(x, y)$. For $\mathcal{R}_0 \leq 1$, since $\omega^T > 0, x \geq 0, V^{-1} \geq 0$, and $f(x, y) \geq 0, Q' \leq 0$. Now we consider the set $S = \{z \in \mathbb{R}_{15} : Q' = 0\}$. When $Q' = 0$, we must have that $(\mathcal{R}_0 - 1)\omega^T x = \omega^T V^{-1} f(x, y)$. Using the same reasoning as above, $\omega^T x = 0$. This implies that $E_B = I_B = E_W = A_W = I_W = E_V = I_V = 0$, that is, the diseased compartment $x = 0$. Then the set S can be rewritten as $\{z \in \mathbb{R}_{15} : E_B = I_B = E_W = A_W = I_W = E_V = I_V = 0\}$.

On this set S, we are left with the following disease-free system:

$$
\begin{aligned}
S_B'(t) &= \mu_H(N_B - S_B(t)) \\
A_B'(t) &= -(\gamma_B + \mu_H)A_B(t) \\
I_{BM}'(t) &= -(\alpha + \mu_H)I_{BM}(t) \\
R_B'(t) &= \gamma_B A_B(t) - \mu_H R_B(t) \\
S_W'(t) &= \mu_H(N_W - S_W(t)) \\
I_{WM}'(t) &= \alpha I_{BM}(t) - \mu_H I_{WM}(t) \\
R_W'(t) &= -\mu_H R_W(t) \\
S_V'(t) &= (\pi_V - \frac{(\pi_V - \mu_V)S_V(t)}{K_V})S_V(t) - \mu_V S_V(t)
\end{aligned}
$$

We can show that everything goes to the DFE. Thus, E_0 is the largest and only invariant set in S. Also, since our region Γ_3 is compact and positively invariant, we can apply LaSalle's Invariance Principle to conclude that the DFE is globally asymptotically stable.

□

Existence of an Endemic Equilibrium

Shuai's Theorem 2.2

Theorem (Shuai's Theorem 2.2)

Let F, V, $f(x, y)$ be defined as above, and let $\Gamma \subset \mathbb{R}_+^{n+m}$ be compact such that $(0, y_0) \in \Gamma$ and Γ is positively invariant with respect to the system. Suppose that $f(x, y) \geq 0$ with $f(x, y_0) = 0$ in Γ, $F \geq 0$, $V^{-1} \geq 0$, and $V^{-1}F$ is irreducible. Assume that the disease-free system $y' = g(0, y)$ has a unique equilibrium $y = y_0 > 0$ that is GAS in $\mathbb{R}_+^m$. Then the following holds:

- *If $R_0 > 1$, then the DFE is unstable and there exists at least one EE.*

As seen before, our system satisfies all the assumptions in this theorem. Thus, when $R_0 > 1$ our system has an endemic equilibrium:

$$E^* := (S_B^*, E_B^*, A_B^*, I_B^*, I_{BM}^*, R_B^*, S_W^*, E_W^*, A_W^*, I_W^*, I_{WM}^*, R_W^*, S_V^*, E_V^*, I_V^*)$$

Note: We could no apply this theorem to the original model because the matrix $V^{-1}F$ was not irreducible

Given a weighted digraph with m vertices, we define the $m \times m$ weighted matrix A with $a_{ij} > 0$ if a link exists from node j to node i and $a_{ij} = 0$ otherwise, and we will denote such weighted digraph as $(\mathcal{G}, A)$. The Laplacian of $(\mathcal{G}, A)$ is defined as

$$L = l_{ij} = \begin{cases} -a_{ij}, & i \neq j \\ \sum_{k \neq i} a_{ik}, & i = j \end{cases}$$

From Kirchhoff's matrix tree theorem, we let c_i be the cofactor of l_{ii} in L. If $(\mathcal{G}, A)$ is strongly connected, then $c_i > 0$ for $1 \leq i \leq n$.

Theorem (Shuai Theorem 3.5)

Suppose that the following assumptions are satisfied:

- *There exist functions* $D_i : U \to \mathbb{R}$, $G_{ij} : U \to \mathbb{R}$ *and constants* $a_{ij} \geq 0$ *such that for every* $1 \leq i \leq n$, $D_i' = D'|_{(solutions)} \leq \sum_{j=1}^{n} a_{ij} G_{ij}(z)$ *for* $z \in U$.
- *For* $A = [a_{ij}]$, *each directed cycle* $\mathcal{C}$ *of* $(\mathcal{G}, A)$ *has* $\sum_{(s,r)\in\mathcal{E}(\mathcal{C})} G_{rs}(z) \leq 0$ *for* $z \in U$, *where* $\mathcal{E}(\mathcal{C})$ *denotes the arc set of the directed cycle* $\mathcal{C}$.

Then, the function

$$D(z) = \sum_{i=1}^{n} c_i D_i(z)$$

with constants $c_i \geq 0$ *as defined before, satisfies* $D' = D'|_{(solutions)} \leq 0$; *that is,* D *is a Lyapunov function for the system.*

Note: This theorem was applied because the matrix-theoretic method used to prove global asymptotic stability for the DFE cannot be applied to the EE.

Theorem (WE DID IT)

For $\mathcal{R}_0 > 1$, the endemic equilibrium point E^* is globally asymptotically stable in Γ_3.

Proof.

Define functions:

$$D_1 = S_B - S_B^* - S_B^* \ln \frac{S_B}{S_B^*} + E_B - E_B^* - E_B^* \ln \frac{E_B}{E_B^*}$$

$$D_2 = I_B - I_B^* - I_B^* \ln \frac{I_B}{I_B^*}$$

$$D_3 = S_W - S_W^* - S_W^* \ln \frac{S_W}{S_W^*} + E_W - E_W^* - E_W^* \ln \frac{E_W}{E_W^*}$$

$$D_4 = A_W - A_W^* - A_W^* \ln \frac{A_W}{A_W^*}$$

$$D_{5a} = I_W - I_W^* - I_W^* \ln \frac{I_W}{I_W^*}$$

$$D_{5b} = I_W - I_W^* - I_W^* \ln \frac{I_W}{I_W^*}$$

$$D_{5c} = I_W - I_W^* - I_W^* \ln \frac{I_W}{I_W^*}$$

$$D_6 = S_V - S_V^* - S_V^* \ln \frac{S_V}{S_V^*} + E_V - E_V^* - E_V^* \ln \frac{E_V}{E_V^*}$$

$$D_7 = I_V - I_V^* - I_V^* \ln \frac{I_V}{I_V^*}$$

Differentiating, treating N_B, N_W, N_V as constants, applying the inequality $1 - x + \ln x \le 0$, and simplifying yields:

$$\begin{aligned}
D_1' \le\ & q_A \frac{A_W^* S_B^*}{N_W^*}\left(\frac{A_W}{A_W^*} - \ln\frac{A_W}{A_W^*} - \frac{E_B}{E_B^*} + \ln\frac{E_B}{E_B^*}\right) \\
& + q_I \frac{I_W^* S_B^*}{N_W^*}\left(\frac{I_W}{I_W^*} - \ln\frac{I_W}{I_W^*} - \frac{E_B}{E_B^*} + \ln\frac{E_B}{E_B^*}\right) \\
& + q_E \frac{E_W^* S_B^*}{N_W^*}\left(\frac{E_W}{E_W^*} - \ln\frac{E_W}{E_W^*} - \frac{E_B}{E_B^*} + \ln\frac{E_B}{E_B^*}\right) \\
& + \eta\beta_B b_V \frac{I_V^* S_B^*}{N_B^*}\left(\frac{I_V}{I_V^*} - \ln\frac{I_V}{I_V^*} - \frac{E_B}{E_B^*} + \ln\frac{E_B}{E_B^*}\right) \\
& + \eta\beta_B b_V \theta \frac{E_V^* S_B^*}{N_B^*}\left(\frac{E_V}{E_V^*} - \ln\frac{E_V}{E_V^*} - \frac{E_B}{E_B^*} + \ln\frac{E_B}{E_B^*}\right) \\
:=\ & a_{1,4}G_{1,4} + a_{1,5a}G_{1,5a} + a_{1,3}G_{1,3} + a_{1,7}G_{1,7} + a_{1,6}G_{1,6}
\end{aligned}$$

$$D_2' \leq c\sigma_B E_B^* \left(\frac{E_B}{E_B^*} - \ln \frac{E_B}{E_B^*} - \frac{I_B}{I_B^*} + \ln \frac{I_B}{I_B^*} \right)$$

$$:= a_{2,1} G_{2,1}$$

$$D_3' \leq \beta_W b_V \frac{I_V^* S_W^*}{N_W^*} \left(\frac{I_V}{I_V^*} - \ln \frac{I_V}{I_V^*} - \frac{E_W}{E_W^*} + \ln \frac{E_W}{E_W^*} \right)$$

$$+\beta_W b_V \theta \frac{E_V^* S_W^*}{N_W^*} \left(\frac{E_V}{E_V^*} - \ln \frac{E_V}{E_V^*} - \frac{E_W}{E_W^*} + \ln \frac{E_W}{E_W^*} \right)$$

$$+\chi \frac{I_W^* S_W^*}{N_W^*} \left(\frac{I_W}{I_W^*} - \ln \frac{I_W}{I_W^*} - \frac{E_W}{E_W^*} + \ln \frac{E_W}{E_W^*} \right)$$

$$+\chi\psi \frac{A_W^* S_W^*}{N_W^*} \left(\frac{A_W}{A_W^*} - \ln \frac{A_W}{A_W^*} - \frac{E_W}{E_W^*} + \ln \frac{E_W}{E_W^*} \right)$$

$$:= a_{3,7} G_{3,7} + a_{3,6} G_{3,6} + a_{3,5b} G_{3,5b} + a_{3,4} G_{3,4}$$

$$D_4' \leq (1-p)\sigma_W E_W^* \left(\frac{E_W}{E_W^*} - \ln \frac{E_W}{E_W^*} - \frac{A_W}{A_W^*} + \ln \frac{A_W}{A_W^*} \right)$$

$$:= a_{4,3} G_{4,3}$$

$$D_{5a}' \leq p\sigma_W E_W^* \left(\frac{E_W}{E_W^*} - \ln \frac{E_W}{E_W^*} - \frac{I_W}{I_W^*} + \ln \frac{I_W}{I_W^*} \right)$$

$$:= a_{5a,3} G_{5a,3}$$

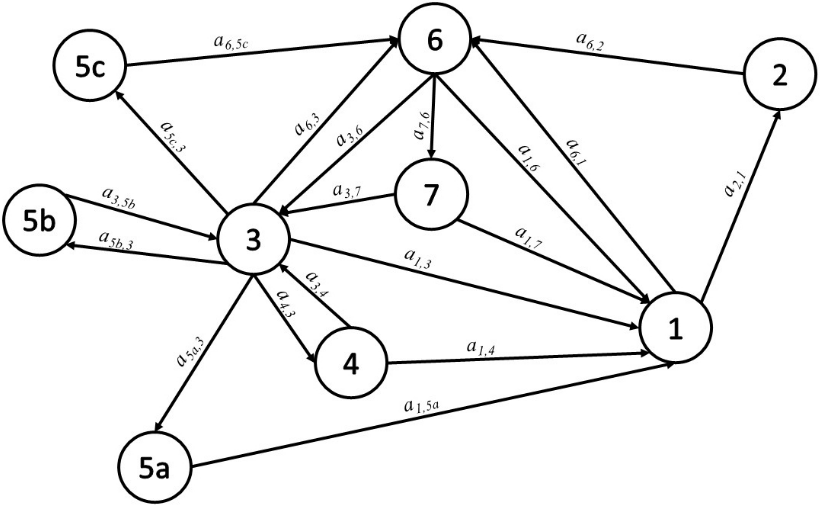
$$D_{5b}' \leq p\sigma_W E_W^* \left(\frac{E_W}{E_W^*} - \ln \frac{E_W}{E_W^*} - \frac{I_W}{I_W^*} + \ln \frac{I_W}{I_W^*} \right)$$

$$:= a_{5b,3} G_{5b,3}$$

$$D_{5c}' \leq p\sigma_W E_W^* \left(\frac{E_W}{E_W^*} - \ln \frac{E_W}{E_W^*} - \frac{I_W}{I_W^*} + \ln \frac{I_W}{I_W^*} \right)$$

$$:= a_{5c,3} G_{5c,3}$$

$$
\begin{aligned}
D_6' \leq\ & \beta_V b_V \phi \frac{E_W^* S_V^*}{N_W^* + \eta N_B^*}\left(\frac{E_W}{E_W^*} - \ln\frac{E_W}{E_W^*} - \frac{E_V}{E_V^*} + \ln\frac{E_V}{E_V^*}\right) \\
& + \beta_V b_V \phi \eta \frac{E_B^* S_V^*}{N_W^* + \eta N_B^*}\left(\frac{E_B}{E_B^*} - \ln\frac{E_B}{E_B^*} - \frac{E_V}{E_V^*} + \ln\frac{E_V}{E_V^*}\right) \\
& + \beta_V b_V \frac{I_W^* S_V^*}{N_W^* + \eta N_B^*}\left(\frac{I_W}{I_W^*} - \ln\frac{I_W}{I_W^*} - \frac{E_V}{E_V^*} + \ln\frac{E_V}{E_V^*}\right) \\
& + \beta_V b_V \eta \frac{I_B^* S_V^*}{N_W^* + \eta N_B^*}\left(\frac{I_B}{I_B^*} - \ln\frac{I_B}{I_B^*} - \frac{E_V}{E_V^*} + \ln\frac{E_V}{E_V^*}\right) \\
& := a_{6,3} G_{6,3} + a_{6,1} G_{6,1} + a_{6,5c} G_{6,5c} + a_{6,2} G_{6,2} \\
D_7' \leq\ & \sigma_V E_V^* \left(\frac{E_V}{E_V^*} - \ln\frac{E_V}{E_V^*} - \frac{I_V}{I_V^*} + \ln\frac{I_V}{I_V^*}\right) \\
& := a_{7,6} G_{7,6}
\end{aligned}
$$


6
5c
2
7
5b
3
1
4
5a
$a_{6,5c}$
$a_{6,2}$
$a_{5c,3}$
$a_{6,3}$
$a_{3,6}$
$a_{7,6}$
$a_{1,6}$
$a_{6,1}$
$a_{2,1}$
$a_{3,5b}$
$a_{3,7}$
$a_{5b,3}$
$a_{1,7}$
$a_{1,3}$
$a_{3,4}$
$a_{4,3}$
$a_{5a,3}$
$a_{1,4}$
$a_{1,5a}$

Cycle 1: $G_{6,1} + G_{7,6} + G_{3,7} + G_{5a,3} + G_{1,5a} = 0$
Cycle 2: $G_{6,1} + G_{7,6} + G_{3,7} + G_{4,3} + G_{1,4} = 0$
Cycle 3: $G_{6,1} + G_{7,6} + G_{3,7} + G_{1,3} = 0$
Cycle 4: $G_{6,1} + G_{7,6} + G_{1,7} = 0$
Cycle 5: $G_{6,1} + G_{3,6} + G_{5a,3} + G_{1,5a} = 0$
Cycle 6: $G_{6,1} + G_{3,6} + G_{4,3} + G_{1,4} = 0$
Cycle 7: $G_{6,1} + G_{3,6} + G_{1,3} = 0$
Cycle 8: $G_{6,1} + G_{1,6} = 0$
Cycle 9: $G_{2,1} + G_{6,2} + G_{7,6} + G_{3,7} + G_{5a,3} + G_{1,5a} = 0$
Cycle 10: $G_{2,1} + G_{6,2} + G_{7,6} + G_{3,7} + G_{4,3} + G_{1,4} = 0$
Cycle 11: $G_{2,1} + G_{6,2} + G_{7,6} + G_{3,7} + G_{1,3} = 0$
Cycle 12: $G_{2,1} + G_{6,2} + G_{7,6} + G_{1,7} = 0$
Cycle 13: $G_{2,1} + G_{6,2} + G_{3,6} + G_{5a,3} + G_{1,5a} = 0$
Cycle 14: $G_{2,1} + G_{6,2} + G_{3,6} + G_{4,3} + G_{1,4} = 0$
Cycle 15: $G_{2,1} + G_{6,2} + G_{3,6} + G_{1,3} = 0$
Cycle 16: $G_{2,1} + G_{6,2} + G_{1,6} = 0$
Cycle 17: $G_{5b,3} + G_{3,5b} = 0$
Cycle 18: $G_{5c,3} + G_{6,5c} + G_{7,6} + G_{3,7} = 0$
Cycle 19: $G_{5c,3} + G_{6,5c} + G_{3,6} = 0$
Cycle 20: $G_{6,3} + G_{7,6} + G_{3,7} = 0$
Cycle 21: $G_{6,3} + G_{3,6} = 0$
Cycle 22: $G_{4,3} + G_{3,4} = 0$

Then, by Shuai's Theorem 3.5, there exists constants c_i such that

$$D = \sum_{i=1}^{n} c_i D_i$$

is a Lyapunov function for the given system.

Next step: finding c_i values.

Theorem (Shuai's Theorem 3.3)

Let c_i be defined as before. If $a_{ij} > 0$ and $d^+(j) = 1$ for some i, j, then

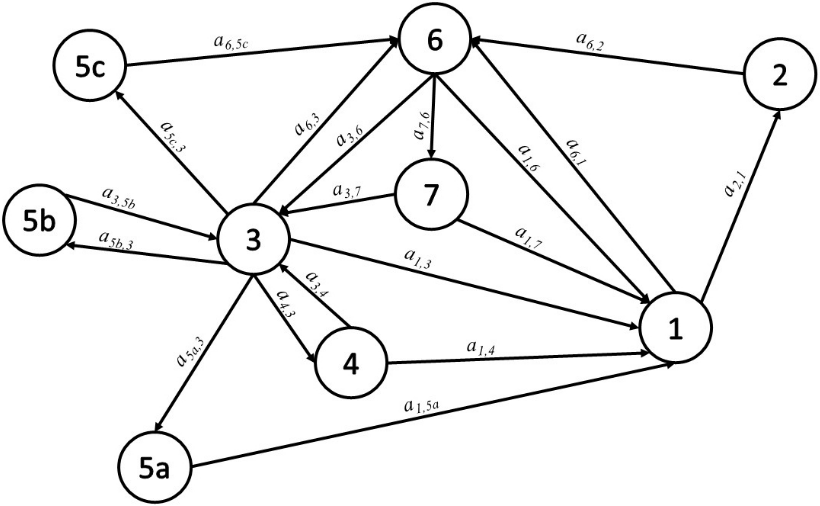
$$c_i a_{ij} = \sum_{k=1}^{m} c_j a_{jk}$$

Theorem (Shuai's Theorem 3.4)

Let c_i be defined as before. If $a_{ij} > 0$ and $d^-(i) = 1$ for some i, j, then

$$c_i a_{ij} = \sum_{k=1}^{m} c_k a_{ki}$$

Global Asymptotic Stability
Weighted Connected Graph



Taking node 2, we see that both the in-degree $d^{-}(i) = 1$ and the out-degree $d^{+}(j) = 1$. Therefore either theorem 3.3 or theorem 3.4 can be applied.

We have $a_{6,2} > 0$, so $i = 6$ and $j = 2$. Therefore, we see

$$c_6 a_{6,2} = \sum_{k=1}^{m} c_2 a_{2,k} = c_2 a_{2,1} + c_2 a_{2,2} + c_2 a_{2,3} + c_2 a_{2,4} + c_2 a_{2,5a} + c_2 a_{2,5b} + c_2 a_{2,5c} + c_2 a_{2,6} + c_2 a_{2,7}$$

Because the edges $a_{2,2}$, $a_{2,3}$, $a_{2,4}$, $a_{2,5a}$, $a_{2,5b}$, $a_{2,5c}$, $a_{2,6}$, $a_{2,7}$ do not exist, these quantities all equal 0, and thus we are left with

$$c_6 a_{6,2} = c_2 a_{2,1}$$

Similarly, we have $a_{2,1} > 0$, so $i = 2$ and $j = 1$. Therefore, we see

$$c_2 a_{2,1} = \sum_{k=1}^{m} c_k a_{k,2} = c_1 a_{1,2} + c_2 a_{2,2} + c_3 a_{3,2} + c_4 a_{4,2} + c_{5a} a_{5a,2} + c_{5b} a_{5b,2} + c_{5c} a_{5c,2} + c_6 a_{6,2} + c_7 a_{7,2}$$

Because the edges $a_{1,2}$, $a_{2,2}$, $a_{3,2}$, $a_{4,2}$, $a_{5a,2}$, $a_{5b,2}$, $a_{5c,2}$, $a_{7,2}$ do not exist in figure 2, these quantities all equal 0, and thus we are left with

$$c_2 a_{2,1} = c_6 a_{6,2}$$

We apply these two theorems to each node where $d^+(j) = 1$ or $d^-(i) = 1$, and we find that

$$\begin{aligned} c_2 a_{2,1} &= c_6 a_{6,2} \\ c_4 a_{4,3} &= c_1 a_{1,4} + c_3 a_{3,4} \\ c_{5a} a_{5a,3} &= c_1 a_{1,5a} \\ c_{5b} a_{5b,3} &= c_3 a_{3,5b} \\ c_{5c} a_{5c,3} &= c_3 a_{6,5c} \\ c_7 a_{7,6} &= c_1 a_{1,7} + c_3 a_{3,7} \end{aligned}$$

Global Asymptotic Stability

Finding the c_i Values

We then set $c_1 = 1$, $c_3 = 1$, and $c_6 = 1$ and solve for the remaining c_i values:

$$c_1 = 1$$

$$c_2 = c_6 \frac{a_{6,2}}{a_{2,1}} = \frac{\beta_V b_V \eta I_B^* S_V^*}{c\sigma_B E_B^* (N_W^* + \eta N_B^*)}$$

$$c_3 = 1$$

$$c_4 = \frac{c_1 a_{1,4} + c_3 a_{3,4}}{a_{4,3}} = \frac{q_A A_W^* S_B^* + \chi\psi A_W^* S_W^*}{N_W^*(1-p)\sigma_W E_W^*}$$

$$c_{5a} = c_1 \frac{a_{1,5a}}{a_{5a,3}} = \frac{q_I I_W^* S_B^*}{p\sigma_W E_W^* N_W^*}$$

$$c_{5b} = c_3 \frac{a_{3,5b}}{a_{5b,3}} = \frac{\chi I_W^* S_W^*}{p\sigma_W E_W^* N_W^*}$$

$$c_{5c} = c_6 \frac{a_{6,5c}}{a_{5c,3}} = \frac{\beta_V b_V I_W^* S_V^*}{p\sigma_W E_W^* (N_W^* + \eta N_B^*)}$$

$$c_6 = 1$$

$$c_7 = \frac{c_1 a_{1,7} + c_3 a_{3,7}}{a_{7,6}} = \frac{\eta\beta_B b_V I_V^* S_B^* N_W^* + \beta_W b_V I_V^* S_W^* N_B^*}{\sigma_V E_V^* N_B^* N_W^*}$$

So we have

$$\begin{aligned}
D &= c_1 D_1 + c_2 D_2 + c_3 D_3 + c_4 D_4 + c_{5a} D_{5a} + c_{5b} D_{5b} + c_{5c} D_{5c} + c_6 D_6 + c_7 D_7 \\
&= \left(S_B - S_B^* - S_B^* \ln \frac{S_B}{S_B^*} + E_B - E_B^* - E_B^* \ln \frac{E_B}{E_B^*} \right) + c_2 \left(I_B - I_B^* - I_B^* \ln \frac{I_B}{I_B^*} \right) \\
&\quad + \left(S_W - S_W^* - S_W^* \ln \frac{S_W}{S_W^*} + E_W - E_W^* - E_W^* \ln \frac{E_W}{E_W^*} \right) + c_4 \left(A_W - A_W^* - A_W^* \ln \frac{A_W}{A_W^*} \right) \\
&\quad + c_{5a} \left(I_W - I_W^* - I_W^* \ln \frac{I_W}{I_W^*} \right) + c_{5b} \left(I_W - I_W^* - I_W^* \ln \frac{I_W}{I_W^*} \right) + c_{5c} \left(I_W - I_W^* - I_W^* \ln \frac{I_W}{I_W^*} \right) \\
&\quad + \left(S_V - S_V^* - S_V^* \ln \frac{S_V}{S_V^*} + E_V - E_V^* - E_V^* \ln \frac{E_V}{E_V^*} \right) + c_7 \left(I_V - I_V^* - I_V^* \ln \frac{I_V}{I_V^*} \right)
\end{aligned}$$

This is our Lyapunov function.

Now we consider the set $S = \{x \in \mathbb{R}^{+}_{15} : D' = 0\}$. Differentiating, we get

$$D' = \left(\frac{S_B - S_B^*}{S_B} S_B' + \frac{E_B - E_B^*}{E_B} E_B' \right) + c_2 \left(\frac{I_B - I_B^*}{I_B} I_B' \right)$$

$$+ \left(\frac{S_W - S_W^*}{S_W} S_W' + \frac{E_W - E_W^*}{E_W} E_W' \right) + c_4 \left(\frac{A_W - A_W^*}{A_W} A_W' \right)$$

$$+ (c_{5a} + c_{5b} + c_{5c}) \left(\frac{I_W - I_W^*}{I_W} I_W' \right) + \left(\frac{S_V - S_V^*}{S_V} S_V' + \frac{E_V - E_V^*}{E_V} E_V' \right)$$

$$+ c_7 \left(\frac{I_V - I_V^*}{I_V} I_V' \right)$$

Global Asymptotic Stability

$D' = 0$ Converging to the Endemic Equilibrium

Since $c_i > 0$ for all i, when $D' = 0$, we have $\left(\frac{I_B - I_B^*}{I_B} I_B'\right) = 0$. Then there are two cases: (1) $I_B - I_B^* = 0$ or (2) $I_B' = c\sigma_B E_B - \frac{c\sigma_B E_B^* I_B}{I_B^*} = 0$. In case 1, we get $I_B = I_B^*$ as desired. In case 2, solving yields $E_B = \frac{E_B^*}{I_B^*} I_B$. Since $\frac{E_B^*}{I_B^*}$ is a positive constant, this means that E_B and I_B are positively correlated, a biological contradiction, except when $I_B = I_B^*$ and $E_B = E_B^*$. In either case, we have $I_B = I_B^*$.

Similarly, considering

$$\left(\frac{I_V - I_V^*}{I_V} I_V'\right) = \left(\frac{A_W - A_W^*}{A_W} A_W'\right) = \left(\frac{I_W - I_W^*}{I_W} I_W'\right) = 0 \text{ and}$$

using the same reasoning, we can deduce that $I_V = I_V^*$, $A_W = A_W^*$, $I_W = I_W^*$. In addition, we know that $\left(\frac{S_B - S_B^*}{S_B} S_B'\right) = 0$. Then either $S_B = S_B^*$ or $S_B' = 0$. S_B' can be written as

$$P(S_B^* - S_B) + q_E\left(\frac{E_W^* S_B^*}{N_W} - \frac{E_W S_B}{N_W}\right) + \eta\beta_B b_V \theta\left(\frac{E_V^* S_B^*}{N_B} - \frac{E_V S_B}{N_B}\right),$$

where P is some positive constant. Setting this expression equal to zero, we can see that in any case, we must have $S_B = S_B^*$. We can similarly conclude that $S_W = S_W^*$ and $S_V = S_V^*$. Now, given this, we can reason that $E_B = E_B^*$, $E_W = E_W^*$, and $E_V = E_V^*$.

Thus far, we have $S_B = S_B^*$, $E_B = E_B^*$, $I_B = I_B^*$, $S_W = S_W^*$, $E_W = E_W^*$, $A_W = A_W^*$, $I_W = I_W^*$, $S_V = S_V^*$, $E_V = E_V^*$, and $I_V = I_V^*$. Plugging these values into the original system, we are left with the following:

$$
\begin{aligned}
A_B'(t) &= (1 - c - d)\sigma_B E_B^* - (\gamma_B + \mu_H)A_B(t)\\
I_{BM}'(t) &= d\sigma_B E_B^* - (\alpha + \mu_H)I_{BM}(t)\\
R_B'(t) &= \gamma_B A_B(t) + \gamma_B I_B^* - \mu_H R_B(t)\\
I_{WM}'(t) &= \alpha I_{BM}(t) - \mu_H I_{WM}(t)\\
R_W'(t) &= \gamma_W A_W^* + \gamma_W I_W^* - \mu_H R_W(t)
\end{aligned}
$$

Now, we use an integrating factor and take limits.

(i)

$$A_B'(t) + (\gamma_B + \mu_H)A_B(t) = (1 - c - d)\sigma_B E_B^*$$

$$A_B(t) = e^{-(\gamma_B+\mu_H)t} \int_0^t e^{(\gamma_B+\mu_H)s}[(1 - c - d)\sigma_B E_B^*]ds + Ce^{-(\gamma_B+\mu_H)t}$$

$$A_B(t) = \frac{(1 - c - d)\sigma_B E_B^*}{\gamma_B + \mu_H} - \frac{(1 - c - d)\sigma_B E_B^*}{\gamma_B + \mu_H} e^{-(\gamma_B+\mu_H)t} + Ce^{-(\gamma_B+\mu_H)t}$$

Then

$$\lim_{t\to\infty} A_B(t) = \frac{(1 - c - d)\sigma_B E_B^*}{\gamma_B + \mu_H} = A_B^*$$

Similarly,

(ii)

$$\lim_{t \to \infty} I_{BM}(t) = \frac{d\sigma_B E_B^*}{\alpha + \mu_H} = I_{BM}^*$$

(iii)

$$\lim_{t \to \infty} R_B(t) = \frac{\gamma_B A_B^* + \gamma_B I_B^*}{\mu_H} = R_B^*$$

(iv)

$$\lim_{t \to \infty} I_{WM}(t) = \frac{\alpha I_{BM}^*}{\mu_H} = I_{WM}^*$$

(v)

$$\lim_{t \to \infty} R_W(t) = \frac{\gamma_W A_W^* + \gamma_W I_W^*}{\mu_H} = R_W^*$$

Therefore, we have shown that all trajectories in S go to the endemic equilibrium,

$$E^* = (S_B^*, E_B^*, A_B^*, I_B^*, I_{BM}^*, R_B^*, S_W^*, E_W^*, A_W^*, I_W^*, I_{WM}^*, R_W^*, S_V^*, E_V^*, I_V^*)$$

we did it fellas

Thus, we can see that the largest and only invariant set in S is exactly equal to the endemic equilibrium, E^*. Therefore, invoking LaSalle's Invariance Principle, we conclude that the endemic equilibrium E^* is globally asymptotically stable in $\text{int}(\Gamma_3)$ and therefore is unique.

$\square$

Model Graveyard

This project is dedicated to the many models that did not work, including:

- The Super Special Awesome Modified Model
- Morgan's Marvelous Modified Model, Maybe
- The Model that We Think Will Work
- GAAH HELP US THIS IS SO HARD GAAHHHHHHHH!!!!!!!!!!!!!!!!!
- McDonald's Combo Meal Model

Accomplishments

- Provided a more rigorous proof for the model from Agusto
- Created a more generalized model including all three types of transmission of the Zika virus
- Proved the existence of a DFE and an EE for the new, generalized model
- Proved global asymptotic stability of the DFE and the EE of the new, generalized model using matrix and graph-theoretic methods, respectively.
- Had lots of fun

Future Plans

- Use Xppaut to find numerical evidence of the existence of any bifurcations
- Attempt to prove the existence of such bifurcations
- Revisit the model once more biological data and samples have been collected to check for accuracy
- Dinner at Civil Kitchen and Brunch at Vandivort
- Pack
- Delete GroupMe
- Invest in mosquito repellent
- Get into grad school

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The End

Hasta la vista

#babies