Modeling the mitigation of dengue fever, chikungunya and Zika by infecting mosquitoes with Wolbachia bacteria

Zhuolin Qu¹, Ling Xue² and James Mac Hyman¹

¹ Center for Computational Science, Department of Mathematics, Tulane University  ² Department of Mathematics, University of Manitoba, Canada

Abstract

- The ongoing mosquito-borne epidemics are of increasing concern worldwide. Wolbachia bacteria is a natural parasitic microbe that reduces the disease transmission.
- It is difficult to sustain an infection of the maternally transmitted Wolbachia bacteria in a wild mosquito population due to the reduced fitness of the infected mosquitoes and incompatibility in the maternal transmission.
- We identify important dimensionless numbers and analyze the critical threshold condition for achieving a sustained Wolbachia infection.

Mosquito-borne Diseases v.s. Wolbachia

"Mosquitoes cause more human suffering than any other organism."

- American Mosquito Control Association
- nearly 700 million people get a mosquito-borne disease each year resulting in greater than one million deaths
- Aedes aegypti mosquito: the primary vector for dengue fever, chikungunya and Zika

Wolbachia bacteria  A promising strategy to stop diseases at source.
- a natural parasitic microbe, found in 60% insects, but not in the wild Aedes aegypti mosquitoes
- stops the proliferation of harmful viruses inside the mosquito \( \Rightarrow \) reduces the disease transmission in dengue fever, chikungunya and Zika
- fitness-cost in the infected female mosquitoes

Maternal transmission Wolbachia is maternally transmitted from infected mothers to offspring.

Schematic of the complex maternal transmission mating

Mosquito-borne Diseases

- bacteria in infection dies out
- The ongoing mosquito-borne epidemics are of increasing concern worldwide.
- It is difficult to sustain an infection of the maternally transmitted Wolbachia bacteria in a wild mosquito population due to the reduced fitness of the infected mosquitoes and incompatibility in the maternal transmission.

Our new model captures the complex transmission cycle by accounting for:

- heterosexual contact
- multiple pregnant stages for females
- aquatic-stage with carrying capacity

Maternal Transmission Wolbachia Model

Ordinary differential equation model

\[
\begin{align*}
\frac{dA}{dt} &= (\psi F_{u} + \sigma F_{a}) (1 - \frac{A_{u} + A_{w}}{K_{a}}) - (\mu_{a} + \psi) A_{u} \\
\frac{dA}{dt} &= \nu \phi_{u} (1 - A_{u} + \sigma A_{w}) - (\mu_{u} + \psi) A_{u} \\
\frac{dF_{u}}{dt} &= b F_{u} - (\sigma + \mu_{u}) F_{u} \\
\frac{dF_{w}}{dt} &= b F_{w} - (\sigma + \mu_{w}) F_{w} \\
\frac{dF_{pu}}{dt} &= \sigma F_{pu} - \mu_{pu} F_{pu} \\
\frac{dF_{pw}}{dt} &= \sigma F_{pw} - \mu_{pw} F_{pw} \\
\frac{dM_{u}}{dt} &= b_{u} F_{u} - \mu_{mu} M_{u} \\
\frac{dM_{w}}{dt} &= b_{u} F_{w} - \mu_{mu} M_{w} \\
\end{align*}
\]

Model parameters

\( \psi \) Female birth probability
\( \sigma \) Mating rate
\( \phi_{u} \) Egg-laying rate of \( F_{u} \)
\( \phi_{w} \) Egg-laying rate of \( F_{w} \)
\( \nu \) Maternal transmission rate

\( \mu_{u} \) Death rate of aquatic-stage
\( \mu_{a} \) Death rate of uninfected females
\( \mu_{w} \) Death rate of infected females
\( \mu_{pu} \) Death rate of infected males
\( K_{a} \) Carrying capacity of aquatic-stage

Bifurcation Analysis

Important dimensionless numbers

next generation number for the uninfected

\[
G_{0w} = \frac{b_{u} \psi \sigma \phi_{u}}{\mu_{a} + \psi + \sigma + \mu_{f}} M_{w}
\]

next generation number for the infected

\[
G_{0w} = \frac{\nu \phi_{u} \sigma \phi_{w}}{\mu_{a} + \psi + \sigma + \mu_{f}} M_{w}
\]

Comparison using different pre-release mitigations

Approach

Target

Threshold condition: backward bifurcation

\[ k = \frac{a}{b} \]

Sensitivity analysis

sensitivity index: \( S_{k} = \frac{\partial k}{\partial r} \times 100\% \)

Bifurcation Analysis

Threshold condition: backward bifurcation

Integrated mosquito management

- pre-release mitigations
  - kill aquatic-stage mosquitoes: larval control
  - kill adult mosquitoes: residual spraying, sticky ovitraps
- release Wolbachia-infected mosquitoes

At day 10, we release 0.5X infected adult mosquitoes to the field. However, it is not sufficient to surpass the threshold condition. The initial infection is eventually wiped out by natural population.

We then release more infected population (0.9X). The system is able to surpass the threshold condition. 90% of female population is infected at day 261, and a stable Wolbachia-endemic state is achieved.

Acknowledgment: This research was partially supported by the NSF-MPS/NIH-NIGMS award NSF-1563531 and the NIH-NIGMS MIDAS award U01GM097661.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NSF or the NIH.

Author: Zhuolin Qu  zqu1@tulane.edu