Reducing mathematical models for *Wolbachia* transmission in mosquitoes to control mosquito-borne diseases

Zhuolin Qu and James Mac Hyman
Center for Computational Science, Department of Mathematics, Tulane University

Abstract

▶ The ongoing mosquito-borne epidemics are of great concern worldwide. ***Wolbachia* bacteria** is a natural parasitic microbe that blocks disease transmission.
▶ **Mathematical models** provide new insight into a successful *Wolbchia*-based mitigation: a critical threshold of *Wolbachia* infection must be exceeded in mosquitoes.
▶ The large-scale nature of the system prevents further extensions that provide **more practical guidelines**.
▶ We create an ensemble of reduced models to cut the analysis burden, yet capture the important properties of the original system.
▶ **The parameters for the reduced models are defined in terms of the ones in the full model.**

Mosquito-born Diseases v.s. *Wolbachia*

- 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

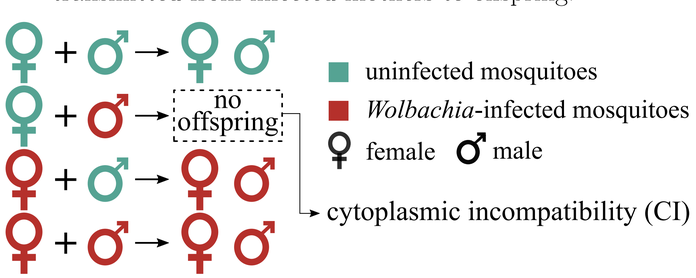
Wolbachia A promising strategy to stop diseases at source.

- a natural parasitic microbe, found in 60% insects species
- inhibits the proliferation of viruses inside the mosquito ⇒ blocks the disease transmission
- is not found in the wild *Aedes aegypti* mosquitoes

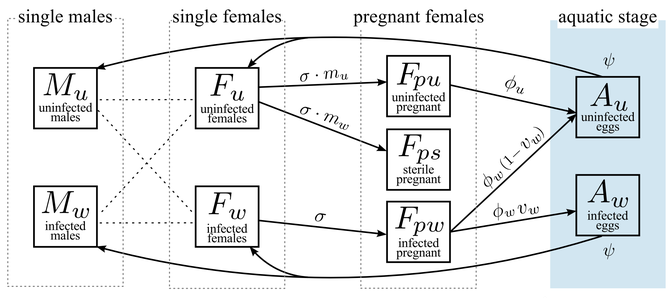
We need to create a *stable* infection in wild mosquitoes.

- field trials in Australia, Brazil, Colombia, Indonesia, Vietnam to control dengue/Zika epidemics
- Fraction of infection has to exceed a critical threshold.

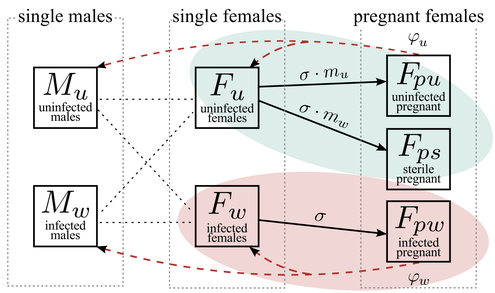
Maternal transmission *Wolbachia* is maternally transmitted from infected mothers to offspring.



Model Reductions 9-ODEs → 2-ODEs



σ	Mating rate
ϕ_u	Egg-laying rate for F_{pu}
ϕ_w	Egg-laying rate for F_{pw}
v_w	Maternal transmission rate
ψ	Development rate
μ_a	Death rate for aquatic
μ_{fu}	Death rate for uninf. females
μ_{fw}	Death rate for inf. females
μ_{mu}	Death rate for uninf. males
μ_{mw}	Death rate for inf. males
K_a	Carrying capacity of aquatic

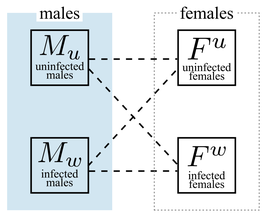


- perfect maternal transmission $v_w = 1$
- remove aquatic (pregnant → adult)

$$\left.\begin{aligned}\varphi_u &= \frac{\psi}{\psi+\mu_a}\phi_u \\ \varphi_w &= \frac{\psi}{\psi+\mu_a}\phi_w\end{aligned}\right\} \textit{Natural} \text{ reproduction rate}$$

- carrying capacity on pregnant females

$$K_p = \frac{\sigma}{\sigma+\mu_{fu}}\frac{b_f\psi}{\mu_{fu}}K_a$$



- combine infection groups

$$F^u = F_u + F_{pu} + F_{ps}$$
$$F^w = F_w + F_{pw}$$

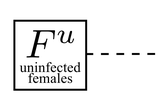
- single females ≈ 0

$$F_{pu} \to F^u\frac{M_u}{M_u+M_w} \qquad F_{ps} \to F^u\frac{M_w}{M_u+M_w} \qquad F_{pw} \to F^w$$

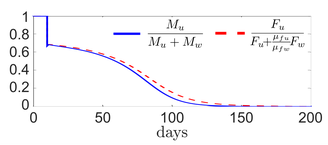
$$\left.\begin{aligned}\varphi'_u &= \frac{\psi}{\psi+\mu_a}\frac{\sigma}{\sigma+\mu_{fu}}\phi_u \\ \varphi'_w &= \frac{\psi}{\psi+\mu_a}\frac{\sigma}{\sigma+\mu_{fw}}\phi_w\end{aligned}\right\} \textit{Mixing} \text{ reproduction rate}$$

- carrying capacity on all the females

$$K_f = \frac{b_f\psi}{\mu_{fu}}K_a$$



- remove males
- proportional infection fraction in males and females



Reduced model

$$(F^u)_t = b_f\varphi'_u\frac{F^u}{F^u+\frac{\mu_{fw}}{\mu_{fu}}F^w}\left(1-\frac{F^u+F^w}{K_f}\right)F^u - \mu_{fu}F^u + d(F^u_{xx}+F^u_{yy})$$

$$(F^w)_t = b_f\varphi'_w\left(1-\frac{F^u+F^w}{K_f}\right)F^w - \mu_{fw}F^w + d(F^w_{xx}+F^w_{yy})$$

Future work

Include practical extensions

- spatial heterogeneity
- temporal variation

Model Comparisons

Reduced models preserve two important properties of the complex 9-compartment model.

Basic reproductive number $\mathbb{R}_0$

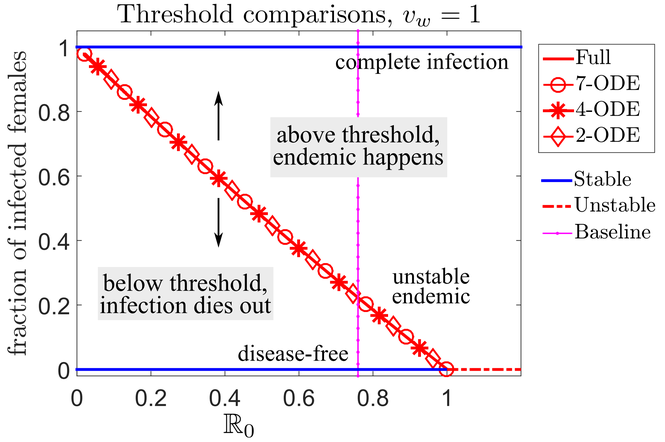
- number of new infections created by a single *Wolbachia*-infected mosquito, given all the rest mosquitoes are fully susceptible
- often used as a threshold condition for disease outbreak (predict early epidemic)
- Full model: $\mathbb{R}_0^{(9)} = v_w\frac{\mu_{fu}\,\phi_w\,(\sigma+\mu_{fu})}{\mu_{fw}\,\phi_u\,(\sigma+\mu_{fw})} \approx 0.722$

$$\mathbb{R}_0^{(9)} = \mathbb{R}_0^{(7)} = \mathbb{R}_0^{(4)} = \mathbb{R}_0^{(2)}$$

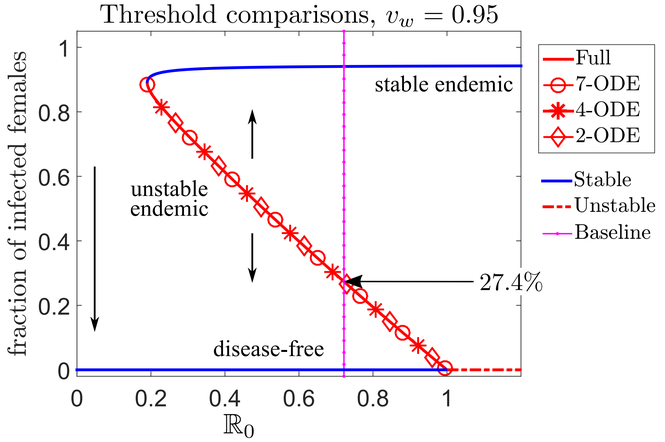
Critical threshold for stable *Wolbachia* infection

- a critical threshold must be exceeded to create a stable infection in wild mosquitoes
- backward bifurcation with an unstable endemic state

Threshold comparisons, $v_w = 1$



Threshold comparisons, $v_w = 0.95$



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