Wolbachia invasion in wild mosquito populations: a modeling framework apt for different strains

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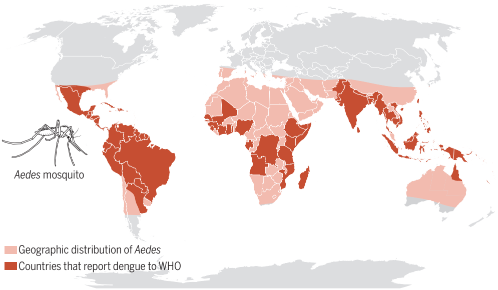
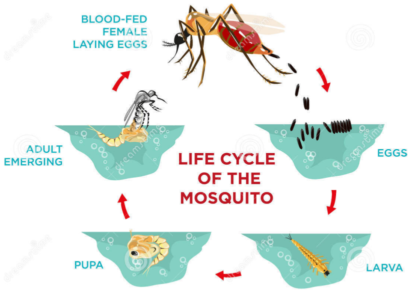




- *Ae. aegypti* females are transmitters of DENV and other arboviruses (they bite people)
- *Ae. aegypti* males do not transmit arboviruses (they do not bite people)

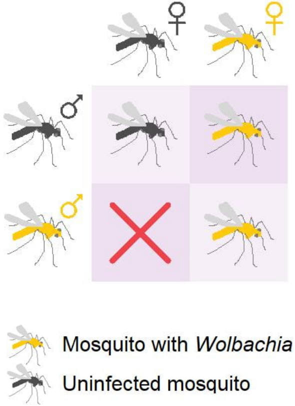
NO MOSQUITO = NO DENGUE

Image source: Wilder-Smith and Gubler, 2015, DOI: 10.1126science.aab4047

Image source: https://www.peststrategies.com/

What is *Wolbachia*?

- *Wolbachia* is a symbiotic bacterium naturally found in up to 60-70% of insect species.
- *Wolbachia* is **not** found in *Ae. aegypti* mosquitoes.
- *Wolbachia* is transmitted maternally *(female ⇢ eggs)*
- *Wolbachia* induces *cytoplasmic incompatibility (CI-phenotype)*
- *Wolbachia* suppresses replication of different viruses inside *Ae. aegypti* females.



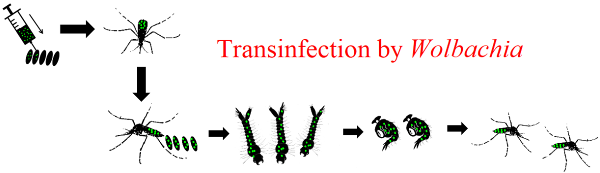


Image sources: Ross *et al.*, 2020; DOI: 10.1002/ece3.6012 & https://www.nea.gov.sg/

Major Wolbachia strains for the prevention of *Aedes*-borne diseases

Key features \ ***Wolbachia* strains**	***w*MelPop**	***w*Mel**	***w*AlbB**	***w*Au**
Virus inhibition or blockage (VI)	**High**	Medium	Medium	**High**
Fitness cost (FC)	High	Low	Medium	Low
Imperfect maternal transmission (IMT)	High	High	High	High
Cytoplasmic incompatibility (CI)	High	High	High	**None**
Wolbachia infection retention under thermal stress (WIR)	**Low**	**Low**	Medium	High

Sources: **???**

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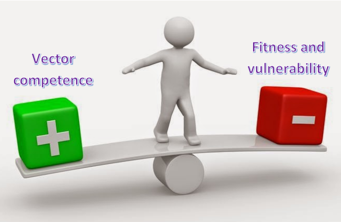
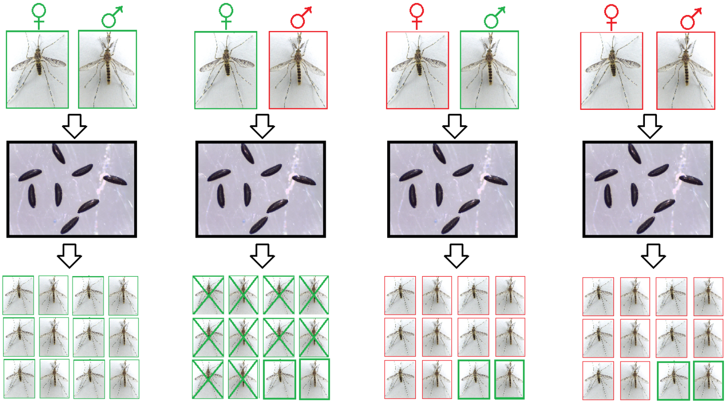


Imperfect maternal transmission and cytoplasmic incompatibility



Wild population: females (♀) and males (♂)

Wolbachia-carrying population: females (♀) and males (♂)

Extension of the model attributed to ?

Total mosquito population $P(t)$
- *Wolbachia*-free $P_n(t)$
  - Males $M_n(t)$
  - Females $F_n(t)$
- *Wolbachia*-carriers $P_w(t)$
  - Males $M_w(t)$
  - Females $F_w(t)$

Key assumptions for simplification

- Wild and *Wolbachia*-carrying mosquitoes exhibit $(1 \div 1)$ adult sex ratio [?].
- Wild and *Wolbachia*-carrying male mosquitoes are equally capable to mate [??].
- Wild female and male mosquitoes are often evenly distributed and have a similar lifespan [?].
- Let us also suppose that *Wolbachia*-carrying males and females bear similar longevity.

Under these assumptions and in the line of other studies [??], we can then assume that

$$\boxed{X(t) := M_n(t) = F_n(t) \quad \text{and} \quad Y(t) := M_w(t) = F_w(t) \quad \forall t \geq 0}$$

The modeling framework

$$\begin{cases} \dfrac{dX}{dt} = \left[\rho_n X \dfrac{X + (1-\eta)Y}{X+Y} + \rho_w (1-\nu) Y\right] e^{-\sigma(X+Y)} + \omega Y - \delta_n X & \blacktriangleleft \text{ wild mosquitoes} \\ \dfrac{dY}{dt} = \rho_w \nu Y\, e^{-\sigma(X+Y)} - \omega Y - \delta_w Y & \blacktriangleleft \textit{ Wolbachia}\text{-carriers} \end{cases}$$

Parameters of the model:

$\rho_n \geq \rho_w$	–	average fecundity rate of X, Y
$\delta_n \leq \delta_w$	–	death rates of X, Y
$\sigma > 0$	–	competition parameter
$\nu \in (0, 1]$	–	probability of imperfect maternal transmission (IMT);
$\eta \in [0, 1]$	–	strength of CI due to *Wolbachia* infection;
$\omega \geq 0$	–	loss of *Wolbachia* infection due to thermal stress.

NOTE: ρ_w, δ_w and ν, η, ω are strain-dependent.

$$Q_x := \frac{\rho_n}{\delta_n}$$ No. of wild mosquitoes produced by 1 wild mosquito

$$Q_y := \frac{\nu \rho_w}{\omega + \delta_w}$$ No. of *Wolbachia*-carriers produced by 1 *Wolbachia*-carrier

$$Q_{y,x} := \frac{(1-\nu)\rho_w + \omega Q_y}{\delta_n}$$ No. of wild mosquitoes produced by 1 *Wolbachia*-carrier

Equilibria of no interest

- Extinction equilibrium $\mathbf{E}_0 = (0,0)$ always exists; it is GAS if $Q_x \leq 1$ and $Q_y \leq 1$, and is repulsive otherwise.
- Fully non-infected equilibrium $\mathbf{E}_x = \left(X^\sharp, 0\right)$ is a boundary equilibrium with

$$\boxed{X^\sharp = \frac{1}{\sigma} \ln Q_x}$$

that exists if $Q_x > 1$. It is LAS if $Q_y > 1$ and is GAS if $Q_y \leq 1$.

Coexistence equilibria

When $Q_x > Q_y > 1$, two coexistence equilibria arise under this condition:

$$Q_c := \frac{Q_{y,x} + Q_y + \eta Q_x}{Q_x} > 1$$

- Unstable coexistence $\mathbf{E}_u = (X_u, Y_u)$

$$X_u = \frac{\ln Q_y}{2\eta\sigma}\left[(Q_c - 1) + \sqrt{(Q_c-1)^2 - 4\eta\frac{Q_{y,x}}{Q_x}}\right], \qquad Y_u = \frac{1}{\sigma}\ln Q_y - X_u$$

- Stable coexistence $\mathbf{E}_s = (X_s, Y_s)$

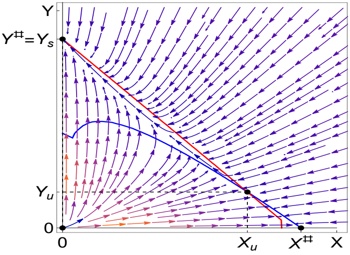
$$X_s = \frac{\ln Q_y}{2\eta\sigma}\left[(Q_c - 1) - \sqrt{(Q_c-1)^2 - 4\eta\frac{Q_{y,x}}{Q_x}}\right], \qquad Y_s = \frac{1}{\sigma}\ln Q_y - X_s$$

NOTE: stable coexistence $\mathbf{E}_s = (X_s, Y_s)$ becomes a *boundary equilibrium* ($X_s \mapsto 0$) if

$$\nu = 1 \quad \text{and} \quad \omega = 0 \quad \text{that is, when} \quad Q_{y,x} = 0.$$

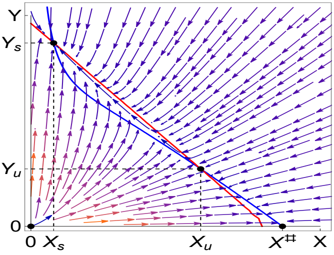
wMel Wolbachia strain: dynamics

Ideal case: 2 boundary LAS equilibria



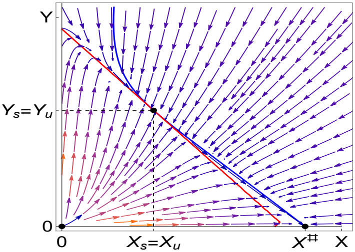
$\nu = 1, \eta = 1, \omega = 0$

Stable coexistence (bistability)



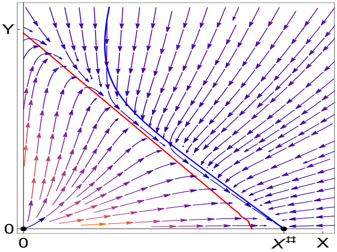
$\nu = 0.95, \eta = 0.98, \omega = 0.1\%$

Unstable coexistence



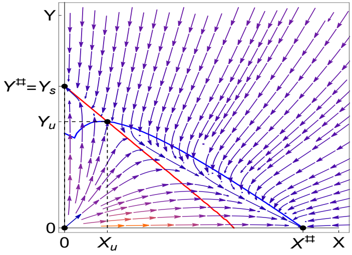
$\nu = 0.95, \eta = 0.98, \omega = 0.61\%$

Wolbachia extinction



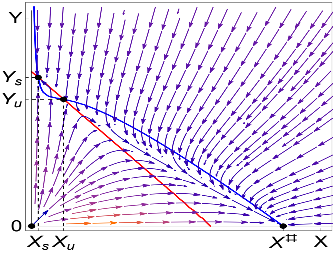
$\nu = 0.95, \eta = 0.98, \omega = 1\%$

Ideal case: 2 boundary LAS equilibria



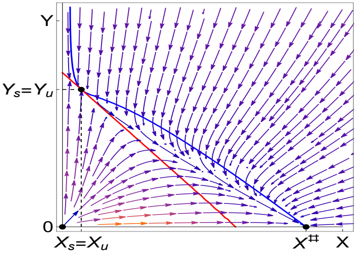
$\nu = 1, \eta = 1, \omega = 0$

Stable coexistence (bistability)



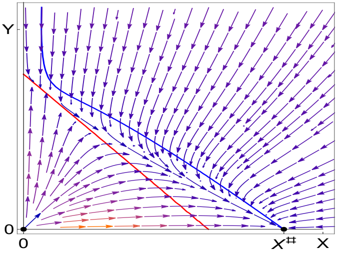
$\nu = 0.99, \eta = 0.95, \omega = 0.015\%$

Unstable coexistence



$\nu = 0.99, \eta = 0.95, \omega = 0.083\%$

Wolbachia extinction



$\nu = 0.99, \eta = 0.95, \omega = 0.5\%$

Genetic algorithm

- - Extinction equilibrium $\mathbf{E}_0 = (0, 0)$ always exists; it is GAS if $Q_x \leq 1$ and $Q_y \leq 1$, and is repulsive otherwise.
  -
- Fully non-infected equilibrium $\mathbf{E}_x = \left(X^\sharp, 0\right)$ is a boundary equilibrium with

$$\boxed{X^\sharp = \frac{1}{\sigma} \ln Q_x}$$

that exists if $Q_x > 1$. It is LAS if $Q_y > 1$ and is GAS if $Q_y \leq 1$.

SUMMARY: existence of the non-trivial equilibria

Maternal transmission (MT)	Infection loss due to thermal stress	Cytoplasmic incompatibility (CI)	Existence of non-trivial equilibria			
			***Wolbachia*-free** $(X^{\#}, 0)$	**Fully infected** $(0, Y^{\#})$	**Stable coexistence** (X_s, Y_s)	**Unstable coexistence** (X_u, Y_u)
$\nu = 1$ (perfect)	$\omega = 0$ (absent)	$\eta = 1$ (perfect)	YES	YES	NO	YES
		$0 < \eta < 1$ (imperfect)		MAYBE		MAYBE
		$\eta = 0$ (absent)		NO		NO
	$\omega > 0$ (present)	$\eta = 1$ (perfect)			MAYBE	MAYBE
		$0 < \eta < 1$ (imperfect)				
		$\eta = 0$ (absent)			NO	NO
$0 < \nu < 1$ (imperfect)	$\omega = 0$ (absent)	$\eta = 1$ (perfect)			MAYBE	MAYBE
		$0 < \eta < 1$ (imperfect)				
		$\eta = 0$ (absent)			NO	NO
	$\omega > 0$ (present)	$\eta = 1$ (perfect)			MAYBE	MAYBE
		$0 < \eta < 1$ (imperfect)				
		$\eta = 0$ (absent)			NO	NO

Conclusions

- The proposed 2-dim model **retains the key properties** of higher-dimensional models of *Wolbachia* invasion.
- The proposed 2-dim system **has rich dynamics and exhibits numerous bifurcations** w.r.t. parameters ν (maternal transmission), η (cytoplasmic incompatibility), and ω (infection loss due to thermal stress).
- The proposed 2-dim model allows to visualize **its phase portrait** for further identification of the **attraction basins** of possible LAS equilibria (bistability).
- The proposed 2-dim model is **applicable to different Wolbachia strains** (*wMel*, *wMelPop*, and *wAu*) that are currently tested for *Wolbachia*-based biocontrol of *Aedes*-borne diseases.

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