IME INSTITUTO DE MATEMÁTICA E ESTATÍSTICA UNIVERSIDADE DE SÃO PAULO

Exploring the impact of temperature over the efficacy of replacing the wild *Ae. aegypti* population by *Wolbachia*-carrying one

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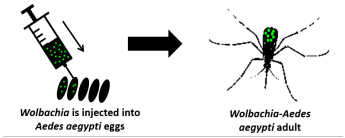
Motivation

Replace the wild population of mosquito *Ae. aegypti* by an infectious one carrying the *Wolbachia* bacteria in order to block *flavivirus* transmission.

Two parameters: maternal inheritance and cytoplasmic incompatibility (CI)

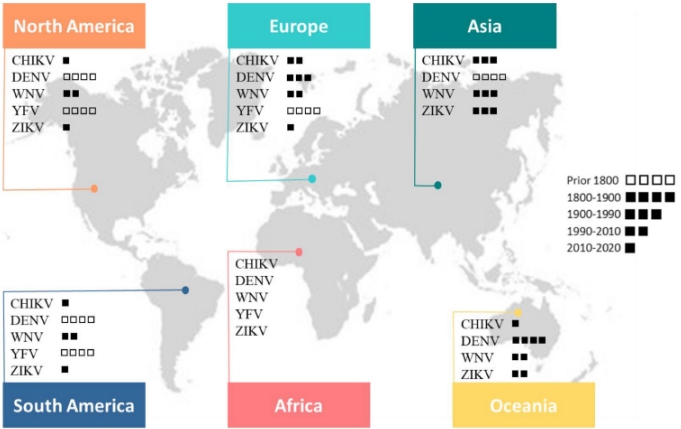


unidirectional

	♂	♂
♀		CI
♀		

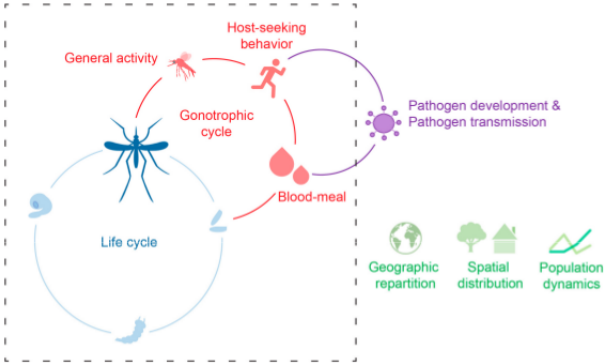
- World Mosquito Program (WMP)
- National Environment Agency (NEA)
- Institute For Medical Research

Arbovirus transmission



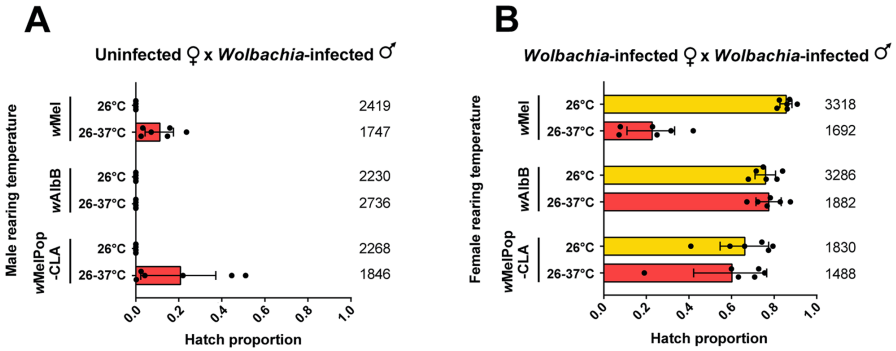
[1] Bellone, R; Failloux, A.B. (2020). The role of temperature in shaping mosquito-borne viruses transmission. Frontiers in Microbiology.

Abiotic factors, mosquito physiology and behavior



[2] Reinhold, JM, *et al.* (2018). Effects of the environmental temperature on Aedes aegypti and Aedes albopictus mosquitoes: a review. Insects, 9(4), 158.

Temperature modulates the infection by *Wolbachia*



[3] Ross, PA; *et al.*(2017). *Wolbachia* infections in *Aedes aegypti* differ markedly in their response to cyclical heat stress. PLoS Pathogens, 13(1), e1006006.

Non-autonomous delay differential model

Table: Parameters of the mathematical model, their meaning, and units. The indices u, w, and J are related to uninfected, infected with *Wolbachia*, and immature (juvenile) phase, respectively.

Notation	Meaning	Units
ξ	maternal inheritance	-
τ	development time	days
q	cytoplasmic incompatibility	-
η	carrying capacity	individual^{-1}
r_u, r_w	sex ratios	-
b_u, b_w	birth rates	days^{-1}
θ, θ_J	rates of *Wolbachia* infection loss	days^{-1}
d_u, d_w, d_{uJ}, d_{wJ}	rates of mortality	days^{-1}
ϵ	mating competitive advantage	-

Non-autonomous delay differential model

States variables

N_u and N_w the total uninfected and infected mosquito population, respectively.

$$
\begin{aligned}
\frac{dN_u(t)}{dt} &= r_u(1-q\nu(t-\tau(t)))b_u(T(t-\tau(t)))N_u(t-\tau(t))S_u(t)\phi(T(t-\tau(t))) \\
&\quad +(1-\xi\sigma(t))r_w b_w(T(t-\tau(t)))N_w(t-\tau(t))S_w(t)\phi(T(t-\tau(t))) \\
&\quad -d_u(T(t))N_u(t)+\theta(T(t))N_w(t), \\
\frac{dN_w(t)}{dt} &= r_w\xi\sigma(t)b_w(T(t-\tau(t)))N_w(t-\tau(t))S_w(t)\phi(T(t-\tau(t))) \\
&\quad -(\theta(T(t))+d_w(T(t)))N_w(t),
\end{aligned}
\tag{1}
$$

where

$$\phi(T(t-\tau(t))) = e^{-\eta(T(t-\tau(t)))(r_u N_u(t-\tau(t))+r_w N_w(t-\tau(t)))}$$

and

$$\nu(t-\tau(t)) = \frac{(1-r_w)N_w(t-\tau(t))}{\epsilon(1-r_u)N_u(t-\tau(t))+(1-r_w)N_w(t-\tau(t))}.$$

[4] Ferreira, C. P. (2020). *Aedes aegypti* and *Wolbachia* interaction: population persistence in an environment changing. Theoretical Ecology, 13(2), 137-148.

Non-autonomous delay differential model

Parameters

S_i - survival of the immature phase, not carrying ($i = u$) or carrying $\left(i = w\right)$ the bacterium;

σ - survival of the infection during the immature phase;

τ - development time.

$$
\begin{aligned}
\frac{dS_u(t)}{dt} &= S_u(t)\left[\frac{m(T(t))d_{uJ}(T(t-\tau(t)))}{m(T(t-\tau(t)))} - d_{uJ}(T(t))\right], \\
\frac{dS_w(t)}{dt} &= S_w(t)\left[\frac{m(T(t))d_{wJ}(T(t-\tau(t)))}{m(T(t-\tau(t)))} - d_{wJ}(T(t))\right], \\
\frac{d\sigma(t)}{dt} &= \sigma(t)\left[\frac{m(T(t))\theta_J(T(t-\tau(t)))}{m(T(t-\tau(t)))} - \theta_J(T(t))\right], \\
\frac{d\tau(t)}{dt} &= 1 - \frac{m(T(t))}{m(T(t-\tau(t)))}.
\end{aligned}
$$

[5] R.M. Nisbet and W.S.C Gurney (1983). The systematic formulation of population models for insects with dynamically vaying instar duration. Theoretical Population Biology 23: 114-135.

[6] P. Amarassekare and R.M. Coutinho (2014). Efects of temperatue on intraspecific competition in ectotherms. The American Naturalist 184: E50-E65.

Theorem (Existence of the steady states)

If $T := T(t) = T(t-\tau)$, $\nu := \nu(t-\tau)$, *and* $r := r_u = r_w$, *then System (1) admits three equilibria:*

(i) $P_1 = (0, 0)$ *which always exists;*

(ii) $P_2 = \left(\dfrac{\ln R_u}{r\eta(T)}, 0\right)$ *that exists if* $R_u > 1$;

(iii) $P_3 = \left(\dfrac{\ln R_w}{r\eta(T)}\left(\dfrac{R_{wu} + \alpha R_w}{R_{wu} + R_w(\alpha+1) - R_u}\right), \dfrac{\ln R_w}{r\eta(T)}\left(\dfrac{R_w - R_u}{R_{wu} + R_w(\alpha+1) - R_u}\right)\right)$ *that exists if* $R_w > max\{1, R_u\}$, *where* $\alpha := \alpha(T) = \dfrac{\theta(T)}{d_u(T)}$.

The three thresholds R_w, R_u *and* R_{wu} *are given by*

$$R_w = \frac{r\xi\sigma b_w(T)S_w}{\theta(T) + d_w(T)}, \quad R_u = \frac{r(1-q\nu)b_u(T)S_u}{d_u(T)} \quad \text{and} \quad R_{wu}(T) = \frac{(1-\xi\sigma)b_w(T)rS_w}{d_u(T)}.$$

where $S_w := S_w(t)$, $S_u := S_u(t)$ *and* $\sigma := \sigma(t)$.

Theorem (Local asymptotic stability of the equilibrium P_1)

Suppose that $T := T(t) = T(t-\tau)$, $\nu := \nu(t-\tau)$, *and* $r := r_u = r_w$. *If* $\max\{R_u, R_w\} < 1$, *then* P_1 *is local asymptotic stable; otherwise it is unstable.*

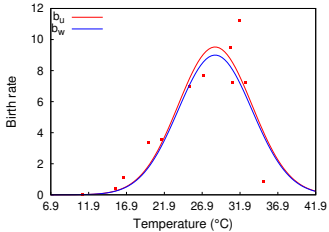
Theorem (Local asymptotic stability of the equilibrium P_2)

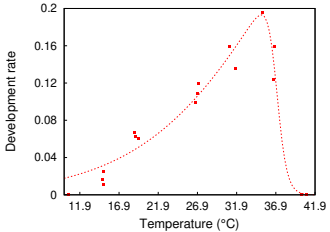
Suppose that $T := T(t) = T(t-\tau)$, $\nu := \nu(t-\tau)$, *and* $r := r_u = r_w$. *If* $R_u > \max\{1, R_w\}$, $R_w/R_u < \tan(\omega_1)\ \sin(\omega_1) + \cos(\omega_1)$ *where* $\omega_1 = -(\theta(T) + d_w(T))\tau\ \tan(\omega_1)$ *and* $1 - \ln R_u < \tan(\omega_2)\ \sin(\omega_2) + \cos(\omega_2)$ *with* $\omega_2 = -d_u(T)\tau\ tan(\omega_2)$, $\omega_1, \omega_2 \in]0, \pi[$, *then* P_2 *is local asymptotic stable; otherwise it is unstable.*

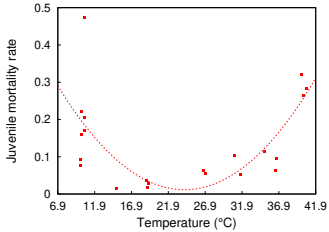
Theorem (Local asymptotic stability of the equilibrium P_3)

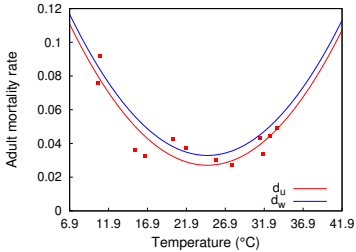
Suppose that $T := T(t) = T(t-\tau)$, $\nu := \nu(t-\tau)$, $\theta(T) = 0$, $\xi\sigma = 1$, *and* $r := r_u = r_w$. *If* $R_w > \max\{1, R_u\}$, $R_u/R_w < \tan(\omega_1)\ \sin(\omega_1) + \cos(\omega_1)$ *where* $\omega_1 = -\ d_u(T)\tau\ \tan(\omega_1)$ *e* $1 - \ln R_w < \tan(\omega_2)\ \sin(\omega_2)\ +\ \cos(\omega_2)$ *with* $\omega_2 = -d_w(T)\tau\ \tan(\omega_2)$, $\omega_1, \omega_2 \in]0, \pi[$, *then* P_3 *is local asymptotic stable; otherwise it is unstable.*

Temperature-driven parameters

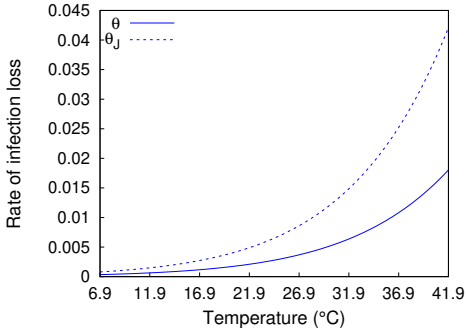








Temperature-driven parameters

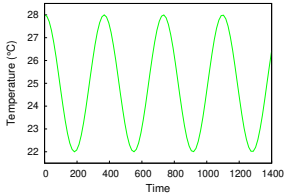


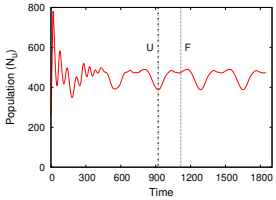
What is the best period of the year to release the *Wolbachia*-carrying mosquitoes?

Assuming a periodic variation of temperature over a year, the temperature function is given by

$$T(t) = T_M - \sigma_T \cos\left(\frac{2\pi t}{365}\right)$$

where T_M and σ_T are the mean temperature and its variation.





The initial condition is $N_u(t) = 200 + 200\left|\cos\left(t + \frac{\pi}{2}\right)\right|$, and $N_w(t) = 0$, for $t \in [-\tau, 0]$, $S_u(0) = e^{-\tau(0)d_{uJ}(T(0))}$, $S_w(0) = e^{-\tau(0)d_{wJ}(T(0))}$, and $\sigma(0) = e^{-\tau(0)\theta_J(T(0))}$ with $\tau(0) = m(T(0))^{-1}$.

What much and how many times we will do it?

One release of *Wolbachia*-carying mosquitoes during favorable or not favorable period.

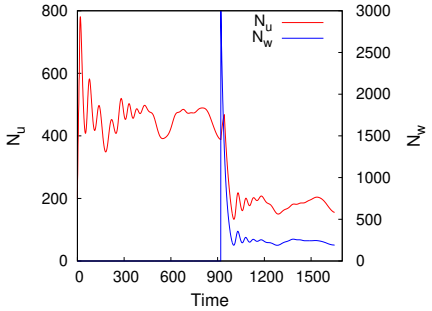


Figure: unfavorable period

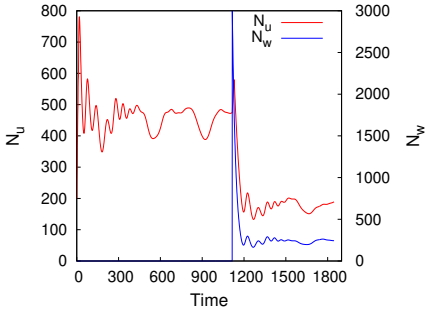


Figure: favorable period

What much and how many times we will do it?

Four releases of *Wolbachia*-carying mosquitoes during favorable or not favorable period.

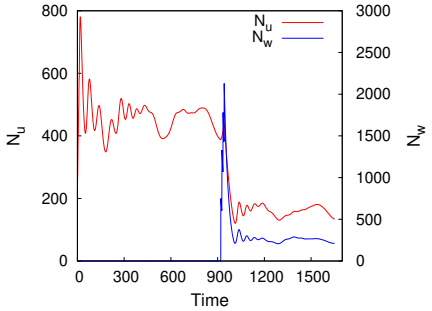


Figure: unfavorable period

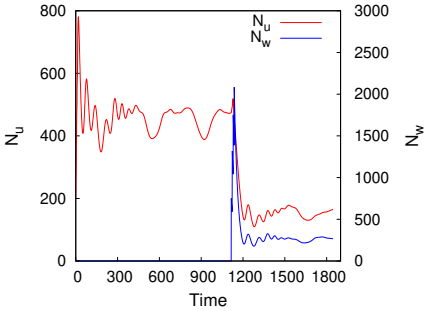


Figure: favorable period

How can we measure the efficiency of the technique?

$$E_k = 1 - \frac{I_c}{I_0}, \quad \text{with} \quad I_j = \int_{t_i}^{t_f} N_u(t)\, dt$$

where I_j with $j = \{0, c\}$ measures the cumulative number of non-infected mosquitoes observed between t_i and t_f.

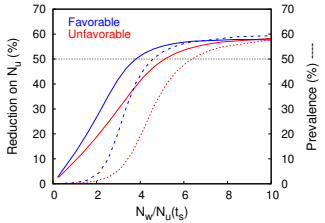


Figure: one infected-mosquito release

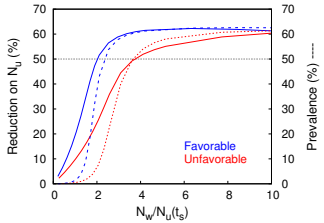


Figure: four infected-mosquito releases

How temperature values impact the dynamics of both population?

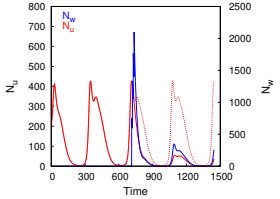


Figure: $T = 18 \pm 3^{\circ}$C

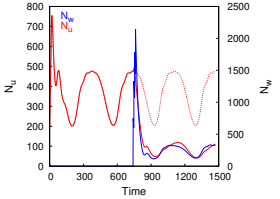


Figure: $T = 22 \pm 3^{\circ}$C

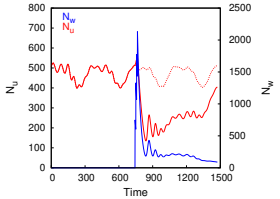


Figure: $T = 28 \pm 3^{\circ}$C

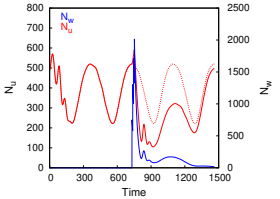


Figure: $T = 32 \pm 3^{\circ}$C

The effect of the bacteria strain

Temperature data in Niterói-RJ from 2020 to 2022 and the dynamics of both populations.

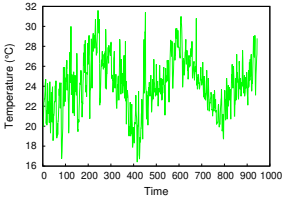


Figure: From 2020 to 2022

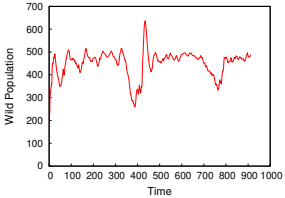


Figure: non-infected one

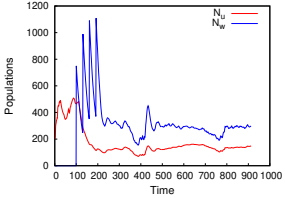


Figure: $\xi = 0.99$ and $q = 0.95$

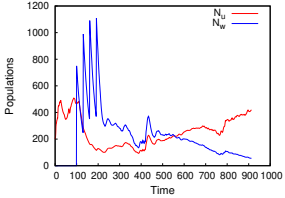
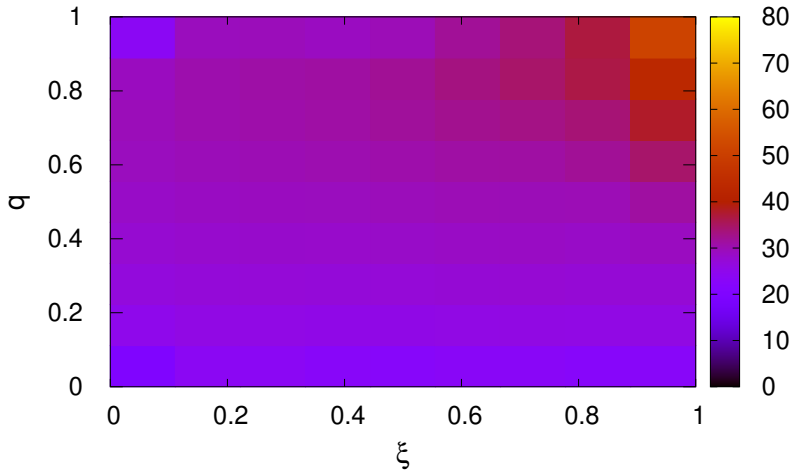


Figure: $\xi = 0.99$ and $q = 0.8$

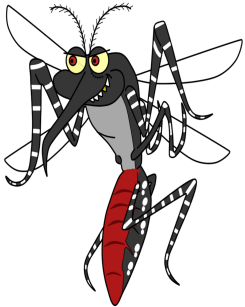
What is the importance of the chosen bacterial strain?



Conclusions

- Four releases delayed by seven days each are more efficient than one.
- When the mosquito population is high is the best moment to implement the releasing of infected mosquitoes.
- Strains with high levels of cytoplasmic incompatibility and maternal inheritance boost the efficacy of the technique.
- High temperature can increase the ratio of infected to non-infected mosquitoes necessary to achieve infection's persistence.
- High temperature can also diminishing the prevalence of the infection in the long run.

Although, the general idea of how all these factors affects the efficacy of the technique, the interaction among them are not trivial. And here, a framework of how this interaction affects the replacement of wild mosquito population by an infected one that is not able to transmit dengue is developed.



Thank you!