

Quelques modèles mathématiques de contrôle de populations de moustiques et de nuisibles agricoles

Luís Almeida (LJLL, CNRS and Sorbonne Univ.)

Chaire Modélisation Mathématique et Biodiversité

Joint work with:

For the Mathematics: Kala Agbo Bidi, Jesus Bellver Arnau, Alexis Léculier and Jean-Michel Coron (LJLL, Sorbonne Univ), & Jorge Estrada and Nicolas Vauchelet (LAGA, Sorbonne Paris Nord)), & Carlota Rebelo (Univ de Lisboa) & Y. Privat (Mines Nancy) & Grégoire Nadin (U. Orléans) & Michel Duprez (INRIA)

For the field applications: Hervé Bossin and Françoise Mathieu-Daudé (ILM, Papeete) & René Gato and Mislady Rodriguez (IPK, La Havana)

October 27th, 2022

- Vector Borne Diseases involve at least 3 components :

Vector-borne Diseases

- Vector Borne Diseases involve at least 3 components :
- Vectors: usually bloodsucking arthropods like mosquitoes (malaria, dengue, chikungunya, yellow fever, west Nile fever), ticks (Lyme disease), fleas (Black Death)....

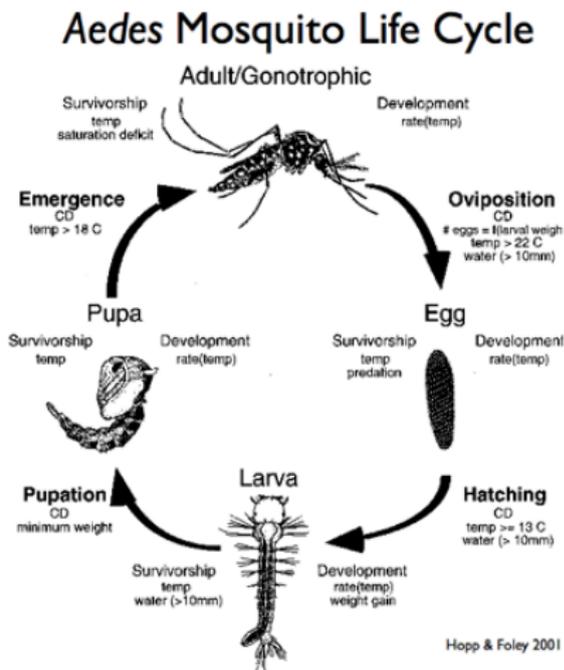
- Vector Borne Diseases involve at least 3 components :
- Vectors: usually bloodsucking arthropods like mosquitoes (malaria, dengue, chikungunya, yellow fever, west Nile fever), ticks (Lyme disease), fleas (Black Death)....
- Hosts (humans for our models)

- Vector Borne Diseases involve at least 3 components :
- Vectors: usually bloodsucking arthropods like mosquitoes (malaria, dengue, chikungunya, yellow fever, west Nile fever), ticks (Lyme disease), fleas (Black Death)....
- Hosts (humans for our models)
- Pathogens: plasmodium (malaria), virus (dengue, chikungunya, Zika), bacteria (Yersinia pestis for the Black Death)

- Vector Borne Diseases involve at least 3 components :
- Vectors: usually bloodsucking arthropods like mosquitoes (malaria, dengue, chikungunya, yellow fever, west Nile fever), ticks (Lyme disease), fleas (Black Death)....
- Hosts (humans for our models)
- Pathogens: plasmodium (malaria), virus (dengue, chikungunya, Zika), bacteria (Yersinia pestis for the Black Death)
- Other species can be involved, for instance as reservoir (like birds for the west Nile fever or rodents for the Black Death)

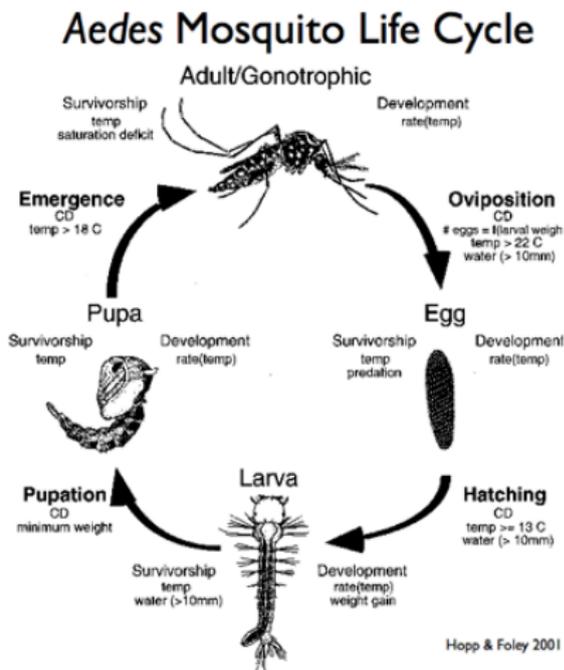
Mosquito-borne Diseases

- Diseases transmitted by hematophagous organisms: 17% of world's infectious diseases (WHO).



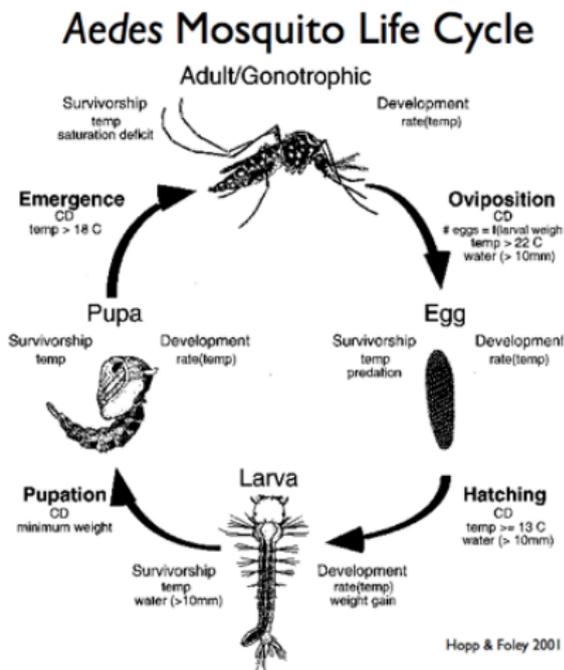
Mosquito-borne Diseases

- Diseases transmitted by hematophagous organisms: 17% of world's infectious diseases (WHO).
- Female mosquitoes need blood to produce the eggs. Transmission through the bite.



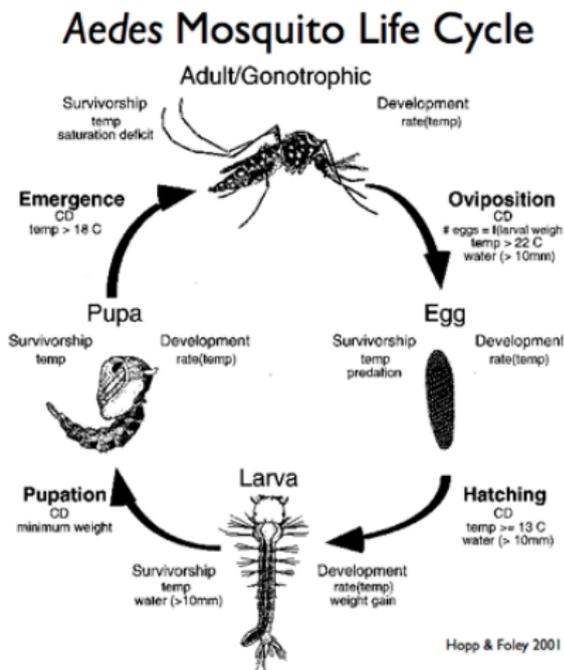
Mosquito-borne Diseases

- Diseases transmitted by hematophagous organisms: 17% of world's infectious diseases (WHO).
- Female mosquitoes need blood to produce the eggs. Transmission through the bite.
- Mosquitoes of the genus Anopheles: Malaria



Mosquito-borne Diseases

- Diseases transmitted by hematophagous organisms: 17% of world's infectious diseases (WHO).
- Female mosquitoes need blood to produce the eggs. Transmission through the bite.
- Mosquitoes of the genus Anopheles: Malaria
- Mosquitoes of the genus Aedes: dengue fever, Zika, Chikungunya, yellow fever.



Aedes mosquitoes: public health problem (Dengue)

- \approx 400 million infections every year.

Aedes mosquitoes: public health problem (Dengue)

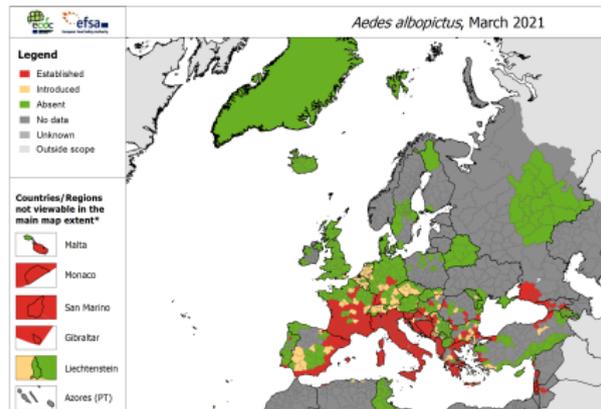
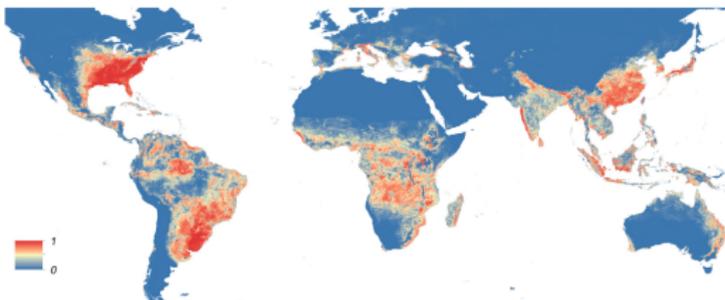
- \approx 400 million infections every year.
- \approx 3.9 billion people at risk in 129 countries.

Aedes mosquitoes: public health problem (Dengue)

- \approx 400 million infections every year.
- \approx 3.9 billion people at risk in 129 countries.
- No efficient vaccine, nor antiviral drugs.

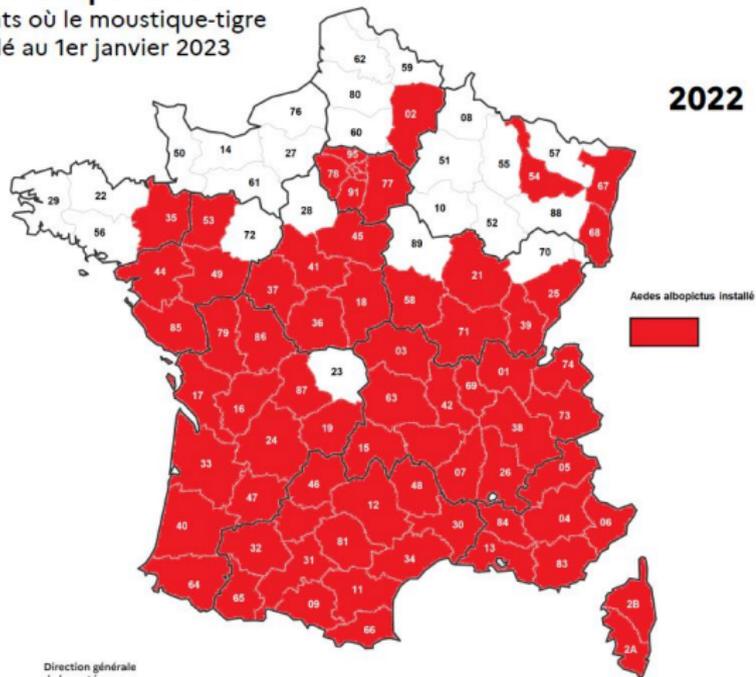
Aedes mosquitoes: public health problem (Dengue)

- \approx 400 million infections every year.
- \approx 3.9 billion people at risk in 129 countries.
- No efficient vaccine, nor antiviral drugs.
- Expansion of vector's habitat (global trade, global warming, reduction of predator populations ...)



Dengue vector population : Tiger mosquito in France

France métropolitaine
Départements où le moustique-tigre est installé au 1er janvier 2023



How to fight it?

- Natural and mechanical control: reduction of egg-laying sites, helping natural predators, removal of larvae - implementation complexity, time-consuming, economic cost...

How to fight it?

- Natural and mechanical control: reduction of egg-laying sites, helping natural predators, removal of larvae - implementation complexity, time-consuming, economic cost...
- Insecticide: ecological drawbacks, not species-specific, indirect effect of predator population which may also lead to mosquito overpopulation in the following season, rapid development of resistance ...

How to fight it?

- Natural and mechanical control: reduction of egg-laying sites, helping natural predators, removal of larvae - implementation complexity, time-consuming, economic cost...
- Insecticide: ecological drawbacks, not species-specific, indirect effect of predator population which may also lead to mosquito overpopulation in the following season, rapid development of resistance ...
- Biological control and Genetically Modified Organisms - past experience should lead us to be cautious and avoid when possible.

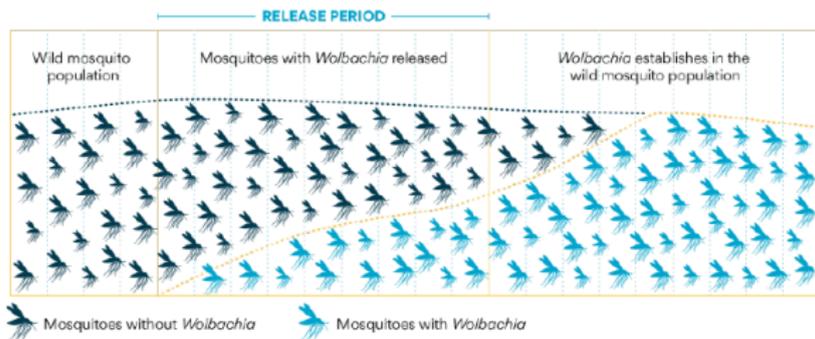
How to fight it?

- Natural and mechanical control: reduction of egg-laying sites, helping natural predators, removal of larvae - implementation complexity, time-consuming, economic cost...
- Insecticide: ecological drawbacks, not species-specific, indirect effect of predator population which may also lead to mosquito overpopulation in the following season, rapid development of resistance ...
- Biological control and Genetically Modified Organisms - past experience should lead us to be cautious and avoid when possible.
- Natural to consider both continuous and impulsive controls.

Species-specific methods we will focus on :

- *Wolbachia* method

- Reduction of the vector capacity.
- *Wolbachia* vertical transmission.
- Cytoplasmic incompatibility.
- Population replacement.



Source: <http://www.eliminatedengue.com/our-research/Wolbachia>

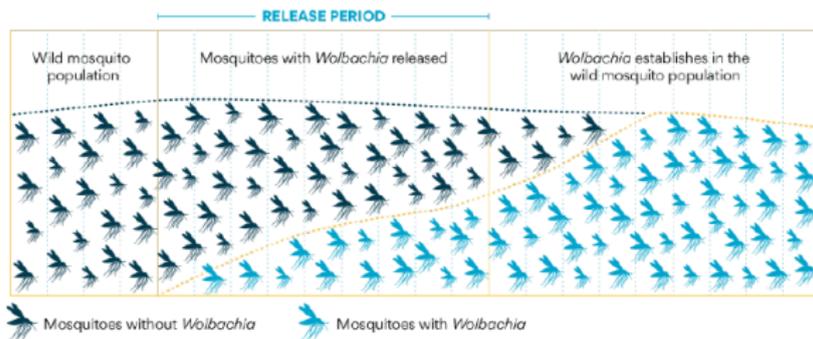
♀ \ ♂	Infecté	Sain
Infecté	I	I
Sain	×	S



Species-specific methods we will focus on :

- *Wolbachia* method

- Reduction of the vector capacity.
- *Wolbachia* vertical transmission.
- Cytoplasmic incompatibility.
- Population replacement.



Source: <http://www.eliminatedengue.com/our-research/Wolbachia>

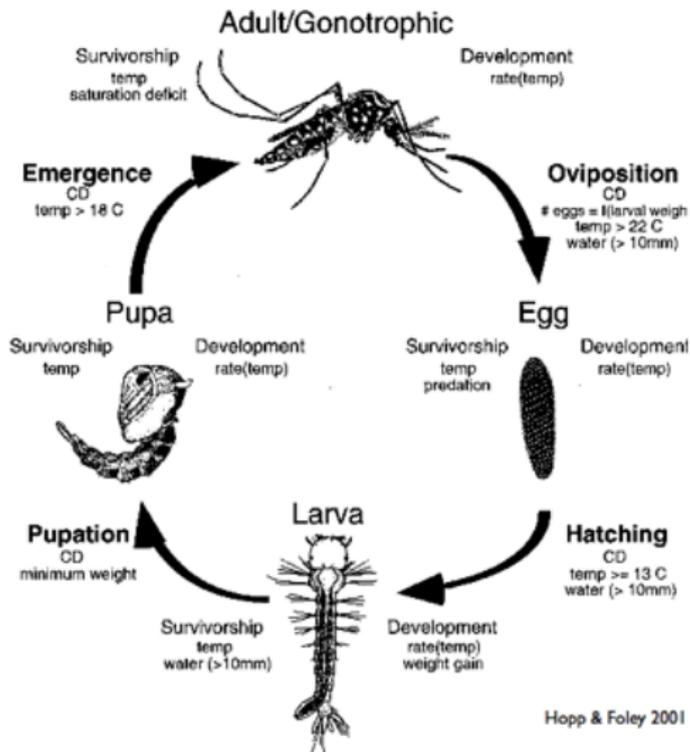
♀ \ ♂	Infecté	Sain
Infecté	I	I
Sain	×	S



- Sterile insect technique

- Population reduction/suppression.
- Recurrent intervention

Aedes Mosquito Life Cycle



Aquatic phase :

egg (few days to several months)

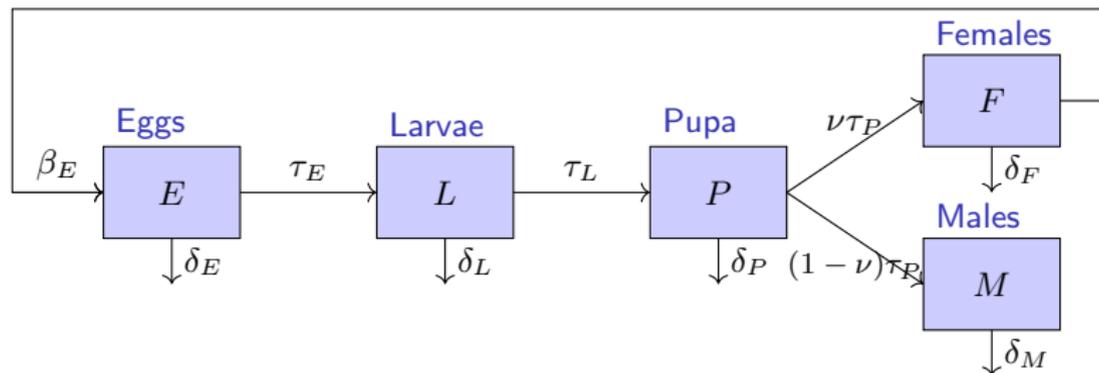
larvae (3 days to several weeks)

pupa (1-3 days)

Adult phase (~ 1 month)

Mosquito life cycle

The life cycle for mosquitos may be schematized as follows



- $\beta_E(M)$ birth rate (per female);
- τ_E, τ_L, τ_P transition rates; ν sex ratio;
- $\delta_E, \delta_L, \delta_P, \delta_M, \delta_F$ death rates.

Mosquito life cycle

$$\frac{d}{dt}E = \underbrace{\beta_E F}_{\text{birth}} \underbrace{\left(1 - \frac{E}{K}\right)}_{\text{competition intraspecific}} - \underbrace{\tau_E E}_{\text{transition to larvae}} - \underbrace{\delta_E E}_{\text{death}},$$

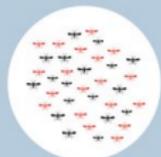
$$\frac{d}{dt}L = \tau_E E - \left(\underbrace{cL}_{\text{competition}} + \underbrace{\tau_L}_{\text{transition}} + \underbrace{\delta_L}_{\text{death}} \right) L,$$

$$\frac{d}{dt}P = \tau_L L - (\tau_P + \delta_P) P,$$

$$\frac{d}{dt}F = \nu \tau_P P - \delta_F F,$$

$$\frac{d}{dt}M = (1 - \nu) \tau_P P - \delta_M M.$$

Sterile Insect Technique



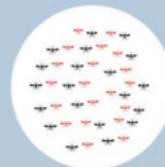
Mass-rearing of insects takes place in special facilities.



Male and female insects are separated. Ionizing radiation is used to sterilize the male insects.



The sterile male insects are released over towns or cities...



...where they compete with wild males to mate with females.



These females lay eggs that are infertile and bear no offspring, reducing the insect population.



Targeting sexual reproduction: SIT

Sterile Insect Technique (SIT) : releases of sterilized male mosquitoes. The release function is denoted u .

Introduce a new compartment for sterilized males, denoted M_s .

Probability for a female to meet a non-sterilized male is proportional to the proportion of them, with a preferential parameter, denoted γ .

$$\frac{d}{dt}E = \beta_E F \frac{M}{M + \gamma M_s} \left(1 - \frac{E}{K}\right) - (\tau_E + \delta_E)E$$

$$\frac{d}{dt}L = \tau_E E - (cL + \tau_L + \delta_L)L$$

$$\frac{d}{dt}P = \tau_L L - (\tau_P + \delta_P)P$$

$$\frac{d}{dt}F = \nu \tau_P P - \delta_F F$$

$$\frac{d}{dt}M = (1 - \nu)\tau_P P - \delta_M M$$

$$\frac{d}{dt}M_s = u - \delta_s M_s.$$

Spatial problem - invasive wave propagation

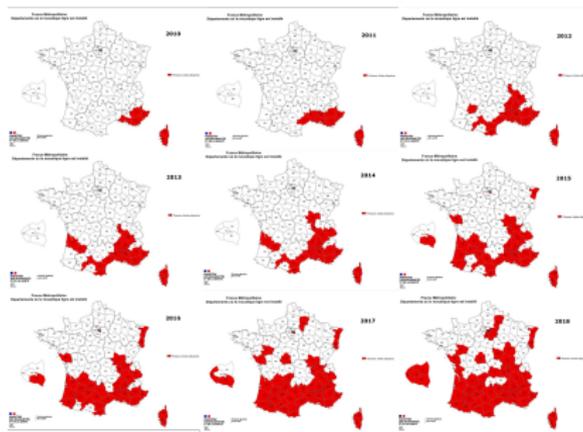


Figure: Expansion of *Aedes albopictus* in mainland France

Global warming and trade help *Aedes* mosquitoes to settle in many temperate regions including Europe. They are not only an invasive species but also vectors for many diseases including dengue, Zika and chikungunya.

Sterile Insect Technique: Rolling carpet strategy

A strategy to avoid the epidemic risk is to repulse the invading wave of mosquitoes (including expanding the mosquito-free area) using a *Rolling Carpet* strategy where we act in a band of width L that moves with speed c against the invading front. Mathematical study helps optimizing this strategy (e.g. the amount of mosquitoes released, M)

SIT as a general technique against pests

Used since the 60's and combined with other control methods, the SIT has been successful in controlling various insect pests, including

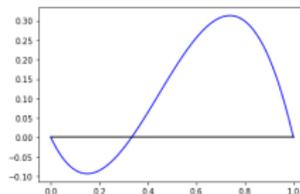
- fruit flies (Mediterranean fruit fly, Mexican fruit fly, oriental fruit fly, melon fly);
- tsetse fly;
- screwworm;
- moths (codling moth, pink bollworm, false codling moth, cactus moth, and the Australian painted apple moth)
- mosquitoes.

With good "return on investment" according to FAO and IAEA.

Bistable Dynamics and Traveling Wave solutions

Assumption : **Bistable dynamics**

$$\underbrace{\partial_t u - \Delta u}_{\text{Diffusion}} = \underbrace{g(u)}_{\text{Growth}}$$



Natural set of solutions : the traveling wave solutions $u(x, t) = \phi(x - c_0 t)$.

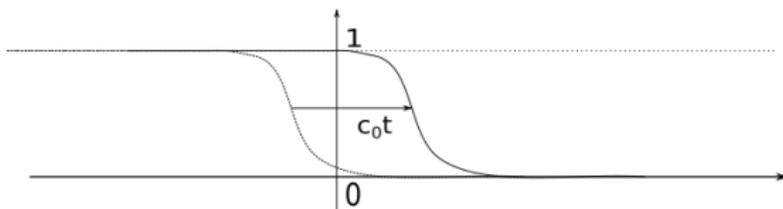
$$\partial_t u - \Delta u = g(u) \quad \longrightarrow \quad -c_0 \phi' - \phi'' = g(\phi).$$

ϕ connects the two stable steady states :

$$\phi(-\infty) = 1 \quad \text{and} \quad \phi(+\infty) = 0.$$

The sense of propagation depends on $\text{sign}(c_0) = \text{sign} \left(\int_0^1 g(v) dv \right)$

Assumption : $\text{sign}(c_0) > 0$: naturally, the mosquitoes invade the territory



The rolling carpet strategy

The idea is to *act* on a finite interval $(0, L)$ and move this *action* like a rolling carpet in the opposite sense to that of the natural invasion traveling wave.

Aim of the work : generate a traveling wave with a negative speed solution of

$$\begin{cases} \partial_t u - \Delta u = g(u)1_{\{x < ct, x > L+ct\}} + Act(u)1_{\{ct < x < L+ct\}}, \\ u(-\infty) = 1, \\ u(+\infty) = 0 \end{cases}$$

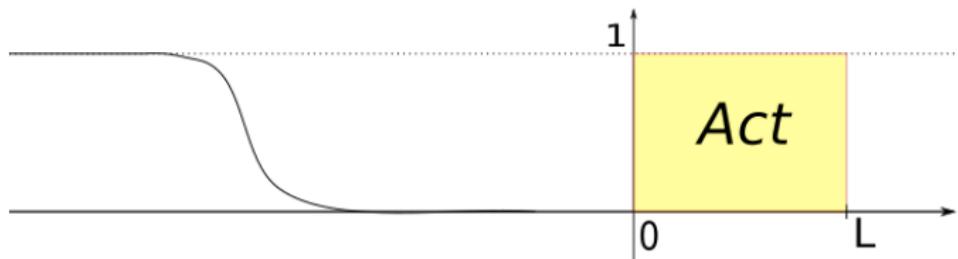


Fig. 1. The system at time $t = 0$

The rolling carpet strategy

The idea is to *act* on a finite interval $(0, L)$ and move this *action* like a rolling carpet in the opposite sense to that of the natural invasion traveling wave.

Aim of the work : generate a traveling wave with a negative speed solution of

$$\begin{cases} \partial_t u - \Delta u = g(u)1_{\{x < ct, x > L+ct\}} + Act(u)1_{\{ct < x < L+ct\}}, \\ u(-\infty) = 1, \\ u(+\infty) = 0 \end{cases}$$

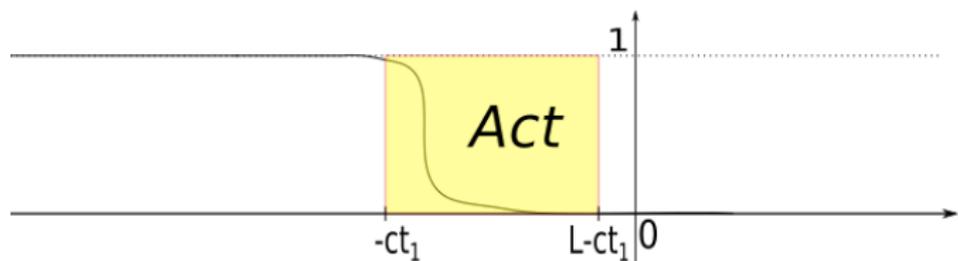


Fig. 1. The system at $t = t_1$

Numerical results

We perform numerical simulations of

$$\partial_t f - \partial_{xx} f = g(f, m_S),$$

for $c = -0.1$, $L = 20$ and two sizes of releases M .

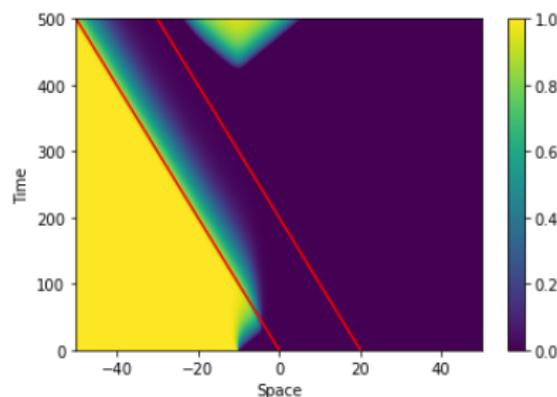


Fig. 4. $M = 3.3$

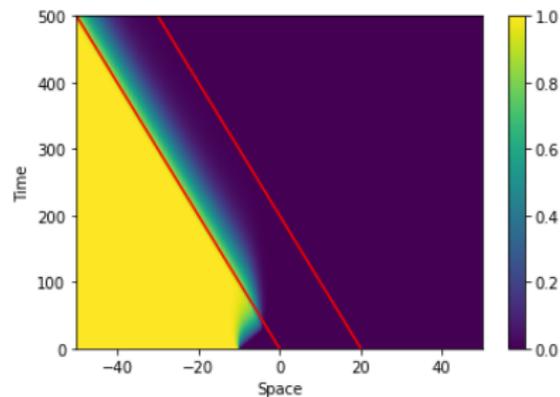
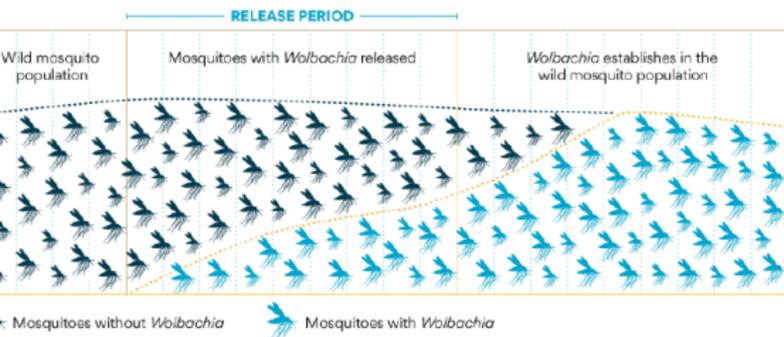


Fig. 5. $M = 3.6$

Wolbachia

In this part, we will mainly focus on the spatial spread of *Wolbachia* bacteria into a wild host population.

- Endo-symbiotic bacteria found in most arthropod species.
- Maternally transmitted from mother to offspring.
- Causes cytoplasmic incompatibility (CI) and blocks transmission of some viruses (Dengue, Chikungunya, Zika) by *Aedes* mosquitoes.
- Several side-effects on its host (reduces fecundity, reduces lifespan, ...).



♀ \ ♂	Infecté	Sain
Infecté	I	I
Sain	×	S



Source: <http://www.eliminatedengue.com/our-research/Wolbachia>

Then, it is a population replacement problem : replacing the wild population by a population carrying the bacteria *Wolbachia*.

Mathematical model

Only adult mosquitoes can fly and their dispersal is estimated to less than 1km during their life time. Then we consider the simplified model for adult mosquitoes:

- n_i : density of Wolbachia-infected mosquitoes;
- n_u : density of uninfected mosquitoes;
- $d_u, d_i = \delta d_u$: death rate, $\delta > 1$;
- $F_u, F_i = (1 - s_f)F_u$: fecundity;
- s_h : cytoplasmic incompatibility parameter (fraction of uninfected females' eggs fertilized by infected males and which will not hatch);
- K : carrying capacity ;
- D : dispersal coefficient (assumed to be constant and normalized $D = 1$).

Model

$$\begin{cases} \partial_t n_i - \Delta n_i &= (1 - s_f)F_u n_i \left(1 - \frac{n_i + n_u}{K}\right) - \delta d_u n_i, \\ \partial_t n_u - \Delta n_u &= F_u n_u \left(1 - s_h \frac{n_i}{n_i + n_u}\right) \left(1 - \frac{n_i + n_u}{K}\right) - d_u n_u, \end{cases}$$

Model

$$\begin{cases} \partial_t n_i - \Delta n_i = f_1(n_i, n_u) := (1 - s_f)F_u n_i \left(1 - \frac{n_i + n_u}{K}\right) - \delta d_u n_i, \\ \partial_t n_u - \Delta n_u = f_2(n_i, n_u) := F_u n_u \left(1 - s_h \frac{n_i}{n_i + n_u}\right) \left(1 - \frac{n_i + n_u}{K}\right) - d_u n_u, \end{cases}$$

- **Nonnegativity:** if at $t = 0$ the densities are nonnegative, then they are nonnegative for any positive time.
- **Bound:** solutions are clearly bounded uniformly by K (if so at $t = 0$).
- This model is **competitive** : $\partial_2 f_1 < 0$ and $\partial_1 f_2 < 0$ on the quadrant $(n_i, n_u) > 0$. Then an increase of n_i (resp. n_u) will affect negatively the population n_u (resp. n_i).

We first consider the steady states (equilibria) for the associated ODE model, with no diffusion.

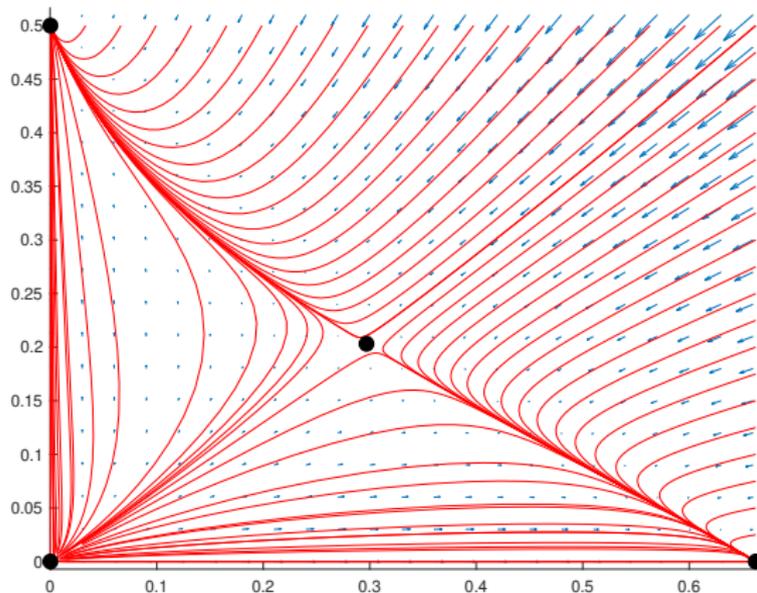
Steady states

As soon as $s_f + \delta - 1 < \delta s_h$, there are four distinct nonnegative equilibria:

- *Wolbachia* invasion $(n_{iW}^*, n_{uW}^*) := (K - \frac{d_u}{F_u} \frac{\delta}{1-s_f}, 0)$ is stable;
- *Wolbachia* extinction $(n_{iE}^*, n_{uE}^*) := (0, K - \frac{d_u}{F_u})$ is stable;
- co-existence steady state $(n_{iC}^*, n_{uC}^*) := ((K - \frac{d_u}{F_u} \frac{\delta}{1-s_f}) \frac{\delta - (1-s_f)}{\delta s_h}, (K - \frac{d_u}{F_u} \frac{\delta}{1-s_f}) \frac{\delta(s_h - 1) + (1-s_f)}{\delta s_h})$ is unstable;
- extinction $(0, 0)$ is unstable.

Dynamical system

The question is to know whether we can pass from the *Wolbachia-free equilibrium* to the *Wolbachia infected equilibrium* thanks to releases of mosquitoes and how to optimize the releases.



Dynamical system

Since the study of the spatial system is complicated, we first consider the dynamical system neglecting the spatial dependency.

Mathematical model

Let u denote the release function. The dynamical system reads

$$\begin{cases} \frac{d}{dt}n_i &= (1 - s_f)F_u n_i \left(1 - \frac{n_i + n_u}{K}\right) - \delta d_u n_i + u, \\ \frac{d}{dt}n_u &= F_u n_u \left(1 - s_h \frac{n_i}{n_i + n_u}\right) \left(1 - \frac{n_i + n_u}{K}\right) - d_u n_u, \\ n_i(t = 0) &= 0, \quad n_u(t = 0) = n_{uE}^* := K - \frac{d_u}{F_u}. \end{cases}$$

where $s_h \in (0, 1]$ is CI rate, K is environmental capacity, b_i and d_i are birth and death rates.

Principle : Two **competing** populations (for breeding sites), with **reproductive interference** by (unidirectional) CI are **exposed to releases** $u \geq 0$.

Dynamical system : an optimal control problem

We want to optimize the release strategy to be as close as possible to the *Wolbachia*-infected equilibrium at the final time of treatment, denoted T :

Cost

$$J(u) = \frac{1}{2}n_u(T)^2 + \frac{1}{2}(n_{iW}^* - n_i(T))_+^2.$$

Constraints

- The local release of mosquitoes is bounded : $0 \leq u \leq \bar{U}$.
- The total number of mosquitoes used is bounded (production limitation) : $0 \leq \int_0^T u(t)dt \leq C$.

Optimization problem

$$\min_{u \in \mathcal{U}_{\bar{U}, C, T}} J(u), \quad \text{with } \mathcal{U}_{\bar{U}, C, T} = \left\{ 0 \leq u \leq \bar{U} \text{ a.e.}, \int_0^T u(t)dt \leq C \right\}.$$

Reduction of the optimal problem

As above, we may try to simplify the system by using the large fertility asymptotics, $\varepsilon \ll 1$,

$$\begin{cases} \frac{d}{dt}n_i &= (1 - s_f) \frac{F_u^0}{\varepsilon} n_i \left(1 - \frac{n_i + n_u}{K}\right) - \delta d_u n_i + u, \\ \frac{d}{dt}n_u &= \frac{F_u^0}{\varepsilon} n_u \left(1 - s_h \frac{n_i}{n_i + n_u}\right) \left(1 - \frac{n_i + n_u}{K}\right) - d_u n_u. \end{cases}$$

As above, when $\varepsilon \rightarrow 0$, we deduce

$$n_i + n_u = K(1 - \varepsilon n) + o(\varepsilon).$$

Then we may compute the system of equation satisfied by n and the proportion

$$p := \frac{n_i}{n_i + n_u}.$$

Reduction of the optimal problem

As above, by passing to the limit $\varepsilon \rightarrow 0$, the system reduces to

Reduced problem

$$\frac{dp}{dt} = f(p) + ug(p),$$

where

$$f(p) = \frac{\delta d_u}{F_u^0} \frac{p(1-p)(p-\theta)}{(1-p)^2 + (1-s_f)p}, \quad \theta = \frac{s_f + \delta - 1}{\delta},$$
$$g(p) = \frac{1}{K} \frac{(1-p)^2}{(1-p)^2 + (1-s_f)p}.$$

For the cost functional, we have

$$J(u) = \frac{1}{2}((n_i + n_u)(T)(1 - p(T)))^2 + \frac{1}{2}\left(K\left(1 - \varepsilon \frac{d_u \delta}{F_u^0(1 - s_f)}\right) - ((n_i + n_u)(T)p(T))\right)^2.$$

Thus, with the fact that $n_i + n_u \rightarrow K$ in $C^0([0, T])$, we deduce that

$$J(u) \xrightarrow{\varepsilon \rightarrow 0} (K(1 - p(T)))^2.$$

Reduced optimal control problem

Reduced optimization problem

$$\min_{u \in \mathcal{U}_{\bar{U}, C, T}} (1 - p(T))^2,$$

with $\mathcal{U}_{\bar{U}, C, T} = \{0 \leq u \leq \bar{U} \text{ a.e.}, \int_0^T u(t) dt \leq C\}$, where p solves the differential equation

$$\frac{d}{dt}p = f(p) + ug(p), \quad f \text{ bistable}, g > 0 \text{ on } (0, 1), g(1) = 0.$$

Reduction of the optimal problem

As a consequence we may prove the following result:

Theorem (LA, Privat, Strugarek, Vauchelet, SIAM Math. Anal. 2018)

Assume $T > C/M$ and above assumptions on the coefficients.

Then, any solution u^* to the reduced optimal problem satisfies $\int_0^T u^*(t)dt = C$ and is **bang-bang** (i.e. equal a.e. to 0 or \bar{U}).

Moreover, if (u^ε) is a family of minimizers for the optimal problem for the full system. Then, as $\varepsilon \rightarrow 0$, it converges in $L^1(0, T)$ to a solution of the reduced problem. Moreover, we have

$$\lim_{\varepsilon \rightarrow 0} \min_{u \in \mathcal{U}_{\bar{U}, C, T}} J^\varepsilon(u) = \min_{u \in \mathcal{U}_{\bar{U}, C, T}} (1 - p(T))^2.$$

This problem is simpler to study than the full system. Indeed, we observe that when $u = 0$,

- if $0 < p < \theta$, then $\frac{d}{dt}p < 0$;
- if $\theta < p < 1$, then $\frac{d}{dt}p > 0$.

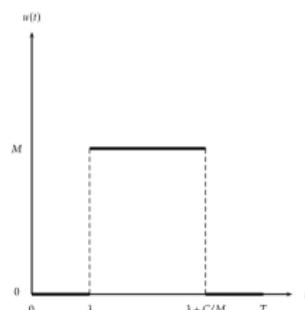
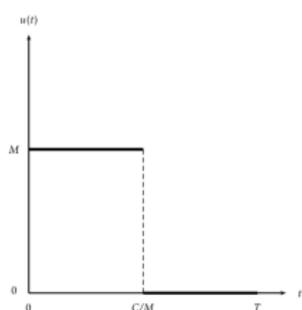
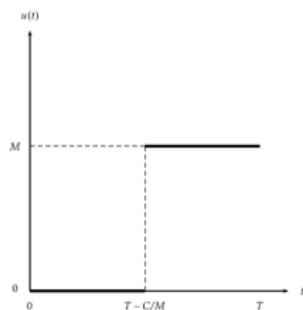
In other words, the basin of attraction of 1 is $(\theta, 1)$, outside this domain, the solution move away from 1. Hence to be optimal one expects the solution to go to this basin of attraction as fast as possible. If the solution cannot reach this basin of attraction, it is better to act at the end of the protocol.

Reduction of the optimal control problem

Actually, we can get a precise description of the optimum:

Theorem (LA, Privat, Strugarek, Vauchelet, SIAM Math. Anal. 2018)

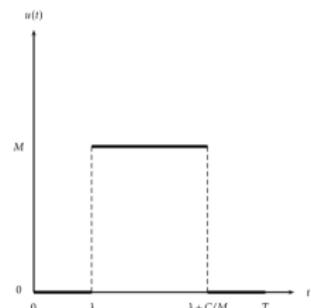
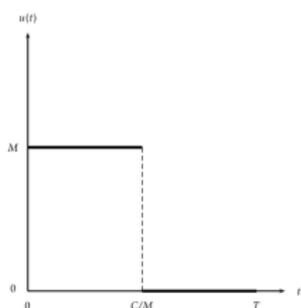
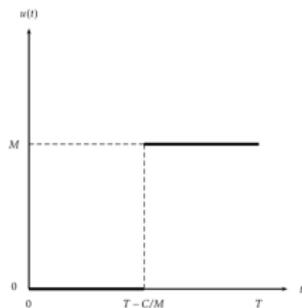
- If $\bar{U} \leq \max_{p \in [0, \theta]} -\frac{f(p)}{g(p)}$ then the unique solution is given by $u^* = \bar{U} \mathbf{1}_{[T-C/\bar{U}, T]}$.
- Otherwise, defining $C^*(\bar{U}) = \int_0^\theta \frac{\bar{U} dp}{f(p) + \bar{U}g(p)}$, one has
 - if $C < C^*(\bar{U})$ then the solution is unique and equal to $u^* = \bar{U} \mathbf{1}_{[T-C/\bar{U}, T]}$;
 - if $C > C^*(\bar{U})$ then the solution is unique and equal to $u^* = \bar{U} \mathbf{1}_{[0, C/\bar{U}]}$;
 - if $C = C^*(\bar{U})$ then there is a continuum of solutions given by $u_\lambda^* = \bar{U} \mathbf{1}_{[\lambda, \lambda+C/\bar{U}]}$ for $\lambda \in [0, T - C/\bar{U}]$.



Reduction of the optimal control problem

Interpretation.

- the best release protocol in the framework of the frequency model consists in a single release phase
- If the amount of mosquitoes available is enough to cross the threshold θ , then it is preferable to make the maximum effort at the beginning of the time protocol. Indeed, p is increasing whenever $p > \theta$, thus it is interesting to cross this threshold as soon as possible
- if the amount of mosquitoes is not enough for p to reach the threshold θ , then $p < \theta$ and p is decreasing when $u = 0$. In this case, the optimum is achieved acting at the end of the time frame to avoid p to decrease



Epidemics: bringing humans and a disease into the picture

$$\begin{aligned}S'_H &= b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H \\E'_H &= \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H \\I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H \\ \\M' &= b_M M \left(1 - \frac{M}{K}\right) - d_M M\end{aligned}$$

Epidemics: bringing humans and a disease into the picture

$$S'_H = b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H$$

$$E'_H = \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H$$

$$I'_H = \gamma_H E_H - \sigma_H I_H - b_H I_H$$

$$S'_M = b_M M \left(1 - \frac{M}{K}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M$$

$$E'_M = \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M$$

$$I'_M = \gamma_M E_M - d_M I_M$$

Epidemics: bringing humans and a disease into the picture

$$S'_H = b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H$$

$$E'_H = \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H$$

$$I'_H = \gamma_H E_H - \sigma_H I_H - b_H I_H$$

$$S'_M = b_M M \left(1 - \frac{M}{K}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M$$

$$E'_M = \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M$$

$$I'_M = \gamma_M E_M - d_M I_M$$

Impulsive control: $u(t) = \sum_{i=1}^n c_i \delta(t - t_i)$ **Constraint:** $\sum_{i=1}^n c_i = C$

Epidemics: bringing humans and a disease into the picture

$$S'_H = b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H$$

$$E'_H = \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H$$

$$I'_H = \gamma_H E_H - \sigma_H I_H - b_H I_H$$

$$S'_M = b_M M \left(1 - \frac{M}{K}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M$$

$$E'_M = \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M$$

$$I'_M = \gamma_M E_M - d_M I_M$$

Impulsive control: $u(t) = \sum_{i=1}^n c_i \delta(t - t_i)$ **Constraint:** $\sum_{i=1}^n c_i = C$

Goal: Minimise $J(u)$ during an outbreak

$$J(u) := \int_0^T I_H(t) dt$$

We add the mosquitoes with Wolbachia:

$$S'_H = b_H H - \frac{\beta_M}{H} I_M S_H - \frac{\beta_{WH}}{H} I_W S_H - b_H S_H$$

$$E'_H = \frac{\beta_M}{H} I_M S_H + \frac{\beta_{WH}}{H} I_W S_H - \gamma_H E_H - b_H E_H$$

$$I'_H = \gamma_H E_H - \sigma I_H - b_H I_H$$

$$S'_M = b_M M \left(1 - \frac{M+W}{K}\right) \left(1 - s_h \frac{W}{M+W}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M$$

$$E'_M = \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M$$

$$I'_M = \gamma_M E_M - d_M I_M$$

$$S'_W = b_W W \left(1 - \frac{M+W}{K}\right) - \frac{\beta_{HW}}{H} S_W I_H - d_W S_W + u$$

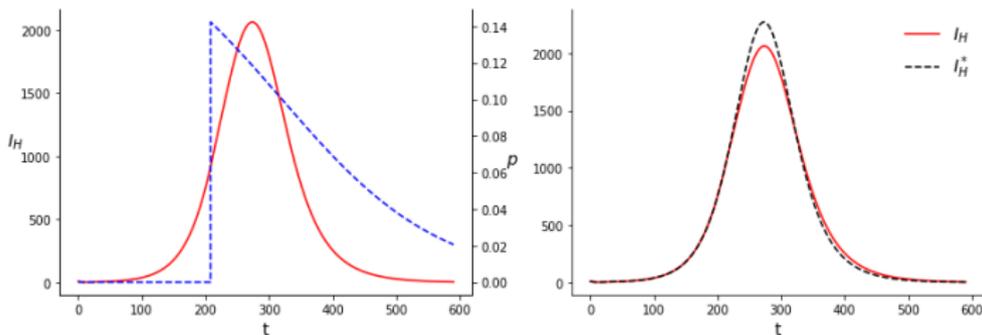
$$E'_W = \frac{\beta_{HW}}{H} S_W I_H - \gamma_W E_W - d_W E_W$$

$$I'_W = \gamma_W E_W - d_W I_W$$

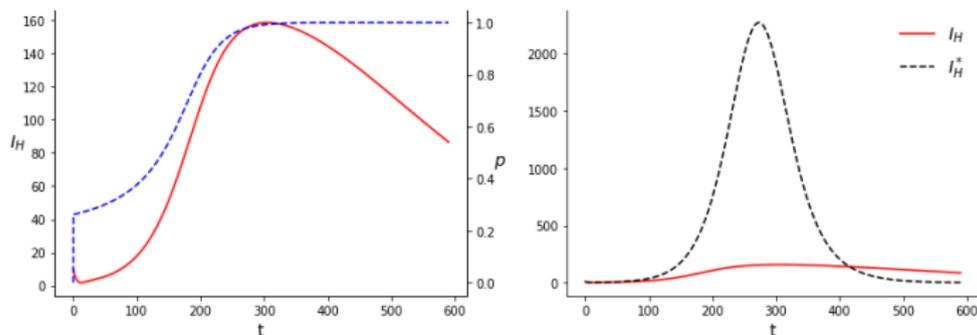
Results: instant releases for Wolbachia

- $C < G(\theta)$: release before the outbreak reaches its peak.
- $C > G(\theta)$: Release at $t = 0$.

$C = 10000$
Reduction:
2.0%



$C = 20000$
Reduction:
80.3%



$G(\theta) \approx 14800$

$$S'_H = b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H$$

$$E'_H = \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H$$

$$I'_H = \gamma_H E_H - \sigma_H I_H - b_H I_H$$

$$S'_M = b_M M \left(1 - \frac{M}{K}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M$$

$$E'_M = \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M$$

$$I'_M = \gamma_M E_M - d_M I_M$$

$$S'_H = b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H$$

$$E'_H = \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H$$

$$I'_H = \gamma_H E_H - \sigma_H I_H - b_H I_H$$

$$S'_M = b_M M \left(1 - \frac{M}{K}\right) \frac{M}{M + s_c M_S} - \frac{\beta_M}{H} S_M I_H - d_M S_M$$

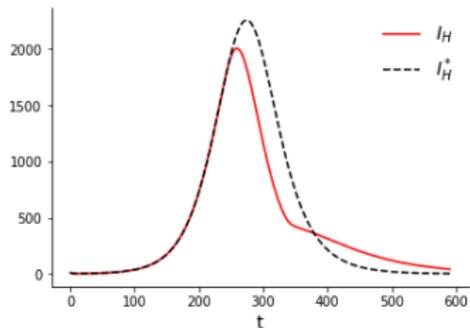
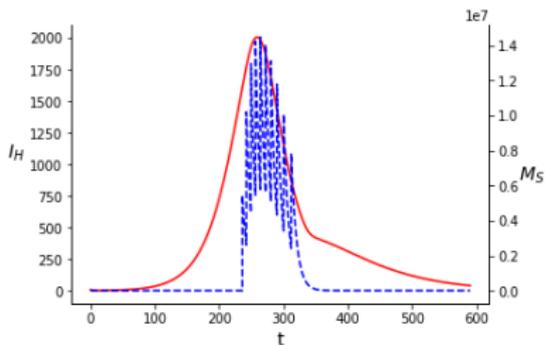
$$E'_M = \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M$$

$$I'_M = \gamma_M E_M - d_M I_M$$

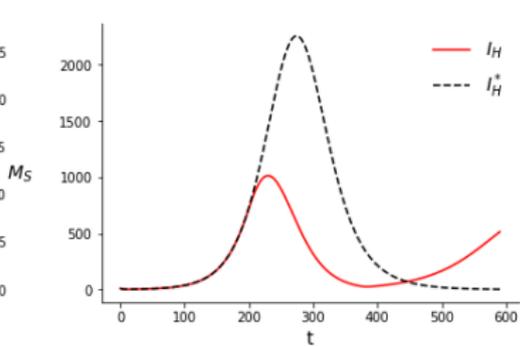
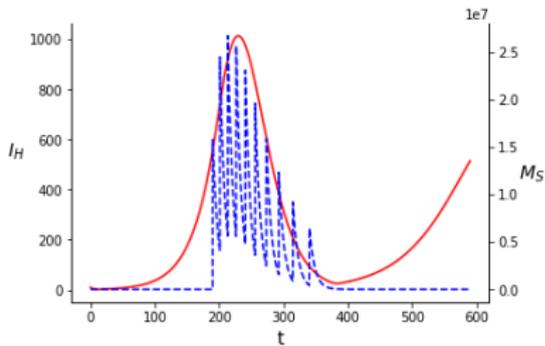
$$M'_S = u - d_S M_S$$

Results: 10 instant releases

$C = 7.5 \cdot 10^7$
Reduction:
12.3%

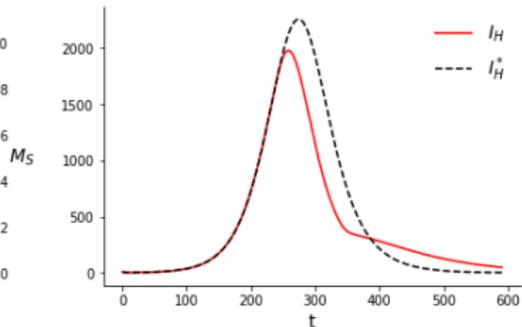
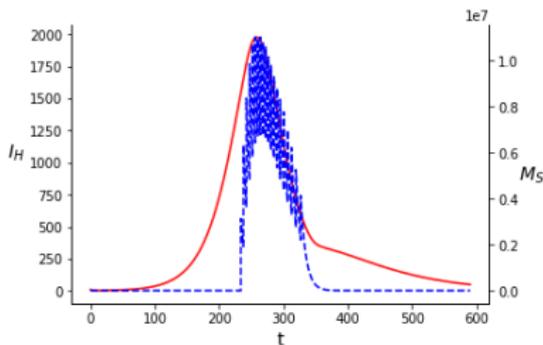


$C = 1.5 \cdot 10^8$
Reduction:
49.1%

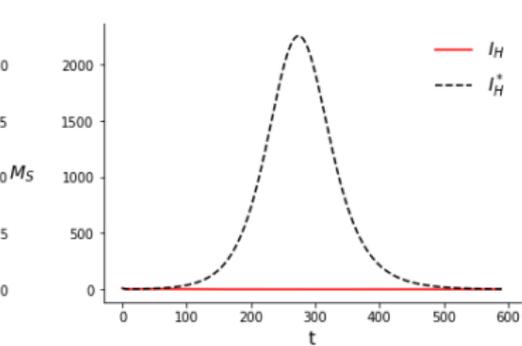
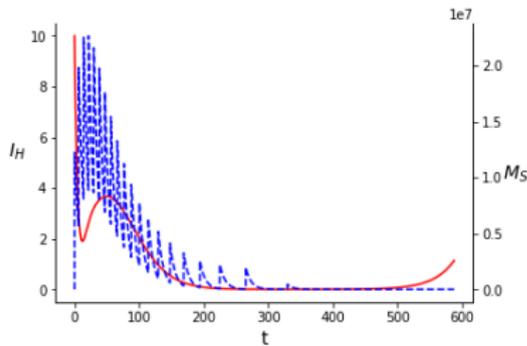


Results: 20 instant releases

$C = 7.5 \cdot 10^7$
Reduction:
13.9%



$C = 1.5 \cdot 10^8$
Reduction:
99.9%



Conclusions for the epidemic model

- Wolbachia:
 - Optimal strategy: One single release
 - If we have enough mosquitoes to trigger a population replacement: release as soon as possible.
 - If we don't have enough: release before the peak of the outbreak.

Conclusions for the epidemic model

- Wolbachia:
 - Optimal strategy: One single release
 - If we have enough mosquitoes to trigger a population replacement: release as soon as possible.
 - If we don't have enough: release before the peak of the outbreak.
- Sterile mosquito:
 - Strategy and results depend highly on the number of releases considered (when low).
 - After ~ 20 releases almost no improvement.
 - With few mosquitoes: spaced releases around the peak.
 - With a lot of mosquitoes: spaced releases from the beginning.

The real map since 50 B.C. !)



The real map since 50 B.C. !)

