Models of mosquito population control strategies for fighting against arboviruses

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FSMP Fondation Sciences Mathématiques de Paris

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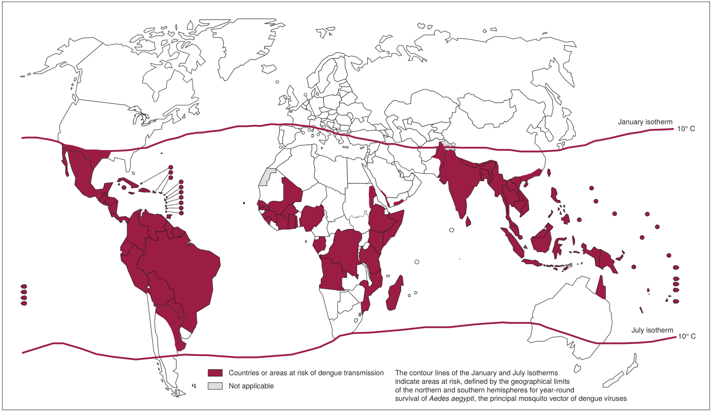
Some fact about the Dengue fever

- Dengue is a tropical vector-borne disease (4 different serotypes)
- Infect >100M, kills 20k annually
- No efficient vaccine
  (up to Dengvaxia : dangerous for seronegative)

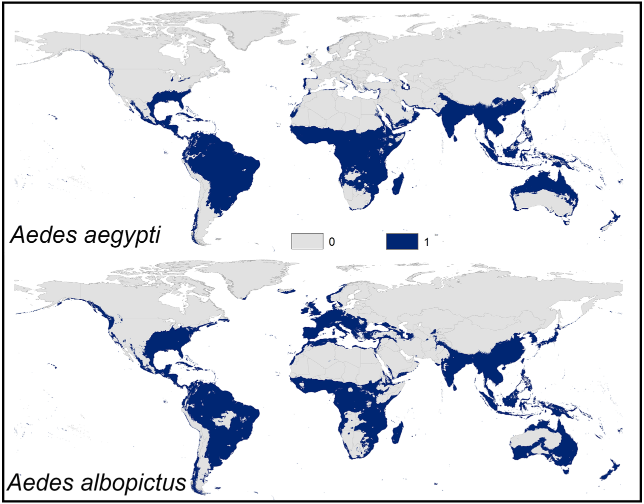


Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

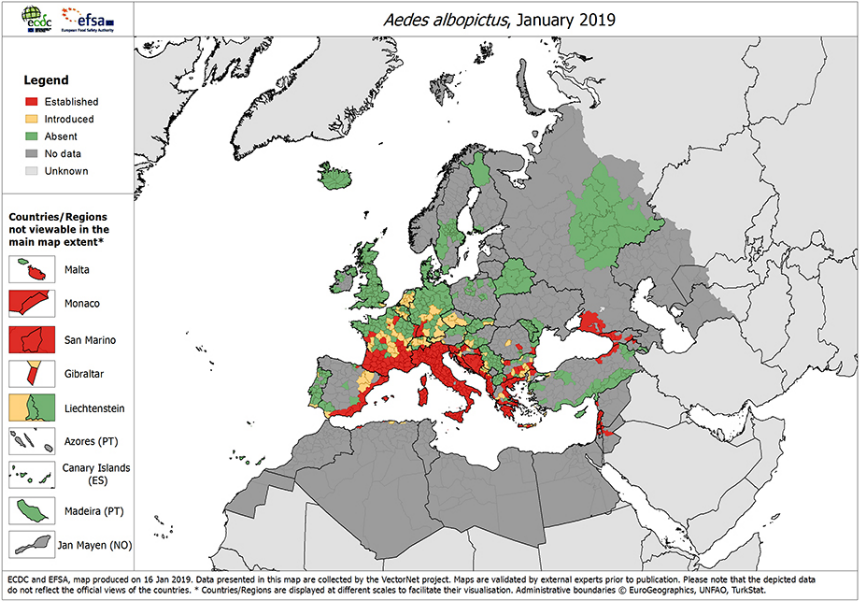
Propagation of the Aedes Aegypti and Aedes Albopictus

The mosquitoes Aedes Aegypti and Aedes Albopictus are the main vectors of dengue fever (also of Chikugunya and Zika).

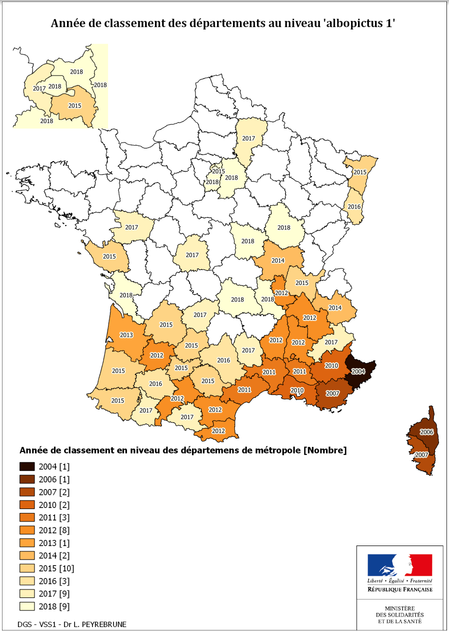


[Kamal et al, *PLOS One*, 2018]

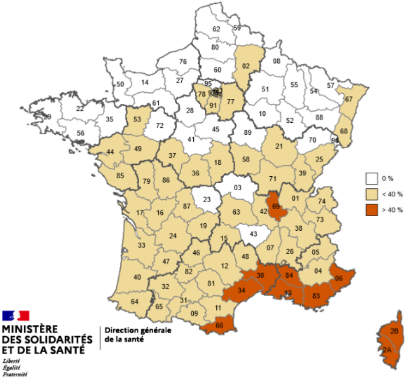
Main vector : Aedes mosquitoes in Europa in 2019



Main vector : Aedes Albopictus in France



Pourcentage de communes colonisées par *Aedes albopictus* des départements en France métropolitaine au 1er janvier 2021



Main vector : Aedes mosquitoes

- More than **100 species**. Major arbovirus vectors :
  → Aedes aegypti (tropical region)
  → Aedes alpopictus (more resistants to low temperature)
- Its life cycle is divided into **two phases** :
  → Aquatic phases (egg, larva,pupa)
  → Aerial phases (adult)
- Female during her life ($\approx$ 1 month) : Several ovipositions of 40-80 eggs
  → **Hatching** : after fews days or several months
- Only **females** suck bloods
  → Preferentially from humans
  → Used to maturate their eggs
- Adults can fly with a **dispersion** of less than 1 km during its lifetime.

Fight against arboviruses

In absence of vaccine or curative treatment, acting on the population of mosquitoes Aedes is essentially the only feasible control method :

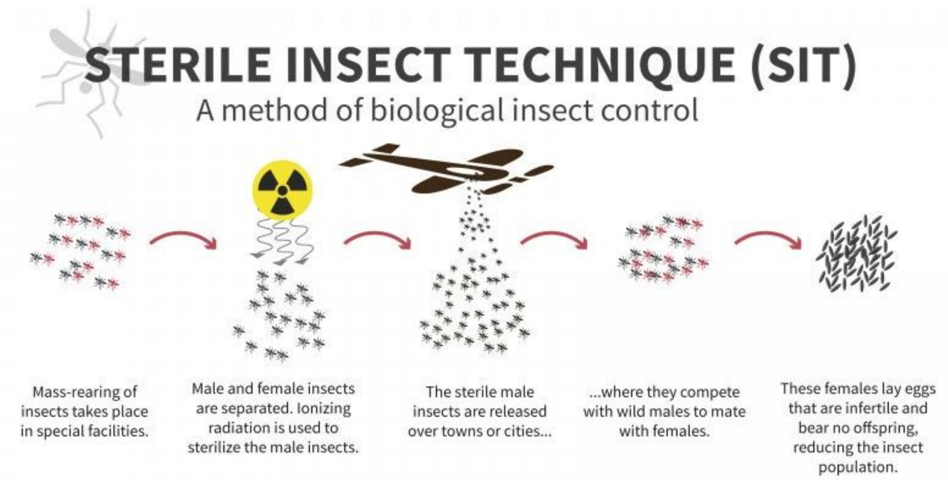
- Mechanical remove of breeding sites.
  - → Difficult to implement to have good efficiency
- Application of insecticides.
  - → Increase of moquito resistance
  - → Negative impact on the environment
- **Sterile insect techniques**
  - → Releases of sterilized (or incompatible) males
- **Population replacement strategies**
  - → Wolbachia bacterium

The two latter techniques have been studied by the HCB (High Council for Biotechnology) in June 2017.

Outline

1. **Introduction**
2. **Sterile Insect Techniques (SIT) : optimal continuous strategy**
3. **Sterile Insect Techniques (SIT) : optimal impulsive strategy**
4. **Replacement strategy : Wolbachia bacterium**
5. **Conclusions and perspectives**

SIT : Sterile Insect Technique



Some mathematical references

Bliman-Cardona-Salgado-Dumont-Vasilieva ’19 (feedback)

Dumont-Bossin-Strugarek ’19 (constant controls)

Releases

Continuous strategy for SIT : objectives

Model of the mosquitoes population : which **complexity** ?

How to **model the optimal control problem** ?

Can we extract mathematical **properties of the optimizers** ?

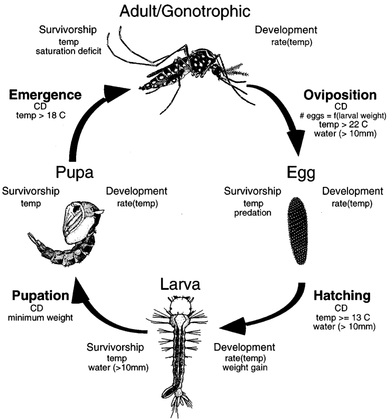
Can we deduce an efficient **numerical scheme** ?

[Almeida-D.-Privat-Vauchelet, *submitted*]

$$\begin{cases} E' = \beta_E F\left(1 - \dfrac{E}{K}\right) - (\nu_E + \delta_E)E, \\ M' = (1-\nu)\nu_E E - \delta_M M, \\ F' = \nu\nu_E E - \delta_F F. \end{cases}$$

where

- E : **eggs, larvae, pupa** density
  - $\rightarrow$ eggs : few days to several months
  - $\rightarrow$ larvae : 3 days to several weeks
  - $\rightarrow$ pupa : 1-3 days
- M, F : density of **adult** males/female
  - $\rightarrow$ males : $\approx$ 10 days
  - $\rightarrow$ females : $\approx$ 15-45 days



Continuous strategy for SIT : model

Model

$$
\begin{cases}
E' = \beta_E F \left(1 - \dfrac{E}{K}\right) - (\nu_E + \delta_E) E, \\
M' = (1-\nu)\nu_E E - \delta_M M, \\
F' = \nu \nu_E E \dfrac{M}{M + \gamma_s M_s} - \delta_F F, \\
M_s' = u - \delta_s M_s
\end{cases}
$$

where

- M_s : density of sterile males.
- $\frac{M}{M+\gamma M_s}$: probability that a female mates with a fertile male
- u : release function of non-sterile male mosquitoes.

Proposition [Almeida-Duprez-Privat-Vauchelet, submitted]

Assume that $u = 0$, $\delta_s > \delta_M$ and $\frac{1}{2}\beta_E\beta_F > \delta_F(\tau_E + \delta_E)$.
Then there are two equilibria for system :

- $(0, 0, 0, 0)$ is **unstable**
- $(\bar{E}, \bar{M}, \bar{F}, 0)$ is **linearly asymptotically stable** with

$$\bar{E} = K\left(1 - \frac{\delta_F(\nu_E + \delta_E)}{\beta_E \nu \nu_E}\right), \quad \bar{M} = \frac{(1-\nu)\nu_E}{\delta_M}\bar{E}, \quad \bar{F} = \frac{\nu\nu_E}{\delta_F}\bar{E}.$$

Moreover,

$$\begin{cases} E_0 \in [0, \bar{E}], \\ M_0 \in [0, \bar{M}], \\ F_0 \in [0, \bar{F}], \\ M_{s0} \geqslant 0 \end{cases} \Rightarrow \begin{cases} E(t) \in [0, \bar{E}], \\ M(t) \in [0, \bar{M}], \\ F(t) \in [0, \bar{F}], \\ M_s(t) \geqslant 0 \end{cases} \quad \text{for each } t \in [0, T].$$

Continuous strategy for SIT : Reduction of the model

Assumptions

the time dynamics of the **aquatic and males compartments** are **fast**

Hence

$$\begin{cases} F' = f(F, M_s), \\ M_s' = u - \delta_s M_s, \end{cases}$$

where $f : \mathbb{R}^2 \to \mathbb{R}$ denotes the nonlinear function

$$f(F, M_s)$$
$$= \frac{\nu(1-\nu)\beta_E^2 \nu_E^2 F^2}{\left(\frac{\beta_E F}{K} + \nu_E + \delta_E\right)\left((1-\nu)\nu_E \beta_E F + \delta_M \gamma_s M_s \left(\frac{\beta_E F}{K} + \nu_E + \delta_E\right)\right)} - \delta_F F,$$

Continuous strategy for SIT : equilibria

Proposition [Almeida-Duprez-Privat-Vauchelet, submitted]

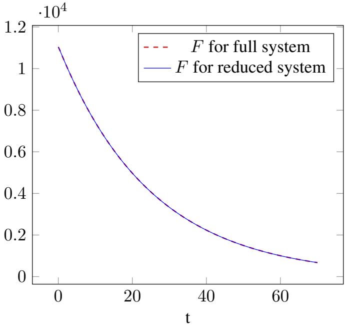
Assume that $u = 0$, $\delta_s > \delta_M$ and $\frac{1}{2}\beta_E\beta_F > \delta_F(\tau_E + \delta_E)$.
Then there are two equilibria for system :

- $(0, 0)$ is **unstable**
- $(\bar{F}, 0)$ is **linearly asymptotically stable** with

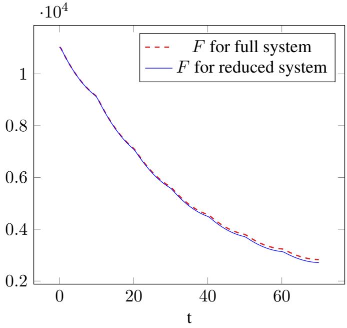
$$\bar{E} = K\left(1 - \frac{\delta_F(\nu_E + \delta_E)}{\beta_E \nu \nu_E}\right), \quad \bar{M} = \frac{(1-\nu)\nu_E}{\delta_M}\bar{E}, \quad \bar{F} = \frac{\nu\nu_E}{\delta_F}\bar{E}.$$

Moreover,

$$\left\{\begin{array}{l} F_0 \in [0, \bar{F}], \\ M_{s0} \geqslant 0 \end{array}\right. \Rightarrow \left\{\begin{array}{l} F(t) \in [0, \bar{F}], \\ M_s(t) \geqslant 0 \end{array}\right. \quad \text{for each } t \in [0, T].$$



$$u(\cdot) = 1.5e4$$



$$u(\cdot) = 2e4 \sum_{k=0}^{6} \mathbb{1}_{[10k,10k+1]}$$

Goals

- Optimize the total number of released sterile mosquitoes over the experiment duration
- Obtain a small density of females at the end of the experiment

Optimization model

$$\inf_{u \in \mathcal{U}_{T,\overline{U},\varepsilon}} \int_0^T u(t)dt,$$

where

$$\mathcal{U}_{T,\bar{U},\varepsilon} := \left\{ u \in L^\infty(0,T) : 0 \leq u \leq \overline{U} \text{ a.e. in } (0,T), F(T) \leqslant \varepsilon \right\}.$$

Remark

$\overline{U}$ is a bound to the instantaneous rate of mosquito release (number of mosquitoes per unit of time)

Continuous strategy for SIT : main results

Optimization model on the reduced system

$$\inf_{u \in \mathcal{U}_{T,\overline{U},\varepsilon}} \int_0^T u(t)dt, \qquad (\mathcal{P})$$

where

$$\mathcal{U}_{T,\bar{U},\varepsilon} := \left\{ u \in L^\infty(0,T) : 0 \leq u \leq \overline{U},\ F(T) \leqslant \varepsilon \right\}.$$

Proposition [Almeida-Duprez-Privat-Vauchelet, submitted]

Under some assumption on the coefficients, for T and $\overline{U}$ large enough, then there exists $t_0, t_1 \in [0,T]$ such that the solutions u^* to problem $\mathcal{P}$ satisfy

- $\boldsymbol{u^* = 0}$ on $(0, t_0)$
- u^* is solution of an **explicite ODE** on (t_0, t_1)
- $\boldsymbol{u^* = 0}$ on (t_1, T) and $t_1 \neq T$

Remark

The infinite dim. problem is reduced to a finite dim. one.

Continuous strategy for SIT : sketch of proof

Dual system :

$$\begin{cases} -\dfrac{d}{dt}\begin{pmatrix} Q \\ R \end{pmatrix} = \begin{pmatrix} \frac{\partial f}{\partial F}(F, M_s) & 0 \\ \frac{\partial f}{\partial M_s}(F, M_s) & -\delta_s \end{pmatrix} \begin{pmatrix} Q \\ R \end{pmatrix}, \\ Q(T) = 1, \ R(T) = 0. \end{cases}$$

Lemma (Pontryagin's maximum principle)

Let $\bar{U} > U^*$ and $T \geqslant \bar{T}(\bar{U})$. Consider u^* a solution to the optimal control reduced problem. Then there exists $\lambda > 0$ such that

$$\begin{cases} \text{a.e. on } \{u^* = 0\}, \text{ one has } 1 + \lambda R(t) \geqslant 0, \\ \text{a.e. on } \{0 < u^* < \overline{U}\}, \text{ one has } 1 + \lambda R(t) = 0, \\ \text{a.e. on } \{u^* = \overline{U}\}, \text{ one has } 1 + \lambda R(t) \leqslant 0. \end{cases}$$

Main idea : We have $Q, \partial^2_{M_s} f > 0$ and

$$-R'' = (\frac{\partial^2 f}{\partial M_s^2} u + \mathcal{G}(F, M_s, Q))Q - \delta_s R'$$

Under some conditions on $\mathcal{G}$, R has no local extremum on $\{u = \overline{U}\}$.
Hence $\{u^* = \overline{U}\} = [0, s_2] \cup [s_3, T]$

Continuous strategy for SIT : sketch of proof

Dual system

$$\begin{cases} -\dfrac{d}{dt}\begin{pmatrix} Q \\ R \end{pmatrix} = \begin{pmatrix} \frac{\partial f}{\partial F}(F, M_s) & 0 \\ \frac{\partial f}{\partial M_s}(F, M_s) & -\delta_s \end{pmatrix} \begin{pmatrix} Q \\ R \end{pmatrix}, \\ Q(T) = 1,\ R(T) = 0. \end{cases}$$

Explicite ODE

Hence, $\{R = -1/\lambda\} = \{0 < u < \overline{U}\} = (t_0, t_1)$. The equation of R gives

$$\left(\frac{\partial^2 f}{\partial M_s \partial F} f + \frac{\partial^2 f}{\partial M_s^2}(u - \delta_s M_s) \right) Q = \frac{\partial f}{\partial M_s} \frac{\partial f}{\partial F} Q.$$

We deduce that

$$u = \left(\frac{\partial^2 f}{\partial M_s^2} \right)^{-1} \left(\frac{\partial f}{\partial M_s} \frac{\partial f}{\partial F} + \frac{\partial^2 f}{\partial M_s^2} \delta_s M_s - \frac{\partial^2 f}{\partial M_s \partial F} f \right),$$

on (t_0, t_1).

$\square$

Continuous strategy for SIT : numerical algorithms

$$\begin{cases} \dfrac{d}{dt}\begin{pmatrix} F^{\tau_1} \\ M_s^{\tau_1} \end{pmatrix} = \begin{pmatrix} f(F^{\tau_1}, M_s^{\tau_1}) \\ u_{\tau_1} - \delta_s M_s \end{pmatrix} \quad \text{in } [0,+\infty), \; F^{\tau_1}(0) = \bar{F}, \; M_s^{\tau_1}(0) = 0 \\ \text{with } u_{\tau_1} = \dfrac{\frac{\partial f}{\partial M_s}(F,M_s)\frac{\partial f}{\partial F}(F,M_s) + \frac{\partial^2 f}{\partial M_s^2}(F,M_s)\delta_s M_s - \frac{\partial^2 f}{\partial M_s \partial F}(F,M_s) f(F,M_s)}{\frac{\partial^2 f}{\partial M_s^2}(F,M_s)} \mathbb{1}_{(0,\tau_1)}, \end{cases}$$

Assumptions

Let $\bar{U}$, T large enough and ε small enough. Then

- $\forall\, \tau_1 \in [0,T)$, $\exists! \tau_2(\tau_1) > \tau_1$ s.t. F^{τ_1} is first strictly decreasing on $(0, \tau_2(\tau_1))$, and then strictly increasing on $(\tau_2(\tau_1), +\infty)$.
- the following value function is decreasing

$$\psi : \tau_1 \in [0,T) \mapsto \min_{t\in[0,\infty]} F^{\tau_1}(t) = F^{\tau_1}(\tau_2(\tau_1))$$

- the optimal control u^* solving the initial reduced Problem satisfies

$$u^*(t) = \begin{cases} 0 & \text{if } t \in (0, T - \tau_2(\tau_1)), \\ u^{\tau_1}(t - T + \tau_2(\tau_1)) & \text{otherwise} \end{cases} \quad (1)$$

on $(0,T)$, where τ_1 is the unique solution on $[0,T)$ to $\psi(\tau_1) = \varepsilon$.

Three algorithms :

- Optimisation on the full system

$$\begin{cases} E' = \beta_E F \left(1 - \frac{E}{K}\right) - (\nu_E + \delta_E) E, \\ M' = (1-\nu)\nu_E E - \delta_M M, \\ F' = \nu \nu_E E \frac{M}{M + \gamma_s M_s} - \delta_F F, \\ M_s' = u - \delta_s M_s \end{cases}$$

- Optimisation on the reduced system

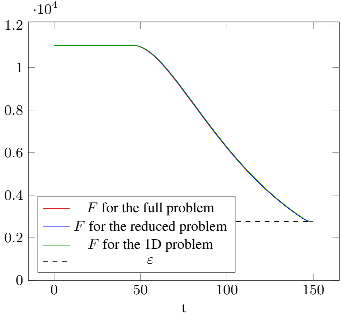
$$\begin{cases} F' = f(F, M_s), \\ M_s' = u - \delta_s M_s, \end{cases}$$

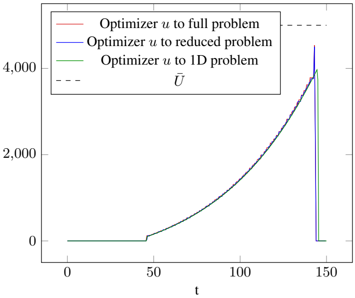
- Dichotomy on the 1D equation $\psi(\tau_1) = \varepsilon$.

Continuous strategy for SIT : numerical simulation

Parameter	*Name*	*Value interval*	*Chosen value*
δ_E	Mosquitoes in Aquatic phase death rate	0.023 - 0.046	0.03
δ_F	Female death rate	0.033 - 0.046	0.04
γ	Preference for the sterile male	(0,1)	1
b	Birth rate	7.46 - 14.85	10
δ_s	Sterile male death rate	0.12	0.12
τ_E	Emergence rate	0.001 - 0.25	0.05
K	Environment capacity		5172

Values of [Strugarek-Bossin-Dumont, *AMM*, 2019]





$$T = 150, \overline{U} = 5000, \nu_E = 0.05, \text{ and } \varepsilon = \bar{F}/4.$$

Continuous strategy for SIT : computation time

Computing Time (CT) in sec. $(\nu_E = 0.05, \varepsilon = \bar{F}/4, \bar{F} = 11037)$

Time discr.	100	200	400	800	1600	3200
CT for full problem	8.11	2.56e1	1.86e2	3.83e4	X	X
CT for reduced problem	6.00	2.94e1	1.13e2	7.37e2	3.53e4	X
CT for 1D problem	6.74e-1	1.44	2.73	5.45	11.7	2.24e1

(Optimization library : Gekko with python)

Remark : The theoretical results lead to a **fast numerical scheme**.

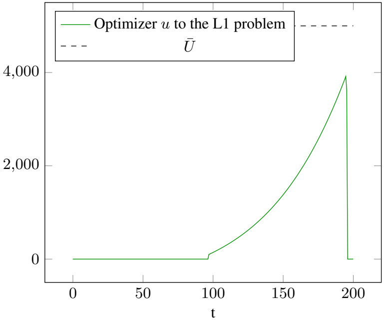
Continuous strategy for SIT : numerical simulation

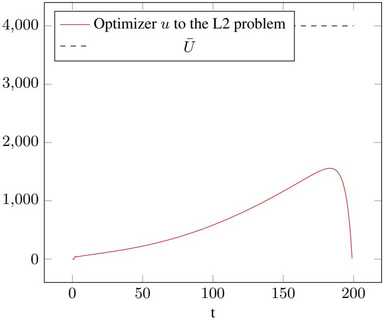
$$J(u) = \int_0^T u(t)dt,$$

$$\begin{cases} 0 \leqslant u \leqslant \overline{U}, \\ F(T) \leqslant \varepsilon, \end{cases}$$

$$J(u) = \int_0^T u^2(t)dt,$$

$$\begin{cases} 0 \leqslant u \leqslant \overline{U}, \\ F(T) \leqslant \varepsilon, \end{cases}$$





Remark : The functional has **strong influence** on the optimal strategy

Outline

Impulsive strategy for SIT : model

Biological questions :

What is the best time in the year to **begin the releases** ?

What is the influence of the **mechanical control** ?

What is the influence of the **residual fertility** ?

Impulsive strategy for SIT : model

Model :

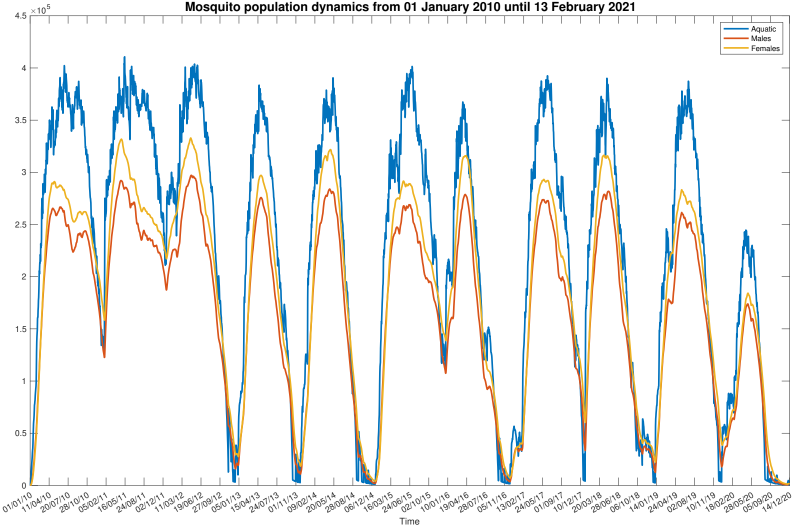
$$
\begin{cases}
A' &= \phi(T)F - \left(\gamma(T) + \mu_{1,A}(T) + \mu_{A,2}(T, Rain)A\right) A,\\
M' &= (1 - r(T))\gamma(T)A - \mu_M(T)M,\\
F' &= r(T)\gamma(T)\dfrac{M + \varepsilon\beta M_S}{M + \beta M_S}A - \mu_F(T)F,\\
M_s' &= u(t) - \mu_s(T)M_s
\end{cases}
$$

where

- $T(t)$: temperature at time t
- $Rain(t))$: rainfall at time t

Parameters : *Aedes albopictus* population in **La Réunion island** [Dumont-Duprez in prep.]

Dynamic of the system :



Impulsive strategy for SIT : control

Large/small impulsive control :

$$u(t) = \tau\Lambda_{\text{large}} \sum_{i=0}^{N} \delta_{t_0+i\tau}(t) + \tau\Lambda_{\text{small}} \sum_{i=N+1}^{\infty} \delta_{t_0+i\tau}(t),$$

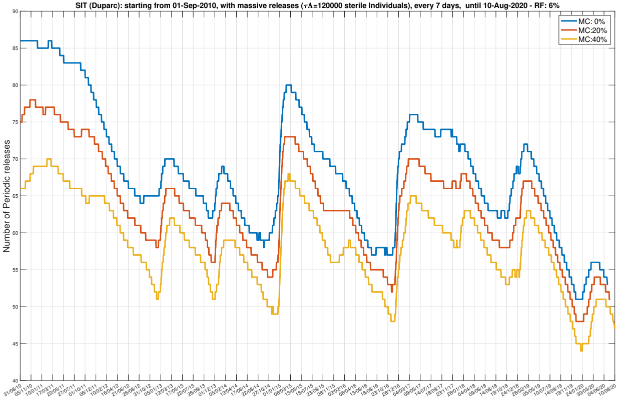
where

- t_0 is the starting time of the massive releases : **control**
- τ the periodicity of the releases (here, $\tau = 7$),
- N the number of weakly massive releases.

For a given t_0 there exists a $t_0 + N_1(t_0)\tau$ such that, after this time, (A, M, F) remains "small".

Gaol : **minimize** the number of large releases N

Optimal number of releases for a beginning between 2010 and 2020



From simulations, best beginning for the releases : July to Nov.

Best biological beginning for the releases : June to Sept.

Impulsive strategy for SIT : control

Constant coefficients : RF : residual fertility, MC : mechanical control

RF=0.6	6000 Ind/ha	12000 Ind/ha
0% of MC	74	63
20% of MC	69	61
40% of MC	64	58

RF=1.2	6000 Ind/ha	12000 Ind/ha
0% of MC	170	156
20% of MC	163	152
40% of MC	156	148

Non-constant coefficients :

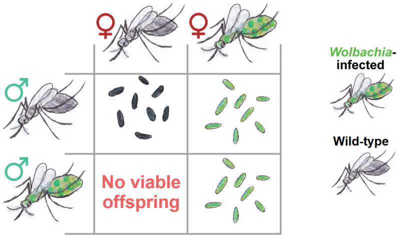
RF=0.6	6000 Ind/ha	12000 Ind/ha
0% of MC	70	61
20% of MC	65	58
40% of MC	60	55

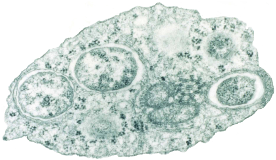
RF=1.2	6000 Ind/ha	12000 Ind/ha
0% of MC	164	152
20% of MC	157	148
40% of MC	150	143

Outline

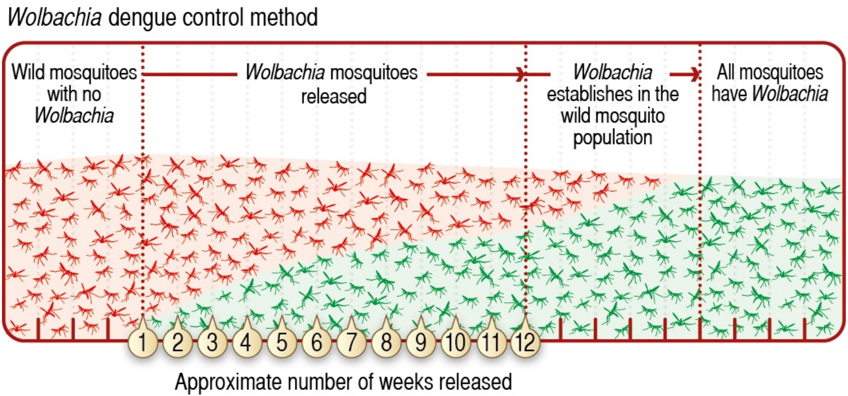
The bacterium Wolbachia

- Common in arthropods, not in Aedes
- Vector competence suppression for key pathogens
  → dengue, zika, chikungunya viruses...
- Typically reduces fecundity and life-span (fitness cost)
- **Cytoplasmic incompatibility** (CI)





Population replacement : Strategy



Some mathematical references

Strugarek-Vauchelet 16', Nadin-Strugarek-Vauchelet 17',
Strugarek-Vauchelet-Zubelli 18', Almaida-Privat-Strugarek-Vauchelet 19'

Population replacement : direct model

Space-time model

$$\begin{cases} \dfrac{d}{dt}F_u - \boldsymbol{\Delta F_u} = \beta_u F_u \left(1 - s_h \dfrac{\boldsymbol{F_i}}{\boldsymbol{F_u + F_i}}\right)\left(1 - \dfrac{F_u + F_i}{K}\right) - \delta_u F_u & \text{in } \Omega \times (0,T), \\ \dfrac{d}{dt}F_i - \boldsymbol{\Delta F_i} = \beta_i F_i \left(1 - \dfrac{F_u + F_i}{K}\right) - \delta_i F_i + \boldsymbol{u} & \text{on } \Omega \times (0,T), \\ \partial_\nu F_i = \partial_\nu F_u = 0 & \text{on } \partial\Omega \times (0,T) \end{cases}$$

where

- F_i : females infected by *Wolbachia*
- F_u : females uninfected
- $\frac{F_i}{F_u+F_i}$: probability for a female to mate with an infected male is equal to the proportion of infected males
- s_h : fraction of uninfected females eggs fertilized by infected males which will not hatch.

  $\longrightarrow$ **cytoplasmic incompatibility**

Population replacement : Steady states

The steady states for the associated ODE model :

Proposition

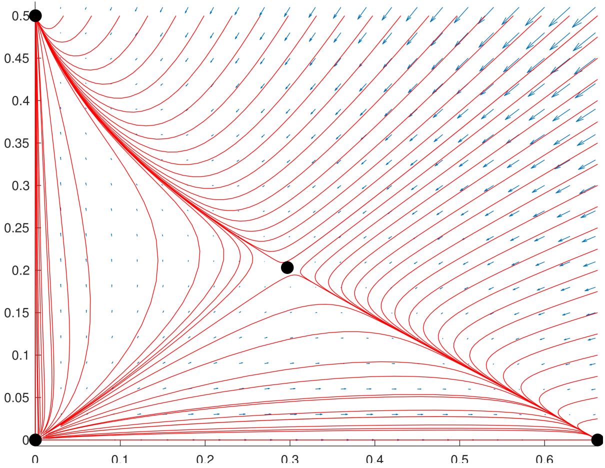
If $S_h > 1 - \delta_u\beta_i/(\delta_i\beta_u)$, then there are four distinct nonnegative equilibria :

- **Wolbachia invasion** $(F_{i1}^*, F_{u1}^*) := (K - \delta_i/\beta_i, 0)$ is stable
- **Wolbachia extinction** $(F_{i2}^*, F_{u2}^*) := (0, K - \delta_u/\beta_u)$ is stable
- **Co-existence** state (F_{i3}^*, F_{u3}^*) is unstable with

$$\begin{cases} F_{i3}^* = (K - \frac{\delta_i}{\beta_i})\frac{1-\delta_u\beta_i/(\delta_i\beta_u)}{s_h}, \\ F_{u3}^* = (K - \frac{\delta_i}{\beta_i})\frac{s_h-1+\delta_u\beta_i/(\delta_i\beta_u)}{s_h} \end{cases}$$

- **Extinction** $(0, 0)$ is unstable

Population replacement : Phase portrait



Assumption

The birth rate is high : $\beta_u = \frac{\beta_u^0}{\varepsilon}$ and $\beta_i = \frac{\beta_i^0}{\varepsilon}$

Simplified model

$$\begin{cases} \frac{d}{dt}F_{u,\varepsilon} - \Delta F_{u,\varepsilon} = \frac{\beta_u^0}{\varepsilon} F_{u,\varepsilon}\left(1 - s_h \frac{F_{i,\varepsilon}}{F_{u,\varepsilon} + F_{i,\varepsilon}}\right)\left(1 - \frac{F_{u,\varepsilon} + F_{i,\varepsilon}}{K}\right) - \delta_u F_{u,\varepsilon}, \\ \frac{d}{dt}F_{i,\varepsilon} - \Delta F_{i,\varepsilon} = \frac{\beta_i^0}{\varepsilon} F_{i,\varepsilon}\left(1 - \frac{F_{u,\varepsilon} + F_{i,\varepsilon}}{K}\right) - \delta_i F_{i,\varepsilon} + \boldsymbol{u}, \end{cases}$$

If $u = 0$, then $F_\varepsilon = \frac{K}{\varepsilon} - F_{i,\varepsilon} - F_{u,\varepsilon}$ and $p_\varepsilon = \frac{F_{i,\varepsilon}}{F_{u,\varepsilon} + F_{i,\varepsilon}}$ are solution to

$$\begin{cases} \partial_t p_\varepsilon - \Delta p_\varepsilon + 2\varepsilon \frac{\nabla F_\varepsilon}{K - \varepsilon F_\varepsilon} . \nabla p_\varepsilon = p_\varepsilon (1 - p_\varepsilon)(G_i(F_\varepsilon, p_\varepsilon) - G_u(F_\varepsilon, p_\varepsilon)) \\ \partial_t F_\varepsilon - \Delta F_\varepsilon = -\left(\frac{K}{\varepsilon} - F_\varepsilon\right)\left[(1 - p_\varepsilon)\, G_u(F_\varepsilon, p_\varepsilon) + p_\varepsilon G_i(F_\varepsilon, p_\varepsilon)\right] \end{cases}$$

where $G_u(F,p) = \beta_u^0 (1 - s_h p)\frac{F}{K} - \delta_u$ and $G_i(F,p) = \beta_i^0 \frac{F}{K} - \delta_i$,

Population replacement : Reduction

Proposition [Duprez-Helie-Privat-Vauchelet, COCV 2021]

When ε goes to zero, the proportion of infected female $p := p_0 = \frac{F_{i,0}}{F_{u,0}+F_{i,0}}$ is solution to

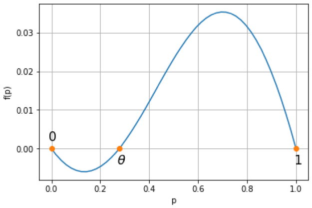
$$\begin{cases} \partial_t p - \Delta p = f(p) + u\, g(p) & \text{in } \Omega \times (0,T), \\ \partial_\nu p = 0 & \text{on } \partial\Omega \times (0,T), \\ p(0) = 0 & \text{in } \Omega, \end{cases}$$

where

$$f(p) = p(1-p)\frac{\delta_u \beta_i^0 - \delta_i \beta_u^0 (1 - s_h p)}{\beta_u^0 (1-p)(1-s_h p) + \beta_i^0 p} \text{ et } g(p) = \frac{1}{K}\frac{\beta_u^0(1-p)(1-s_h p)}{\beta_u^0 (1-p)(1-s_h p) + \beta_i^0 p}.$$

Property

The function f is bistable.



Population replacement : optimization problem and main result

Optimization problem

$$\inf_{v \in \mathcal{U}_{T,C,\overline{U}}} \frac{1}{2} \int_{\Omega} (1 - p(T,x))^2 dx \qquad (\mathcal{P})$$

where

$$\mathcal{U}_{T,C,\overline{U}} = \left\{ \mathbf{u}(\mathbf{t},\mathbf{x}) = \delta_0(\mathbf{t})\mathbf{u_0}(\mathbf{x}) \;\middle|\; 0 \leq u_0 \leq \overline{U} \text{ and } \int_{\Omega} u_0(x)dx \leq C \right\}$$

Theorem [Duprez-Helie-Privat-Vauchelet, COCV 2021]

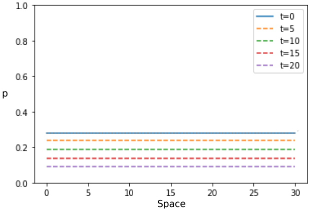
It holds

- Problem $(\mathcal{P})$ admits (at least) a solution.
- If $\overline{U} \leq C/|\Omega|$, then $u^* = M$ satisfy the **optimality conditions of first and second order**.
- If $\overline{U} > C/|\Omega|$ and $C/|\Omega| \leq \theta \leq z$ with z the solution to $f''(z) = 0$, then $u^* = C/|\Omega|$ satisfy the **optimality conditions of first and second order**.

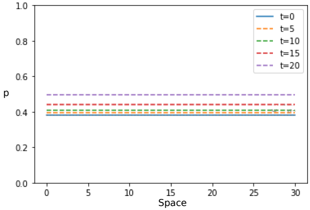
Parameters

$$\Omega = (0,30),\, T = 20,\, D = 1,\, u \in [0, \overline{U}],\, \int u \in [0, C]$$

Local mimimums $\overline{U} \leq C/|\Omega|$



$\overline{U} = 0.02$, C=1.2 : J(u)=12.387, extinction



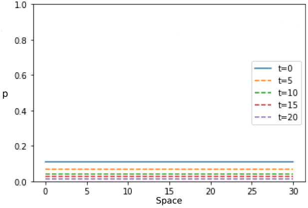
$\overline{U} = 0.03$, C=1.2 : J(u)=0.857, invasion

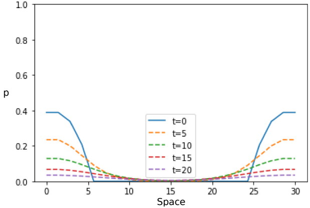
Population replacement : Simulations

Parameters

$\Omega = (0,30)$, $T = 20$, $D = 1$, $u \in [0, \overline{U}]$, $\int u \in [0, C]$

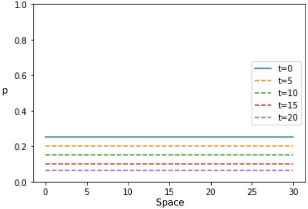
Local mimimums $\overline{U} > C/|\Omega|$ (left : gradient method, right : interior point)

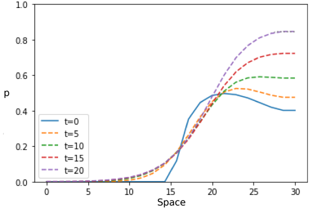




$\overline{U} = 0.2$, C=0.2 : J(u)=14.582, extinction

$\overline{U} = 0.2$, C=0.2 : J(u)=14.424, extinction





$\overline{U} = 0.2$, C=0.5 : J(u)=13.120, extinction

$\overline{U} = 0.2$, C=0.5 : J(u)=8.813, invasion

Outline

Conclusions for TIS with a continuous optimal strategy

- Mathematical description of the optimizer
- Reduction to a finite dim. problem → Fast numerical scheme

Conclusions for TIS with impulsive controls

- Time dependence of the temperature and the rainfall : key role
- The residual fertility has an important impact
- Combining Mechanical control with SIT is recommended
- Beginning of the release : July to November

Conclusions for Wolbachia

The constant in space are good candidates

Perspectives

Take into account the spacial aspect for TIS

Thank you for your attention
and the organization of this workshop !