Mathematical modeling of control techniques for vector borne diseases and their epidemics

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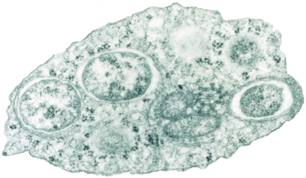
Introduction

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 offsprings.
- 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, ...).



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

Introduction

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

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

Model

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

Outline of lecture 2

1. Reaction-diffusion equations
   - Some mathematical properties for parabolic problems
   - Notion of traveling waves
   - Main results
2. Spatial propagation of Wolbachia
   - Mathematical properties for the reaction-diffusion system
   - Reduction of the system for Wolbachia
   - Spatial spread of Wolbachia
3. Initialisation of the propagation
   - Propagule
   - Application to *Wolbachia* introduction
4. Blocking waves
   - Modelling
   - Blocking waves

PDE model for population dynamics

Let us denote $n(t,x)$ the density of a species at time t, position $x \in \mathbb{R}^d$. We assume that the species move randomly according to Brownian motions. We denote by $B(t,x)$ and $D(t,x)$ respectively the birth and death rate. The system governing the dynamics of the population n reads

$$\partial_t n(t,x) \underbrace{-A(x)\,\Delta n(t,x)}_{\text{Brownian motion}} = \underbrace{B(t,x)n(t,x) - D(t,x)n(t,x)}_{\text{birth and death}}.$$

The quantity $A(x) > 0$ is the diffusion coefficient.

Outline of lecture 2

Second order parabolic equations

Let $\Omega \subset \mathbb{R}^d$, $T > 0$, $Q = (0,T) \times \Omega$. We consider the *second order partial differential operator*

$$Pu = \partial_t u - \sum_{i,j=1}^{d} a_{ij}(t,x) \frac{\partial^2 u}{\partial x_i \partial x_j} - \sum_{i=1}^{d} b_i(t,x) \frac{\partial u}{\partial x_i} - c(t,x)u,$$

where a_{ij}, b_i, c are continuous on $\overline{Q}$, bounded, $a_{ij} = a_{ji}$, and such that

Ellipticity

$$\exists\, \nu_0 > 0, \quad \sum_{i,j=1}^{d} a_{ij}\xi_i\xi_j \geq \nu_0 |\xi|^2, \quad \forall\, \xi \in \mathbb{R}^d, (t,x) \in Q.$$

Examples :

- $\partial_t u - \Delta u = f$ (Heat equation).
- $\partial_t u - \Delta u + \mathrm{div}(bu) = 0$ (Drift-diffusion/Fokker-Planck).
- $\partial_t u - \mathrm{div}(A(x)\nabla u) - b(x) \cdot \nabla u - c(x)u = 0$ with A symmetric, positive definite with eigenvalues bounded from below by ν_0.

Second order parabolic equations

From now on, we will always denote by P a parabolic second order partial differential operator

$$Pu = \partial_t u - \sum_{i,j=1}^{d} a_{ij}(t,x)\frac{\partial^2 u}{\partial x_i \partial x_j} - \sum_{i=1}^{d} b_i(t,x)\frac{\partial u}{\partial x_i} - c(t,x)u.$$

For $\Omega \subset \mathbb{R}^d$, we consider the Cauchy problem

$$\begin{aligned} Pu(t,x) &= f(t,x), && \text{in } Q, \\ u(0,x) &= u_0(x), && \forall\, x \in \Omega, \\ u(t,x) &= g(t,x), && \forall\, t \in (0,T), x \in \partial\Omega. \end{aligned}$$

We will not consider the theory of existence of solution and assume that such problem admits a solution. We will review briefly some important properties of such solutions.

Maximum principle for parabolic equations

Weak maximum principle (corollary)

Let $\Omega \subset \mathbb{R}^d$ be bounded and u a function in C^1 in t and C^2 in x on $Q = (0,T) \times \Omega$, continuous on $\overline{Q}$, such that u is a solution to

$$\begin{aligned} Pu &\geq 0, \qquad \text{on } Q, \\ u &\geq 0, \qquad \text{on } \partial_P Q = (\{0\} \times \overline{\Omega}) \cup ([0,T] \times \partial\Omega). \end{aligned}$$

Then $u \geq 0$ on Q.

Idea of the proof (in the case $Pu > 0$). Let (t_0, x_0) such that $u(t_0, x_0) = \min_{\overline{Q}} u$.

- If $(t_0, x_0) \in \partial_P Q$, then by assumption $u(t_0, x_0) \geq 0$.
- If $(t_0, x_0) \notin \partial_P Q$, we have $\nabla u(t_0, x_0) = 0$, $D^2_{xx} u(t_0, x_0) \geq 0$ and $\partial_t u(t_0, x_0) \leq 0$. Thus $0 \leq Pu(t_0, x_0) \leq -cu(t_0, x_0)$. Then, if $c \leq 0$, $u(t_0, x_0) \geq 0$ and the proof is done. If $c > 0$, we set $u = e^{-\|c\|_\infty t} v$, then we have $Pu = Pv - \|c\|_\infty v = \tilde{P} v$. Since $c - \|c\|_\infty \leq 0$, we may apply the result in the case $c \leq 0$ to the operator $\tilde{P}$. It implies $v \geq 0 \Rightarrow u \geq 0$.

Maximum principle for parabolic equations

Uniqueness for the Cauchy problem

When it exists, the solution to the following problem is unique

$$
\begin{aligned}
Pu = f(t,x), &\qquad \text{in } Q, \\
u(0,x) = u_0(x), &\qquad \forall\, x \in \Omega, \\
u(t,x) = g(t,x), &\qquad \forall\, t \in (0,T), x \in \partial\Omega.
\end{aligned}
$$

Proof. It is an easy consequence of the weak maximum principle. Indeed, if we have two solution u_1 and u_2. Using the above result for $u_1 - u_2$ we deduce $u_1 - u_2 \geq 0$. Doing the same with $u_2 - u_1$, we conclude that $u_1 = u_2$. □

Comparison principle for parabolic equations

We consider non-linear problem

$$Pu = f(t,x,u), \qquad \text{on } Q = (0,T) \times \Omega,$$

with $f : \overline{Q} \times \mathbb{R} \to \mathbb{R}$ continuous and $u \mapsto f(t,x,u)$ is locally Lipschitz, uniformly with respect to (t,x).

Comparison principle

Let Ω bounded. Let u, v in C^1 in t and C^2 in x on Q, continuous on $\overline{Q}$, and such that

$$\begin{aligned} Pu \geq f(t,x,u), \quad Pv \leq f(t,x,v), & \qquad \text{on } Q \\ u(t,x) \geq v(t,x), & \qquad \forall\, t \in (0,T), x \in \partial\Omega, \\ u(0,x) \geq v(0,x), & \qquad \forall\, x \in \Omega. \end{aligned}$$

Then $u \geq v$ on Q.

Comparison principle for parabolic equations

Idea of the proof (when $f \in C^1$).
Let $w = u - v$. We have

$$Pw \geq f(t,x,u) - f(t,x,v) = \gamma(t,x)w,$$

where

$$\gamma(t,x) = \begin{cases} \dfrac{f(t,x,u(t,x)) - f(t,x,v(t,x))}{u(t,x) - v(t,x)}, & \text{if } u(t,x) \neq v(t,x), \\ \partial_u f(t,x,u(t,x)), & \text{if } u(t,x) = v(t,x). \end{cases}$$

For $f \in C^1$, γ is continuous. Thus,

$$\begin{aligned} (P - \gamma(t,x))w \geq 0, \qquad & \text{on } Q, \\ w \geq 0, \qquad & \text{on } \partial_P Q. \end{aligned}$$

By the weak maximum principle, we deduce $w \geq 0$.

Sub- and super-solutions for parabolic equations

We consider the problem

$$\begin{aligned} Pu &= f(t,x,u), && \text{on } Q, \\ u(0,x) &= u_0(x), && \forall\, x \in \Omega, \\ u(t,x) &= g(t,x), && \forall\, t \in (0,T), x \in \partial\Omega. \end{aligned}$$

From the comparison principle, if $\underline{u}$ verifies

$$\begin{aligned} P\underline{u} &\leq f(t,x,\underline{u}), && \text{on } Q, \\ \underline{u}(0,x) &\leq u_0(x), && \forall\, x \in \Omega, \\ \underline{u}(t,x) &\leq g(t,x), && \forall\, t \in (0,T), x \in \partial\Omega. \end{aligned}$$

Then $\underline{u} \leq u$ on Q. It is called a generalized sub-solution.
By the same token, if $\overline{u}$ verifies

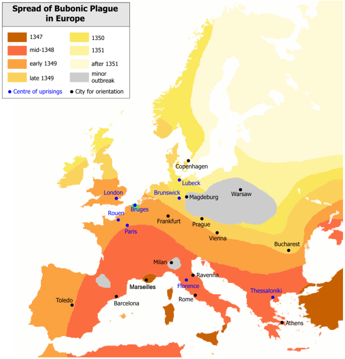
$$\begin{aligned} P\overline{u} &\geq f(t,x,\overline{u}), && \text{on } Q, \\ \overline{u}(0,x) &\geq u_0(x), && \forall\, x \in \Omega, \\ \overline{u}(t,x) &\geq g(t,x), && \forall\, t \in (0,T), x \in \partial\Omega. \end{aligned}$$

Then $u \leq \overline{u}$ on Q. It is called a generalized super-solution.

Outline of lecture 2

Introduction (B. Perthame, Parabolic equations in biology, Springer, 2015.)

An interesting phenomenon modelled by reaction-diffusion equation in full space is propagation, mathematically described thanks to traveling waves. In biology, traveling waves have been used in many situations to explain invasiveness of a species, spread of a genetic trait, propagation of epidemy, ...



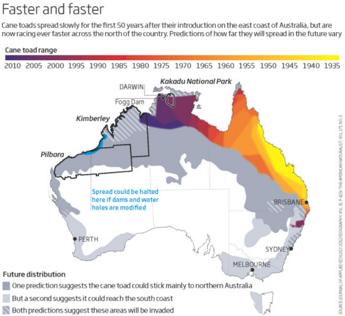


FIGURE – Two examples of invasion phenomena : Left : bubonic plague in Europe during the middle age ; Right : cane toads in Australia nowadays.

Introduction

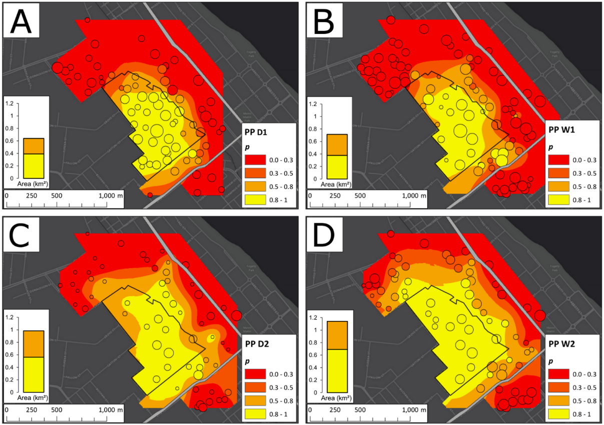


FIGURE – Spread of Wolbachia in a part of the city of Cairns, Australia, where releases of Wolbachia infected mosquitoes have been performed in 2013[2]. A : first dry season, B : first wet season, C : second dry season, D : second wet season.

1. Picture from Schmidt TL, Barton NH, Rasic G, Turley AP, Montgomery BL, Iturbe-Ormaetxe I, et al. (2017) PLoSBiol 15(5) :e2001894.

Setting of the problem

To simplify, we work in one space dimension and consider one species whose dynamics is governed by the reaction-diffusion equation :

$$\partial_t u - \partial_{xx} u = f(u), \quad t > 0, x \in \mathbb{R}.$$

Definition

A traveling wave solution is a solution of the form $u(t,x) = v(x - ct)$ with $c \in \mathbb{R}$ a constant called traveling speed.

We usually consider the case where the function f admits two stationary states $f(0) = f(1) = 0$:

- Fisher/KPP (monostable) equation : $f(u) = u(1-u)$.
- Allen-Cahn (bistable) equation : $f(u) = u(1-u)(u-\theta)$.

We complete the definition by the conditions $v(-\infty) = 1$, and $v(+\infty) = 0$.
When $c > 0$, this expresses the fact that the state $v = 1$ invades the state $v = 0$.
When $c < 0$, the state $v = 0$ invades the state $v = 1$.

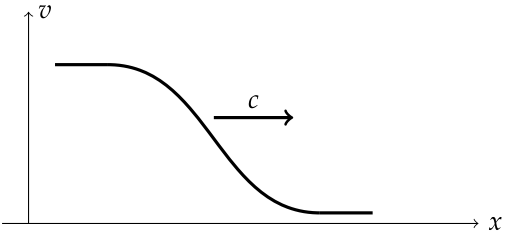
Setting of the problem

Injecting the expression $u(t,x) = v(x-ct)$ into the equation, we arrive at the system :

Problem

We look for a real-valued function v and a real c such that

$$v'' + cv' + f(v) = 0, \quad \text{on } \mathbb{R},$$
$$v(-\infty) = 1, \quad v(+\infty) = 0.$$



When $c = 0$, we say that we have a stationary state or a standing wave.

Setting of the problem

Observations :

- The problem is invariant by translation :
  If $v(x)$ is a solution, then $v(x+a)$ is a solution for any $a \in \mathbb{R}$. Then, we normalize by setting for instance $v(0) = \frac{1}{2}$.
- Multiplying by v', we get

$$\frac{1}{2}((v')^2)' + c(v')^2 + (F(v))' = 0, \qquad \text{where } F(v) = \int_0^v f(s)\,ds.$$

Integrating (using the fact that $v'(\pm\infty) = 0$), we find

$$c\int_{\mathbb{R}} (v'(x))^2\,dx = F(1) = \int_0^1 f(s)\,ds.$$

An important consequence is that

c has the same sign as $\int_0^1 f(s)\,ds$.

For instance, in the Fisher/KPP case, $f(u) = u(1-u) \geq 0$ for $u \in [0,1]$, thus $F(1) > 0$, it means that $v = 1$ is invading.

Outline of lecture 2

The Fisher/KPP (monostable) case

Let us consider the case where $f(u) = u(1-u)$. A famous result is

Theorem

For any $c \geq c^* = 2$, there is a unique traveling wave solution v with $0 \leq v \leq 1$ and v monotically decreasing.

- The quantity c^* is called the minimal propagation speed.
- This result can be extended to general equation

$$\partial_t u - D\partial_{xx} u = f(u), \text{ with } f(0) = f(1) = 0, \; f(u) > 0 \text{ for } 0 < u < 1.$$

In this case, the minimal propagation speed is $c^* = 2\sqrt{f'(0)D}$.

Allen-Cahn (bistable) equation

We consider the *bistable* case, i.e. 0 and 1 are both stable steady state.

Traveling wave solution

We look for $c \in \mathbb{R}$ and a real-valued function v such that

$$v'' + cv' + f(v) = 0$$

$$v(-\infty) = 1, \quad v(+\infty) = 0, \quad v(0) = \frac{1}{2}.$$

We will make use of the notation $F(u) = \int_0^u f(v)\, dv$. We assume that

$$f(0) = 0, \quad f'(0) < 0, \quad f(\theta) = 0, \quad f(1) = 0, \quad f'(1) < 0,$$
$$f(u) < 0 \text{ on } (0,\theta), \qquad f(u) > 0 \text{ on } (\theta,1).$$

Adapting the phase space method, we may prove :

Theorem

Under these assumptions, there exists a unique traveling wave solution (c^*, v) with v decreasing.
We have $c^* > 0$ for $F(1) > 0$, $c^* = 0$ for $F(1) = 0$, $c^* < 0$ for $F(1) < 0$.

Proof

Proof. Such results are known since decades[3]. There are several techniques of proof. We provide here a simple proof based on a phase space method for ODE. The proof is divided into three steps :

1. reduction to a simple ODE ;
2. monotonicity in c ;
3. existence by a continuity argument.

- 1st step : Reduction to a simple ODE

We set $w = -v'$ (so that $w > 0$ since we look for v decreasing). The equation becomes

$$v' = -w \qquad w' = -cw + f(v)$$
$$v(-\infty) = 1,\ w(-\infty) = 0, \quad v(+\infty) = 0,\ w(+\infty) = 0.$$

3. H. Berestycki, B. Nikolaenko, and B. Scheurer, Travelling waves solutions to combustion models and their singular limits, SIAM J. Math. Anal., 16 (1985)
A. Volpert, V. Volpert, V. Volpert. Traveling wave solutions of parabolic systems. Translation of Mathematical Monographs, Vol. 140, Amer. Math. Society, Providence, 1994

Proof

By monotonicity of v, we can invert $v(x)$ as a function $X(v)$, $0 \leq v \leq 1$. We set $\tilde{w}(v) = w(X(v))$. The system becomes

$$\frac{d\tilde{w}}{dv} = \frac{dw}{dx}\left(\frac{dv}{dx}\right)^{-1} = c - \frac{f(v)}{\tilde{w}(v)}, \qquad 0 \leq v \leq 1,$$
$$\tilde{w}(0) = \tilde{w}(1) = 0, \quad \tilde{w} \geq 0.$$

Therefore, the problem reads :

Problem

Can we find a special value for c for which the following boundary value problem admits a solution :

$$\frac{d\tilde{w}}{dv} = c - \frac{f(v)}{\tilde{w}(v)}, \qquad 0 \leq v \leq 1,$$
$$\tilde{w}(0) = \tilde{w}(1) = 0, \qquad \tilde{w} \geq 0.$$

We consider the case $F(1) > 0$ only (otherwise the argument is the same except that we have to argue departing from $v = 1$).

Proof

We first notice that there is a priori a singularity at $v = 0$. This singularity can be handled by computing (L'Hospital rule)

$$\tilde{w}'(0) = c - \frac{f'(0)}{\tilde{w}'(0)} \Longleftrightarrow \tilde{w}'(0) = \frac{1}{2}\Big(c + \sqrt{c^2 + 4|f'(0)|}\Big).$$

A shooting argument

Finally, we arrive at the question to know if the solution to the Cauchy problem

$$\begin{aligned} &\frac{d\tilde{w}}{dv} = c - \frac{f(v)}{\tilde{w}(v)}, \qquad 0 \leq v \leq 1, \\ &\tilde{w}(0) = 0, \end{aligned} \tag{1}$$

can also achieve for a special value of c the conditions $\tilde{w}_c(1) = 0$, $\tilde{w}_c \geq 0$.

For c given, we denote by $\tilde{w}_c$ the solution to (1). Notice that since $f \geq 0$ on $(0, \theta)$, we have

$$\tilde{w}_c(v) \geq cv \qquad \text{on} \quad (0, \theta).$$

Proof

Then the solution can be continued smoothly as a simple ODE until $\tilde{w}_c$ vanishes and the problem is not defined any longer. There are two possibilities :

- either $\tilde{w}_c(v) > 0$ for $0 \leq v \leq 1$, we call this solution *Type 1* and we set $v_c = 1$.
- or there exists $v_c \in (\theta, 1)$ such that $\tilde{w}_c(v_c) = 0$, then the system reaches a singularity where $\tilde{w}_c'(v_c) = -\infty$, we call this solution *Type 2*.

We are interested in the limiting case.

Proof

Then the solution can be continued smoothly as a simple ODE until $\tilde{w}_c$ vanishes and the problem is not defined any longer. There are two possibilities :

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We are interested in the limiting case.

- 2nd step : Monotonicity in c.

Lemma

The mapping $c \mapsto \tilde{w}_c(v)$ is increasing for those v where it is defined, i.e. for $0 < v < v_c$.

Proof. We set $z_c(v) = \frac{d\tilde{w}_c(v)}{dc}$. From (1), it satisfies

$$\frac{dz_c(v)}{dv} = 1 + \frac{f(v)}{(\tilde{w}_c(v))^2} z_c(v), \quad z_c(0) = 0.$$

We deduce that z_c cannot vanish for $v > 0$ and thus $z_c(v) \geq v$ as long as it is defined, i.e. for $v < v_c$. □

Proof

Consequently $\tilde{w}_c(1)$ is an increasing function of c. Therefore there can be at most one value of c satisfying the condition $\tilde{w}_c(1) = 0$.

- 3rd step : Existence.

Let us define

$$\bar{c}^2 = 4 \max_{0 \le v \le 1} \frac{f(v)}{v}.$$

Clearly $\underline{c} < \bar{c}$. Moreover, we have

Lemma

For $c > \bar{c}$, the solution is of *Type 1*. For $c \sim 0$, the solution is of *Type 2*.

Once this lemma is proved, the existence of a c such that $\tilde{w}_c(1) = 0$ will follow by a continuity argument. The uniqueness is a consequence of the monotonicity.

The monostable equation with ignition temperature

Proof of the Lemma.

• *For $c > \bar{c}$ the solution is Type 1 :*

We consider the largest interval $[0, v_0] \subset [0,1]$ on which $\tilde{w}_c(v) \geq \frac{c}{2} v$. Since $\tilde{w}_c(v) \geq cv$ on $[0,\theta]$, clearly $v_0 > \theta$. If $v_0 < 1$, then $\tilde{w}_c'(v_0) \leq \frac{c}{2}$ and we would have

$$\frac{c}{2} \geq \frac{d\tilde{w}_c(v_0)}{dv} = c - 2\frac{f(v_0)}{cv_0} \geq c - \frac{\bar{c}^2}{2c}.$$

This is a contradiction with the fact that $c > \bar{c}$.

• *For $c \sim 0$ the solution is Type 2 :*

Multiplying (1) by $\tilde{w}_c$ and integrating, we obtain the relation

$$\frac{1}{2}\tilde{w}_c(v)^2 = c\int_0^v \tilde{w}_c(z)\,dz - F(v),$$

where we recall that $F' = f$ and $F(1) > 0$. Since $F(1) > 0$, there exists $\beta < 1$ such that $F(\beta) = 0$, $F < 0$ on $(0,\beta)$, and $F > 0$ on $(\beta, 1)$. Thus, for $c = 0$, we have $\tilde{w}_0(v)^2 = -2F(v)$. It allows to define a solution up to β. Therefore the solution ceases to exist for v larger than β, i.e. the solution is *Type 2*.

By continuity, the solution is *Type 2* for $c \sim 0$. □

End of proof

Finally, we conclude by continuity argument, using the monotonicity :

- As c increases from 0, v_c increases from the monotonicity.
  Indeed, from the latter equality taken at $v = v_c$, we have

$$0 = c \int_0^{v_c} \tilde{w}_c(z)\, dz - F(v_c), \qquad \tilde{w}_c(v_c) = 0.$$

  Differentiating in c, we obtain

$$0 = \int_0^{v_c} \tilde{w}_c(z)\, dz + c\tilde{w}_c(v_c)\frac{dv_c}{dc} - f(v_c)\frac{dv_c}{dc} + c\int_0^{v_c} \frac{d\tilde{w}_c(z)}{dc}\, dz.$$

  Hence we get

$$\frac{dv_c}{dc} = \frac{1}{f(v_c)}\left(\int_0^{v_c} \tilde{w}_c(z)\, dz + c\int_0^{v_c} \frac{d\tilde{w}_c(z)}{dc}\, dz\right) > 0.$$

- We define c^* as the maximum of the c corresponding to *Type 2*. It satisfies $\tilde{w}_{c^*}(v_{c^*}) = 0$. By monotonicity, it is also the minimum of c giving solutions of *Type 1*. □

A remark

Remark : an explicit solution.
For the simple choice of bistable function satisfying the assumptions given by

$$f(u) = u(1-u)(u-\theta),$$

we have an explicit expression of the traveling wave solution :

$$v(x) = \frac{e^{-x/\sqrt{2}}}{1+e^{-x/\sqrt{2}}}, \qquad c^* = \sqrt{2}(\frac{1}{2}-\theta).$$

Indeed, we may compute with this expression,

$$v' = \frac{1}{\sqrt{2}}v(v-1), \qquad v'' = \frac{v'}{\sqrt{2}}(2v+1) = v(v-1)(v+\frac{1}{2}).$$

Thus, $-c^*v' - v'' = v(1-v)(v+\frac{c^*}{\sqrt{2}}+\frac{1}{2}) = f(v)$.

Outline of lecture 2

Let us come back to the release of *Wolbachia*-infected mosquitoes. To illustrate we provide some pictures of people releasing *Wolbachia*-infected male mosquitoes (pictures taken in 2017 in Tetiaroa, French Polynesia, courtesy of Hervé Bossin).

Mathematical model

We recall the mathematical model for the dynamics of *Wolbachia* infected mosquitoes and *Wolbachia* free mosquitoes :

- n_i : density of Wolbachia-infected mosquitoes ;
- n_u : density of uninfected mosquitoes ;
- $d_u, d_i = \delta d_u$: death rate, $\delta > 1$;
- $F_u, F_i = (1 - s_f)F_u$: fecondity ;
- s_h : cytoplasmic incompatibility parameter (fraction of uninfected females' eggs fertilized by infected males which will not hatch) ;
- K : carrying capacity ;

Model

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

To simplify, we choose the diffusion coefficient $D = 1$.

Mathematical model

Model

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

- 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.
- 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).
- Comparison principle : if $0 \le n_i^0 \le \widetilde{n}_i^0$, $0 \le \widetilde{n_u}^0 \le n_u^0$, then for any $t > 0$, we have $0 \le n_i(t) \le \widetilde{n}_i(t)$, $0 \le \widetilde{n_u}(t) \le n_u(t)$.

Mathematical model : equilibria

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 $(n_{iC}^*, n_{uC}^*) := \Big(\big(K - \frac{d_u}{F_u}\frac{\delta}{1-s_f}\big)\frac{\delta-(1-s_f)}{\delta s_h}, \big(K - \frac{d_u}{F_u}\frac{\delta}{1-s_f}\big)\frac{\delta(s_h-1)+(1-s_f)}{\delta s_h}\Big)$ is unstable ;
- extinction $(0,0)$ is unstable.

Mathematical model : equilibria

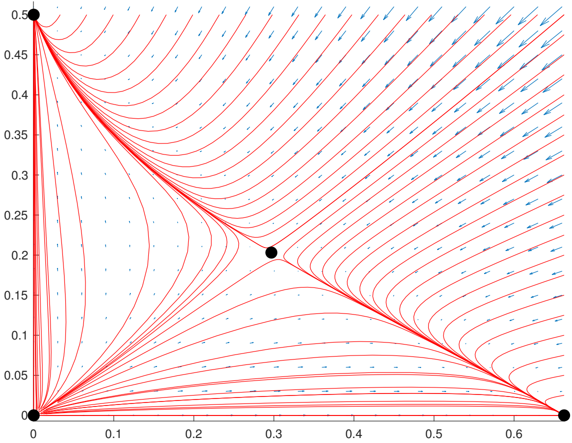

FIGURE – Phase portrait representing the equilibria and their stability for the dynamical system without spatial diffusion

Outline of lecture 2

Large fertility asymptotics

Since we know several results for scalar reaction-diffusion equation, we will try to reduce this system into a scalar equation. To this aim, we consider that the fecundity is large and introduce the parameter ϵ such that $F_u = \frac{F_u^0}{\epsilon}$,

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

We are interested in the limit $\epsilon \to 0$.

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We are interested in the limit $\epsilon \to 0$.
We first observe that

$$n_i + n_u = K + O(\epsilon).$$

Large fertility asymptotics

In order to perform the asymptotics study, we introduce

$$n = \frac{1}{\epsilon}(1 - \frac{n_i + n_u}{K}), \qquad p = \frac{n_i}{n_i + n_u} \text{ (fraction of infected).}$$

After straightforward computations, we find

$$\begin{cases} \partial_t n - \Delta n = -\frac{1-\epsilon n}{\epsilon}\left(F_u^0 n(s_h p^2 - (s_f + s_h)p + 1) - d_u((\delta - 1)p + 1)\right), \\ \partial_t p - \Delta p + \frac{2\epsilon}{1-\epsilon n}\nabla p \cdot \nabla n = p(1-p)(F_u n(s_h p - s_f) + (1-\delta)d_u). \end{cases}$$

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Formally, when $\epsilon \to 0$, we deduce from the first equation that

$$n \to n_0 = \frac{d_u((\delta - 1)p_0 + 1)}{F_u(s_h {p_0}^2 - (s_f + s_h)p_0 + 1)}.$$

Reduction of the model

Injecting this expression into the second equation, we obtain after letting $\epsilon \to 0$,

$$\partial_t p_0 - \Delta p_0 = \delta d_u s_h \frac{p_0(1-p_0)(p_0-\theta)}{F_u(s_h {p_0}^2 - (s_f+s_h)p_0+1)}, \quad \theta = \frac{s_f+\delta-1}{\delta s_h}.$$

Notice that for $\delta \geq 1$ and $s_f < s_h$, we have $\theta \in (0,1)$ and the denominator never vanishes on $(0,1)$.
This is the celebrated model proposed by *Barton & Turelli*.[4]

4. *Spatial Waves of Advance with Bistable Dynamics : Cytoplasmic and Genetic Analogues of Allee Effects*, The American Naturalist, 2011

Reduction of the model

Theorem

Assuming 'well-prepared' initial data, then when $\epsilon \to 0$, we have $p := \frac{n_i}{n_i+n_u} \to p_0$ strongly in $L^2_{loc}(\mathbb{R}^+; L^2(\mathbb{R}^d))$, weakly in $L^2_{loc}(\mathbb{R}^+; H^1(\mathbb{R}^d))$ where p_0 is the unique solution to

$$\partial_t p_0 - \Delta p_0 = f(p_0),$$

$$f(p_0) = \frac{\delta d_u s_h}{F_u} \frac{p_0(1-p_0)(p_0-\theta)}{s_h p_0^2 - (s_f+s_h)p_0 + 1}, \qquad \theta = \frac{s_f+\delta-1}{\delta s_h} \in (0,1).$$

Steps for the proof[5] :

- Uniform estimates of n and p and their gradient in L^2 ;
- Relative strong compactness thanks to a 'Aubin-Lions' Lemma ;
- Passing to the limit.

5. M. Strugarek, N. V., *Reduction to a single closed equation for 2 by 2 reaction-diffusion systems of Lotka-Volterra type, SIAM J. Appl. Math. (2016)*

Outline of lecture 2

Traveling waves for the Wolbachia propagation

A consequence of this latter Theorem is that the solution of the system for *Wolbachia* may be approximated by the scalar reaction-diffusion equation for the proportion of infected

$$\partial_t p - \Delta p = f(p), \quad \text{with } f(p) = \frac{\delta d_u s_h}{F_u} \frac{p(1-p)(p-\theta)}{s_h p^2 - (s_f + s_h)p + 1}.$$

We observe that f is bistable, i.e. $f(0) = 0$, $f(\theta) = 0$ and $f(1) = 0$, $f < 0$ on $(0, \theta)$, and $f > 0$ on $(\theta, 1)$.

Traveling waves for the Wolbachia propagation

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Thus, we may apply the previous Theorem of existence of traveling waves in one dimension.

Proposition

There exists a decreasing traveling wave for the reduced model for Wolbachia,

$$\partial_t p - \partial_{xx} p = f(p), \quad f \text{ bistable as above.}$$

Moreover the speed c^* of the wave has the sign of $\int_0^1 f(\xi)\, d\xi$.

Traveling waves for the Wolbachia propagation

Consequences

We recall that p is the proportion of *Wolbachia*-infected mosquitoes. Thus,

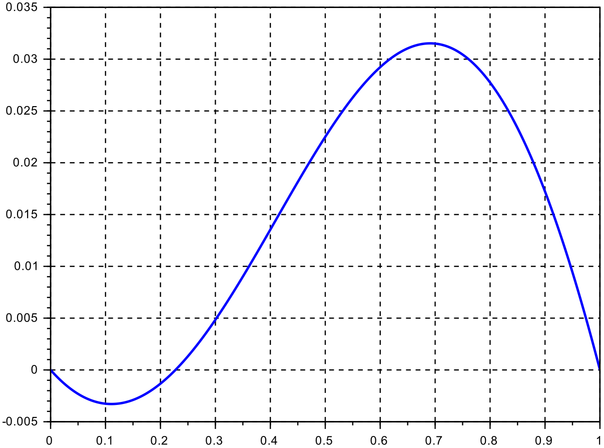
- the stable steady state $p = 0$ corresponds to the *Wolbachia*-free equilibrium ;
- the stable steady state $p = 1$ corresponds to the *Wolbachia*-infected equilibrium ;
- the unstable steady state $p = \theta$ corresponds to the coexistence equilibrium.

Thus, $c > 0$ implies the invasion of *Wolbachia* into the host population, which can occurs if and only if $\int_0^1 f(\xi)d\xi > 0$.

Fortunately, with the numerical data taken from literature, we have $\int_0^1 f(\xi)d\xi > 0$ for the above model for Wolbachia.

Traveling waves for the Wolbachia propagation

Possible shape for f :



Outline of lecture 2

Critical propagule

Question :

How to spatially introduce *Wolbachia*-infected mosquitoes to guarantee invasion ?
How to initiate a wave ?

Critical propagule

Question :

How to spatially introduce *Wolbachia*-infected mosquitoes to guarantee invasion ? How to initiate a wave ?

Answer

There exists a family of functions $(v_\alpha)_\alpha$, compactly supported, radially symmetric and decreasing, such that if there exists a time $\tau > 0$, for which we have $p(\tau) \geq v_\alpha$, then $p(t) \to 1$ uniformly on every compact as $t \to +\infty$. We call them α-bubbles.

References :

- A. Zlatos. *Sharp transition between extinction and propagation of reaction*. J. Amer. Math. Soc., 2006.
- P. Polacik. *Threshold solutions and sharp transitions for nonautonomous parabolic equations on* $\mathbb{R}^N$. Archive for Rational Mechanics and Analysis, 2011.
- Y. Du, H. Matano, *Convergence and sharp thresholds for propagation in nonlinear diffusion problems*. J. Eur. Math. Soc., 2010.
- C. Muratov, X. Zhong, *Threshold phenomena for symmetric-decreasing radial solutions of reaction-diffusion equations*, Discr. Cont. Dyn. Syst. A, 2017.

Critical bubble in one dimension

Idea : *Construct a family of subsolutions for* $\partial_t u - \partial_{xx} u = f(u)$.
To do so, we notice that 0 is a solution, and we consider u_α a stationary solution. Thus $v_\alpha := \max\{0, u_\alpha\}$ is a subsolution. As a consequence, if $u(t=0) \geq v_\alpha$ then $\forall\, t \geq 0$, $u(t) \geq v_\alpha$.

- **Construction of compactly supported bubbles :** The idea is to use the symmetry and to solve the Cauchy problem on $[0, +\infty)$,

$$u_\alpha'' + f(u_\alpha) = 0, \qquad u_\alpha(0) = \alpha, \quad u_\alpha'(0) = 0.$$

We recall that $\boxed{F(1) := \int_0^1 f(\xi)\, d\xi > 0}$, thus $\exists\, \beta > \theta$ such that $F(\beta) = 0$.
Multiplying by u_α' and integrating we obtain

$$\frac{1}{2}(u_\alpha')^2 + F(u_\alpha) = F(\alpha).$$

Since we are looking for u_α decreasing, we have

$$u_\alpha' = -\sqrt{2(F(\alpha) - F(u_\alpha))}, \qquad u_\alpha(0) = \alpha.$$

For $\alpha > \beta$, this function is well-defined and decreasing.

Critical bubble in one dimension

We may invert it into a function X_α. Then

$$X'_\alpha(u) = \frac{-1}{\sqrt{2(F(\alpha)-F(u))}}, \qquad X_\alpha(\alpha) = 0.$$

Integrating, we deduce

$$X_\alpha(u) = \int_u^\alpha \frac{d\xi}{\sqrt{2(F(\alpha)-F(\xi))}}.$$

Hence, the position where the function u_α vanishes is given by

$$L_\alpha = \int_0^\alpha \frac{d\xi}{\sqrt{2(F(\alpha)-F(\xi))}}, \qquad F(\xi) = \int_0^\xi f(z)dz.$$

The α-bubble is defined by

$$v_\alpha(x) = \begin{cases} u_\alpha(-x), & \text{on } (-L_\alpha, 0), \\ u_\alpha(x), & \text{on } (0, L_\alpha), \\ 0 & \text{else.} \end{cases}$$

Critical bubble in one dimension

Lemma

Let u solve the bistable reaction-diffusion equation $\partial_t u - \partial_{xx} u = f(u)$. If there exists $\alpha > \beta$ and $\xi \in \mathbb{R}$ such that $u(t=0,x) \geq v_\alpha(x-\xi)$. Then $u \to 1$ locally uniformly as $t \to +\infty$.

Sketch of the proof :

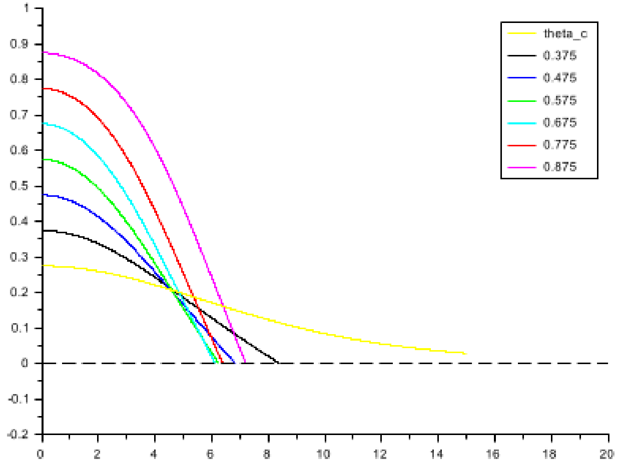
- Let us introduce u_α the solution to the bistable reaction diffusion equation with initial data v_α. Then we have $\partial_t u_\alpha \geq 0$ (Indeed $\partial_t u_\alpha(t=0) = \partial_{xx} v_\alpha + f(v_\alpha) \geq 0$, since v_α is a subsolution, and by comparison principle it is true for any $t > 0$).
- By comparison principle, we have $u(t,x) \geq u_\alpha(t, x-\xi)$ for any $t > 0$ and $x \in \mathbb{R}$. Thus, it suffices to show that $u_\alpha \underset{t\to+\infty}{\longrightarrow} 1$ loc. unif.
- Define $\theta^* = \lim_{t\to+\infty} u_\alpha(t,0)$. It is well-defined since u_α is nondecreasing with respect to time (and bounded by 1).
  Moreover, by comparison principle $1 \geq \theta^* \geq \alpha = v_\alpha(0) > \beta$.

Critical bubble in one dimension

- Let $t \mapsto s(t)$ be a smooth increasing function on $\mathbb{R}^+$ such that $s(t) \leq u_\alpha(t,0)$, and $s(t) \underset{t\to+\infty}{\longrightarrow} \theta^*$. We introduce the solution to
$$\partial_t S - \partial_{xx} S = f(S), \quad \text{on } \mathbb{R}^+, \qquad S(t,0) = s(t), \quad S(0,x) = 0.$$
  - Since s is increasing, we have that $t \mapsto S(t)$ is increasing. In particular $S \geq 0$.
  - Moreover, for any $x \geq 0$ and $t > 0$, $u_\alpha(t,x) \geq S(t,x)$.
- From standard parabolic regularity results, $S(t) \underset{t\to+\infty}{\longrightarrow} \tilde{S}$ loc. unif., where
$$0 = \partial_{xx}\tilde{S} + f(\tilde{S}), \text{ on } \mathbb{R}^+, \quad \tilde{S}(0) = \theta^*.$$
If $\theta^* < 1$, then $\partial_{xx}\tilde{S}(0) > 0$ and the derivative never vanishes since
$$(\tilde{S}'(x))^2 = (\tilde{S}'(0))^2 + \int_{\tilde{S}(x)}^{\theta^*} f(\zeta)\, d\zeta > 0.$$
Thus, $\tilde{S}$ is a decreasing function. Then, let $0 < x_0$, for all $x > x_0$, $(\tilde{S}'(x))^2 \geq (\tilde{S}'(0))^2 + \int_{\max\{\beta, \tilde{S}(x_0))\}}^{\theta^*} f(\zeta)\, d\zeta > 0$. Then, for $x > x_0$, $|\tilde{S}'(x)|$ is bounded from below by a uniform positive constant : It should take negative values. CONTRADICTION since $S \geq 0$.
Thus $\theta^* = 1$, then $\tilde{S} = 1$. Therefore $u \underset{t\to+\infty}{\longrightarrow} 1$ loc. unif. $\square$

Critical bubble in one dimension

Example of a family of initial data (u_α) above which invasion occurs for the function f corresponding to the one for *Wolbachia* (one dimensional case, to symmetrize with respect to zero) :



General result in any dimension

Actually, a more general result is available. More precisely, there exists a critical threshold between ignition and propagation. Let us first define the energy :

$$E[u] := \int_{\mathbb{R}^d} \left(\frac{1}{2}|\nabla u|^2 - F(u)\right) dx.$$

Then, we have[6] :

Theorem

For f a bistable function with $\int_0^1 f(z)\,dz > 0$. Let u be a solution to the scalar reaction-diffusion equation. Let $(\phi_\lambda)_{\lambda\in[0,\lambda^+]}$ be a sequence of nonnegative initial data such that $\lambda \mapsto \phi_\lambda$ is nondecreasing and continuous, $\phi_0 = 0$, and $E[\phi_{\lambda^+}] < 0$. Then, there exists $\lambda^* \in (0, \lambda^+)$ such that

1. $\lim_{t\to+\infty} u = 1$ locally uniformly in $\mathbb{R}^d$ and $\lim_{t\to+\infty} E[u] = -\infty$, for all $\lambda > \lambda_*$.
2. $\lim_{t\to+\infty} u = 0$ uniformly in $\mathbb{R}^d$ and $\lim_{t\to+\infty} E[u] = 0$, for all $\lambda < \lambda_*$.
3. $\lim_{t\to+\infty} u = v^*$ uniformly in $\mathbb{R}^d$ and $\lim_{t\to+\infty} E[u] = E[v^*] > 0$ where v^* is the ground state, for $\lambda = \lambda^*$.

6. Y. Du, H. Matano, J. Eur. Math. Soc., 2010 ; C. Muratov, X. Zhong, Discr. Cont. Dyn. Syst. A, 2017.

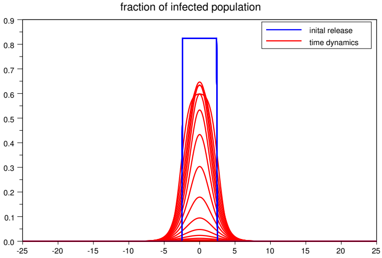
Outline of lecture 2

Numerical results in one dimension

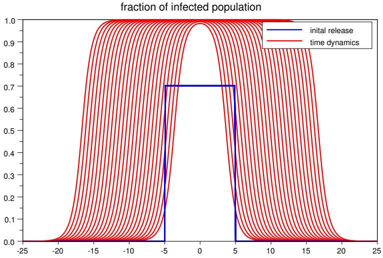
A direct consequence is that the initial repartition of the release of *Wolbachia*-infected mosquitoes should be done in a wide enough domain with a sufficient amount of mosquitoes.

Numerical example : With the same amount of mosquitoes, we consider two different initial repartitions :

Extinction



Invasion

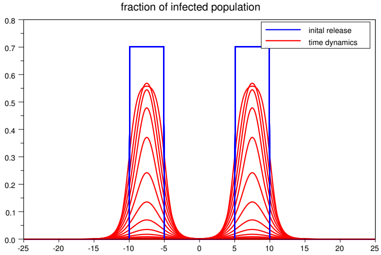


Spatial distribution is important.

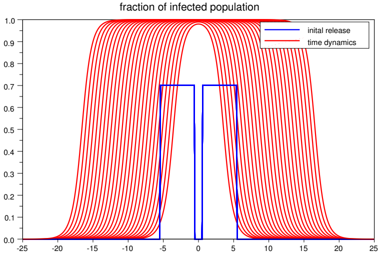
Numerical results in one dimension

Other examples to emphasize the importance of the spatial distribution :

Extinction



Invasion

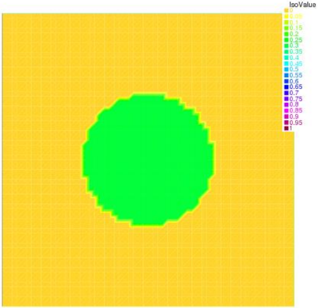


Multiple releases : movie

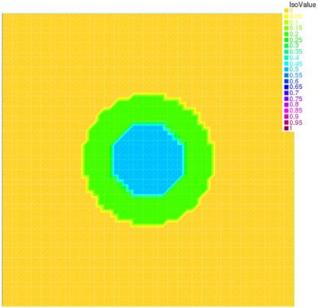
Numerical results in two dimension

We can have similar results in higher dimension.
With the same total amount of mosquitoes on the same area :

Extinction



Invasion



Uncertainty quantification of the releases

Using the same idea, with radial symmetry, we may prove that such result holds also in higher dimension[7].

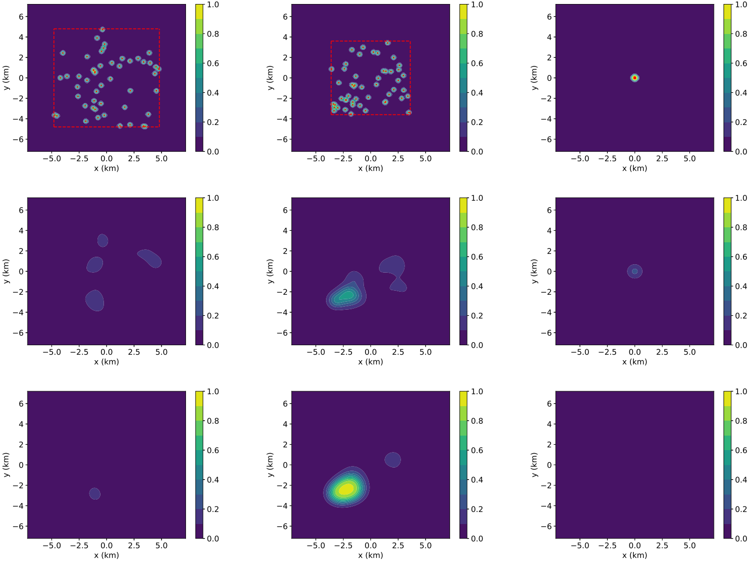
Consequence

Let Ω be a bounded domain containing the support of one bubble.
Let us assume that we perform some random point releases in Ω. Then, the probability of success of invasion tends to 1 as the number of releases goes to $+\infty$.

Indeed each release covers a small ball around its position of release. Then it suffices to show that the probability to cover a domain containing a critical bubble goes to 1 as the number of releases increases.

7. M. Strugarek, N. V., J. Zubelli, *Quantifying the survival uncertainty of Wolbachia-infected mosquitoes in a spatial model*, Math. Biosci. Eng.

Uncertainty quantification of the release



Initial time

after 25 days

after 50 days

Active control

Let us consider the problem of active control with a function u (which may depend on p : feedback control)

$$\partial_t p - \Delta p = f(p) + u\mathbf{1}_{[0,T]\times\Omega}, \qquad p(t=0) = 0.$$

Due to the existence of bubble, it is easy to prove[8] :

Theorem

There exist a time $T > 0$, a bounded open set $\Omega \subset \mathbb{R}^d$ and an active control $u = g(p)$ such that the solution p to the above equation converges to 1 as t goes to $+\infty$, locally uniformly on $\mathbb{R}^d$.

8. P.A. Bliman, N. V., *Establishing traveling wave in bistable reaction-diffusion system by feedback*, IEEE Control Systems Letter, 2017.

Active control

Idea of the proof :

- We look for $g(p) = \mu(1-p) - f(p)$.
- Comparison of the bubble with solution to the linear equation

$$\partial_t u - \Delta u = \mu(1-u) \quad \text{on } \Omega, \quad u = 0 \text{ on } \partial\Omega.$$

Solution to this linear equation may be computed explicitely thanks to eigenmodes. It suffices to show that $u(T) \geq v_\alpha$ on Ω.

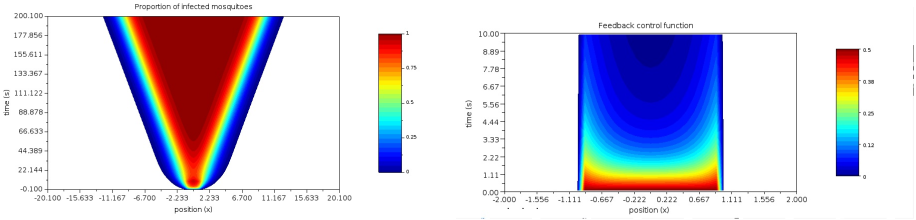
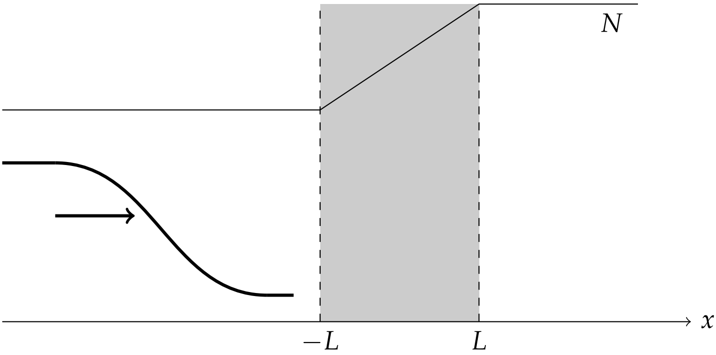


FIGURE – Left : Dynamics of the proportion of infected (in x-axis) as a function of time (y-axis). The domain $\Omega = [-1, 1]$, $u = \frac{1}{2}(1-p)$, $T = 10$. Right : Zoom of the time dynamics of the control input.

Outline of lecture 2

Heterogeneous environment

The environment is heterogeneous. Can strong variations in the total density of mosquitoes stop the propagation ?



Modelling

In order to model this phenomenon, we come back to the initial model for *Wolbachia*-infected mosquitoes n_i and uninfected mosquitoes n_u with space-varying carrying capacity :

$$\partial_t n_i - \Delta n_i = (1 - s_f) F_u n_i \big(1 - \frac{n_i + n_u}{K(x)}\big) - \delta d_u n_i,$$

$$\partial_t n_u - \Delta n_u = F_u n_u (1 - s_h \frac{n_i}{n_i + n_u}) \big(1 - \frac{n_i + n_u}{K(x)}\big) - d_u n_u.$$

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$$\partial_t n_i - \Delta n_i = (1 - s_f)\frac{F_u^0}{\epsilon} n_i \big(1 - \frac{n_i + n_u}{K(x)}\big) - \delta d_u n_i,$$

$$\partial_t n_u - \Delta n_u = \frac{F_u^0}{\epsilon} n_u (1 - s_h \frac{n_i}{n_i + n_u})\big(1 - \frac{n_i + n_u}{K(x)}\big) - d_u n_u.$$

As above, we consider the asymptotics of large fertility $F_u = \frac{F_u^0}{\epsilon}$ with $\epsilon \ll 1$.

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$$\partial_t n_u - \Delta n_u = \frac{F_u^0}{\epsilon} n_u \big(1 - s_h \frac{n_i}{n_i+n_u}\big)\big(1 - \frac{n_i+n_u}{K(x)}\big) - d_u n_u.$$

As above, we consider the asymptotics of large fertility $F_u = \frac{F_u^0}{\epsilon}$ with $\epsilon \ll 1$.
We recall the notations

$$N = n_i + n_u \text{ (total density of mosquitoes)}, \quad p = \frac{n_i}{n_i+n_u} \text{ (fraction of infected)}.$$

Modelling

After straightforward computations, (N, p) solves the system

$$\partial_t N - \Delta N = N\left(\frac{F_u^0}{\epsilon}(1 - \frac{N}{K})\big((1-s_f)p + (1-p)(1-s_h p)\big) - d_u(\delta p + 1 - p)\right),$$

$$\partial_t p - \Delta p - 2\frac{\nabla p \cdot \nabla N}{N} = p(1-p)\left(\frac{F_u^0}{\epsilon}(1 - \frac{N}{K})(s_h p - s_f) + d_u(1-\delta)\right).$$

Modelling

After straightforward computations, (N, p) solves the system

$$\partial_t N - \Delta N = N\left(\frac{F_u^0}{\epsilon}(1-\frac{N}{K})\big((1-s_f)p+(1-p)(1-s_h p)\big) - d_u(\delta p + 1 - p)\right),$$
$$\partial_t p - \Delta p - 2\frac{\nabla p \cdot \nabla N}{N} = p(1-p)\left(\frac{F_u^0}{\epsilon}(1-\frac{N}{K})(s_h p - s_f) + d_u(1-\delta)\right).$$

- Formally, we introduce a development of $N = N^\varepsilon(t,x)$ by setting

$$N = N^\varepsilon(t,x) = K(x)\Big(1 - \epsilon n^\varepsilon(t,x) + \epsilon^2 w^\varepsilon(t,x)\Big).$$

- Equating the leading terms in the equation for N yields

$$n^\varepsilon(t,x) = \frac{d_u\big((\delta-1)p(t,x)+1\big) - \Delta K(x)/K(x)}{(1-s_f)p(t,x) + (1-p(t,x))(1-s_h p(t,x))}.$$

Modelling

- Injecting this latter expression into equation for p leads to

$$\partial_t p - \Delta p - 2\frac{\nabla K}{K}\cdot\nabla p - 2\nabla p\cdot\nabla\ln\left(1-\epsilon n^\varepsilon+\epsilon^2 w^\varepsilon\right)$$
$$= p(1-p)\Big((s_h p - s_f)\frac{d_u\big((\delta-1)p+1\big)-\Delta K/K}{(1-s_f)p+(1-p)(1-s_h p)} - d_u(\delta-1)\Big).$$

- Passing formally to the limit $\epsilon\to 0$, we obtain

$$\partial_t p - \Delta p - 2\frac{\nabla K}{K}\cdot\nabla p$$
$$= p(1-p)\Big((s_h p - s_f)\frac{d_u\big((\delta-1)p+1\big)-\Delta K/K}{(1-s_f)p+(1-p)(1-s_h p)} - d_u(\delta-1)\Big).$$

We assume to be in a range of parameters such that the term $\Delta K/K$ is negligeable with respect to d_u. Then, the equation reduces to study

$$\partial_t p - D\Delta p - 2\frac{\nabla K}{K}\cdot\nabla p = f(p).$$

Outline of lecture 2

Blocking waves

In one dimension, we are left to study the existence of blocking waves for the following scalar equation for the proportion of infected mosquitoes [9]

$$\partial_t p - \partial_{xx} p - 2\partial_x(\log N)\partial_x p = f(p),$$

where we recall that f is bistable (i.e. $f(0) = f(\theta) = f(1) = 0$, $f < 0$ on $(0, \theta)$, $f > 0$ on $(\theta, 1)$), and $\int_0^1 f(x)dx > 0$.

For the sake of simplicity, we assume that we have exponential variation of the density in a domain $[-L, L]$,

$$\partial_x \log(N) = \begin{cases} \frac{C}{2}, & \text{on } [-L, L]; \\ 0, & \text{on } \mathbb{R} \setminus [-L, L]. \end{cases}$$

9. The term $\partial_x(\log N)$ is usually called the *gene flow*.

Blocking waves

Existence of a stationary wave boils down to existence for

$$\begin{aligned} & -p'' - Cp' = f(p), && \text{on } [-L, L], \\ & -p'' = f(p), && \text{on } \mathbb{R} \setminus [-L, L], \\ & p(-\infty) = 1, p(+\infty) = 0, p > 0. && \end{aligned}$$

For C and L given, we call (C, L)-barrier a solution to this system.

Blocking waves

Assume that there exists a (C, L)-barrier, denoted p_B. Then any solution to

$$\partial_t p - \partial_{xx} p - 2\partial_x(\log N)\partial_x p = f(p),$$

with initial data such that $p^{ini} \leq p_B$, has stopped propagation, i.e. $\forall\, t \geq 0, p(t) \leq p_B$.

Blocking waves

We recall that, for bistable equation, there exists a unique traveling wave solution $(\tilde{p}, c^*)$ solution to

$$-\tilde{p}'' - c^*\tilde{p}' = f(\tilde{p}), \qquad \text{on } \mathbb{R},$$
$$\tilde{p}(-\infty) = 1, \quad \tilde{p}(+\infty) = 0.$$

Moreover, since we have assumed $\int_0^1 f(x)dx > 0$, we have $c^* > 0$.
This is the particular case $L = \infty$ in our blocking wave problem.
It seems then natural to have $C \geq c^*$.

Blocking waves

More precisely, we have the following result [10]

Theorem

Let $C > 0$ and $L > 0$. For $C > c^*$, there exists $L_*(C) > 0$ such that there exists a (C, L)-barrier if and only if $L \geq L_*(C)$.
Moreover, $C \mapsto L_*(C)$ is decreasing and

$$\lim_{C \to c^*} L_*(C) = +\infty,$$
$$L_*(C) \sim \frac{1}{4C} \log\left(1 - \frac{F(1)}{F(\theta)}\right), \text{ when } C \to +\infty,$$

where $F(x) = \int_0^x f(z)dz$ (thus $F(1) > 0$ and $F(\theta) < 0$).

10. G. Nadin, M. Strugarek, N. V., *Hindrances to bistable front propagation : application to Wolbachia invasion*, J. Math. Biol. 76 (2018), no 6, 1489-1533.

Blocking waves

Proposition

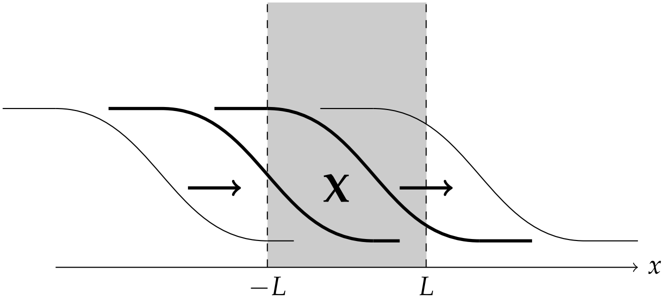
Let $C > 0$ and $L > 0$. We have the following characterisation of $(C, L)-$barrier :

1. Any $(C, L)-$barrier is decreasing.
2. Il $L > L_*(C)$, then there exists at least two $(C, L)-$barriers and they are totally ordered. Then we can define a maximal and a minimal $(C, L)-$barrier.
3. The maximal $(C, L)-$barrier is unstable from above and the minimal $(C, L)-$barrier is stable from below.

Blocking waves

We can draw the following consequences, if $L > L_*(C)$:

- The front cannot cross the minimal $(C, L)-$barrier if it is initially below it.
- The extra cost we have to pay to cross the obstacle is to create a profile above the maximal $(C, L)-$barrier.



Blocking waves : Idea of the proof

1st step : Reduction of the problem.

$$\begin{aligned} & -p'' - Cp' = f(p), && \text{on } [-L, L], \\ & -p'' = f(p), && \text{on } \mathbb{R} \setminus [-L, L], \\ & p(-\infty) = 1, p(+\infty) = 0, p > 0. && \end{aligned}$$

This problem may be reduced to $[-L, L]$ by introcuding $\beta = p(-L)$ and $\alpha = p(L)$. Moreover, since we have conservation of the energy on $(-\infty, -L)$ and $(L, +\infty)$, we obtain the reduced problem

$$\begin{cases} -p'' - Cp' = f(p), \qquad \text{on } [-L, L], \\ p(-L) = \beta, \quad p(L) = \alpha, \\ \frac{1}{2} p'(-L)^2 + F(\beta) = F(1), \quad \frac{1}{2} p'(L)^2 + F(\alpha) = 0. \end{cases} \tag{$\mathcal{P}$}$$

Blocking waves : Idea of the proof

System $(\mathcal{P})$ can be easily interpreted in the phase plane (p, p') [11]. Let $X = p$, $Y = p'$, the system rewrites into

$$
\begin{aligned}
&X' = Y, \quad X(0) = X_0,\\
&Y' = -CY - f(X), \quad Y(0) = Y_0.
\end{aligned}
$$

We define an energy $E : \mathbb{R}^2 \to \mathbb{R}$ by : $E(X,Y) := \dfrac{1}{2}Y^2 + F(X)$.
Two interesting curves appear :

$$
E^{-1}\big(F(1)\big) \supset \Gamma_B := \Big\{(x,y) \in [0,1] \times (-\infty, 0],\, y = -\sqrt{2\big(F(1) - F(x)\big)}\Big\},
$$

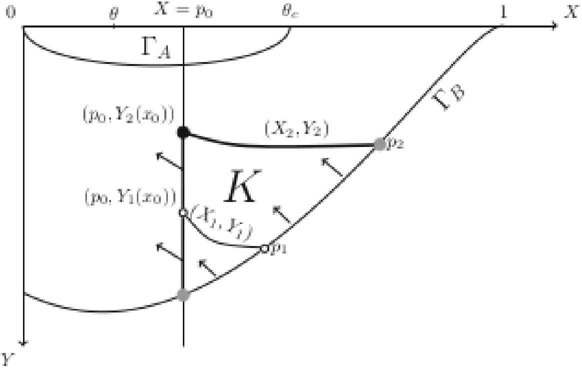
$$
E^{-1}\big(0\big) \supset \Gamma_A := \Big\{(x,y) \in [0,\theta_c] \times (-\infty, 0],\, y = -\sqrt{-2F(x)}\Big\}.
$$

A (C,L)-barrier can be seen there as a trajectory with $\big(X(-L), Y(-L)\big) \in \Gamma_B$ such that $\big(X(L), Y(L)\big) \in \Gamma_A$.

11. T.J. Lewis and J.P. Keener, *Wave-block in excitable media due to regions of depressed excitability*, SIAM Journal on Applied Mathematics, 2000.

Blocking waves : Idea of the proof

Therefore, we are left studying the image of Γ_B by the flow of the differential system.



Blocking waves : Idea of the proof

2nd step : Shooting method.
We assume that $0 < \alpha < \beta < 1$ are given $(\alpha < \theta_c := F^{-1}(0))$. Then we solve the problem : find $C(\alpha,\beta)$ and $L(\alpha,\beta)$ such that the solution to the Cauchy problem

$$
\begin{aligned}
&- p'' - C(\alpha,\beta)p' = f(p), \qquad \text{on } [-L(\alpha,\beta), L(\alpha,\beta)],\\
&p(L(\alpha,\beta)) = \alpha, \quad \frac{1}{2}p'(L(\alpha,\beta))^2 + F(\alpha) = 0,
\end{aligned}
$$

verify $p(-L(\alpha,\beta)) = \beta$, $\frac{1}{2}p'(-L(\alpha,\beta))^2 + F(\beta) = F(1)$.
Because we look for p decreasing, we can invert it into a function $X(p)$. Then we introduce $w(p) = \frac{1}{2}p'(X(p))^2 + F(p)$. We compute

$$
\begin{aligned}
w'(p) &= p''(X(p))X'(p)p'(X(p)) + f(p) = p'' + f(p)\\
&= C(\alpha,\beta)\sqrt{2(w(p) - F(p))}.
\end{aligned}
$$

Blocking waves : Idea of the proof

Thus we look for a function w on $[\alpha, \beta]$ solution to the Cauchy problem

$$w'(p) = C(\alpha, \beta)\sqrt{2(w(p) - F(p))}, \quad w(\alpha) = 0,$$

such that $w(\beta) = F(1)$. We use a shooting method.
Once this function is constructed, we notice that we have

$$L(\alpha, \beta) = \frac{1}{2}(X(\alpha) - X(\beta)) = \frac{1}{2}\int_\beta^\alpha X'(p)\,dp = \frac{1}{2}\int_\beta^\alpha \frac{dp}{p'(X(p))}$$
$$= \frac{1}{2}\int_\alpha^\beta \frac{1}{\sqrt{2(w(p) - F(p))}}dp.$$

Blocking waves : Idea of the proof

Summary

For any $0 < \alpha < \beta < 1$, with $\alpha < \theta_c$, there exists a unique $C(\alpha, \beta)$ such that the reduced problem $(\mathcal{P})$ has a unique solution. Then $L(\alpha, \beta)$ is given by the above expression.

Blocking waves : Idea of the proof

Summary

For any $0 < \alpha < \beta < 1$, with $\alpha < \theta_c$, there exists a unique $C(\alpha, \beta)$ such that the reduced problem $(\mathcal{P})$ has a unique solution. Then $L(\alpha, \beta)$ is given by the above expression.

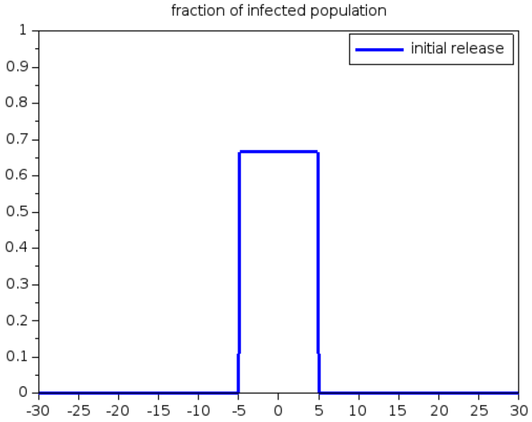
3rd step : For $C > c^*$ and L, find α, β such that $C = C(\alpha, \beta)$ and $L = L(\alpha, \beta) = \frac{1}{2} \int_\alpha^\beta \frac{1}{\sqrt{2(w(p) - F(p))}} dp$.
We use monotony and continuity argument from comparison principles on the system $(\mathcal{P})$.

Some references :

- J. Pauwelussen, *One way traffic of pulses in a neuron*, J. Math. Biol., 1982
- T.J. Lewis and J.P. Keener, *Wave-block in excitable media due to regions of depressed excitability*, SIAM Journal on Applied Mathematics, 2000.
- G. Chapuisat and R. Joly, *Asymptotic profiles for a traveling front solution of a biological equation*, Math. Mod. Methods Appl. Sci., 2011.
- H. Berestycki, N. Rodriguez, L. Ryzhik, *Traveling wave solutions in a reaction-diffusion model for criminal activity*, SIAM MMS, 2013.

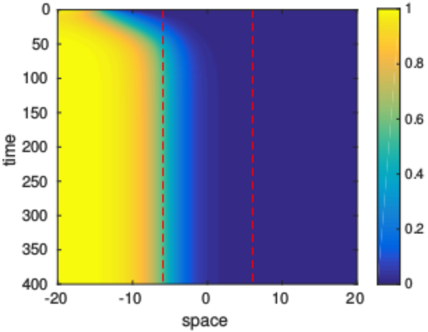
Blocking waves : numerical example

In the following example, we consider the previous model for Wolbachia invasion and consider that $C = 0.07$ on the domain $[-20, -10]$.



Blocking waves : numerical examples

We assume now that $\partial_x \log(N) = \begin{cases} \frac{C}{2}, & \text{on } [-L, L]; \\ 0, & \text{on } \mathbb{R} \setminus [-L, L]. \end{cases}$



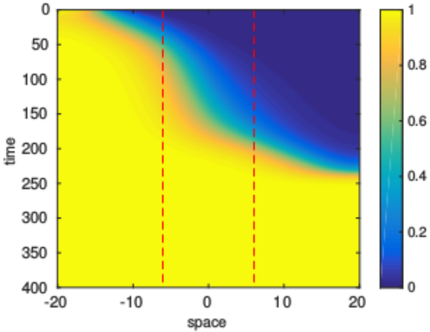


FIGURE – Left : Blocking with $L = 6$ and $C = 0.5$; Right : Propagation with $L = 6$ and $C = 0.2$.

Blocking waves : numerical examples

We assume now that $\partial_x \log(N) = \begin{cases} \frac{C}{2}, & \text{on } [-L,L]; \\ 0, & \text{on } \mathbb{R}\setminus[-L,L]. \end{cases}$

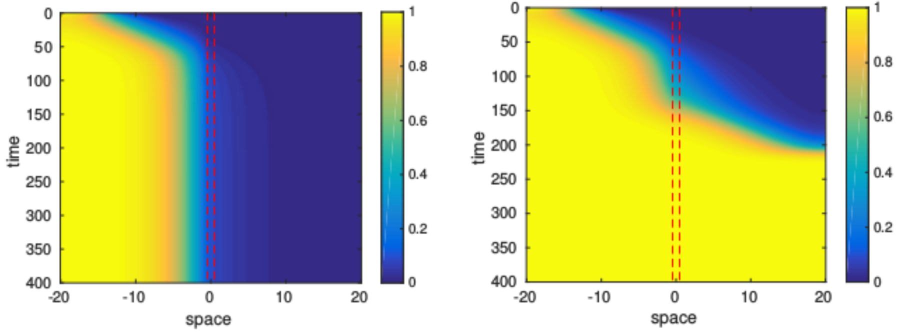


FIGURE – Left : Blocking with $L = 0.5$ and $C = 2$; Right : Propagation with $L = 0.5$ and $C = 1$.

Conclusion and perspectives

With these studies we have answered to some question related to the *replacement strategy* (using *Wolbachia*) and to the *Sterile/Incompatible Insect Technique*. In particular,

- The success of the spatial propagation of the Wolbachia-infected population depends strongly on the position of the releases, which must be done in a sufficiently large area with a sufficient amount of mosquitoes.
- Spatial heterogeneities in the environment may block the propagation.
- Neglecting the spatial dependancy, the study of the success of these strategies may be performed and optimized.

However, this study is not complete and there is still many mathematical questions to solve, for instance :

- Better description of the optimal shape of the release function.
- Extend the study to the system of equation.
- Mathematics are also really useful to study the time dynamics of mosquitoes life cycle.

Conclusion and perspectives

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