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Abstract. In order to prevent the propagation of human diseases transmitted by mosquitoes (as dengue or zika), a solution is to release mosquitoes infected by *Wolbachia*. In this study, we model the release and the propagation over time and space of such infected mosquitoes in a population of uninfected ones. The aim of this study is to investigate the best location in space of the release to ensure invasion by the infected mosquitoes.

Résumé. Afin de prévenir la propagation de maladies transmises à l'homme par les moustiques (comme la dengue ou le zika), une solution consiste à relâcher des moustiques infectés par la bactérie *Wolbachia*. Dans cette étude, nous modélisons le relâcher et la propagation dans le temps et l'espace de ces moustiques infectés dans une population de moustiques hôtes non infectés. Le but de cette étude est d'étudier le meilleur emplacement dans l'espace des relâchers afin d'assurer l'invasion par les moustiques infectés.

Introduction

Aedes aegypti is the main vector transmitting dengue viruses. This mosquito can also transmit chikungunya, yellow fever and Zika infection. According to the World Health Organization, 390 million people are infected by dengue every year and 3.9 billion people, in 128 countries, are at risk of infection by dengue viruses. As there is no treatment for dengue fever, the current method of preventing dengue

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virus transmission and epidemics is to target the vector, i.e. the mosquito. Beyond preventing mosquitoes from accessing egg-laying habitats by environmental management and modification, one of the most promising control techniques is to transform mosquito population with a virus-suppressing *Wolbachia* bacteria. The idea of using *Wolbachia* for disease control was first proposed in the 1960s [8] but applying it to *Aedes aegypti* population is very recent. *Wolbachia* bacterium strains were isolated from *Drosophila melanogaster* in laboratory just before 2000 [7, 10] but were introduced into *Aedes aegypti* embryos only on 2009 [11]. The capability of this bacteria to suppress dengue virus and other pathogens transmission by *Aedes aegypti* was shown in laboratory around 2010 [12, 2, 21]. It was also shown that this bacteria shortens life span [22] and most of the infected adults do not reach the infectious stage. But the most important modification induced by the bacteria is cytoplasmic incompatibility (CI) [11]. Cytoplasmic incompatibility is used by the bacteria to spread rapidly into natural population [18] by producing non-viable eggs when uninfected females mate with infected males. Reproduction between infected males and females lead to infected eggs. As this bacteria is vertically transmitted (from mother to off-springs), uninfected males mating with infected females give rise only to infected eggs.

Formally, a proportion $1 - s_h$ of uninfected female's eggs fertilized by infected males actually hatch. Cytoplasmic incompatibility is complete when $s_h = 1$. We denote by b_1, respectively b_2, the net fecundity rate of uninfected females, respectively infected females. Death rate for uninfected mosquitoes is denoted d_1. As *Wolbachia* decreases lifespan, death rate of infected mosquitoes d_2 verifies $d_2 > d_1$. Is is also observed that *Wolbachia* infected mosquitoes tend to have reduced fertility, then $b_2 \leq b_1$. Finally, we denote κ the carrying capacity. Cytoplasmic incompatibility and vertical transmission drive the spatial spread of the infected population producing a bistable dynamic of *Wolbachia* [19]. If the infected population is installed above a sufficient threshold frequency Θ compared to the uninfected population, it will spread and tend to increase to 1, otherwise it will tend to decline to zero.

We are interested on optimizing the release of *Wolbachia*-infected mosquitoes into a wild host population of mosquitoes. We denote u the release function.

For fixed maximal time $T > 0$ and domain Ω, the system of equation that we consider is the following:

$$
(1) \quad \begin{cases} \partial_t n_1 - D\Delta n_1 = b_1 n_1 (1 - s_h \dfrac{n_2}{n_1+n_2})(1 - \dfrac{n_1+n_2}{\kappa}) - d_1 n_1 & \text{in } \Omega, \\ \partial_t n_2 - D\Delta n_2 = b_2 n_2 (1 - \dfrac{n_1+n_2}{\kappa}) - d_2 n_2 + u & \text{in } \Omega, \\ \partial_\nu n_1 = \partial_\nu n_2 = 0 & \text{on } \partial\Omega, \\ n_1(0,x) = n_1^0(x), \quad n_2(0,x) = n_2^0(x) & \text{in } \Omega. \end{cases}
$$

The system of equations (1) models the propagation across time and space of the infected-mosquito population n_2 into an already existing uninfected mosquito population n_1. The two coupled equation driving the dynamics of n_1 and n_2 are classical bi-stable reaction-diffusion equations. Note that in the reaction term of the first equation the term $-\frac{n_2}{n_1+n_2}$ stands for the vertical transition of the disease whereas the coefficient s_h models that this vertical transmission may or not be perfect because of the cytoplasmic incompatibility. The diffusion coefficient is denoted D; it is assumed to be the same for both population since both populations belongs to

the same genus of mosquitoes. The last term of the second equation $+u$ stands here to model the releases of infected mosquitoes developed in laboratory: it is on this control that we will act upon. More precisely, a question we want to address in this work is to know what should be the shape of the release function u to be as close as possible to the total invasion of the infected population into the domain.

The outline of this paper is the following. In the next section, we introduce the optimal control problem and prove the existence of an optimum for this problem. In Section 2, we consider a toy problem, which is a very simplified version of the full problem, for which we can solve explicitly the optimal problem and find the optimum. In Section 3, we investigate numerically the optimization of the spatial releases of mosquitoes. Finally, we end this paper with a conclusion and perspective for future works. An appendix is devoted to recalling the reduction of system (1).

1. Optimal Control Problem

We are going to simplify the problem. Instead of studying the coupled equations (1), we are going to follow the proportion of mosquitoes $p(t,x) = \frac{n_2(t,x)}{n_1(t,x)+n_2(t,x)}$ as in [15]. This reduction is clearly justified in the limit of large population in [15] (see also [1, Section 2.3]). The formal computation is explained in the Appendix. In order to simplify the reading, we perform the scaling $x = \frac{\tilde{x}}{\sqrt{D}}$ not to keep the diffusion coefficient along the computations. Obviously, for the numerical simulations performed in Section 3, we have to keep in mind this scaling.

Denoting by p the proportion of infected mosquitoes, and u the release function, the dynamics is governed by the reaction-diffusion equation

$$\begin{cases} \dfrac{\partial p}{\partial t} - \Delta p = f(p) + ug(p), & t \in (0,T), \quad x \in \Omega, \\ \partial_\nu p(t,x) = 0, & x \in \partial\Omega, \\ p(0,x) = 0, & x \in \Omega, \end{cases} \tag{2}$$

where

$$f(p) = p(1-p)\frac{d_1b_2 - d_2b_1(1-s_hp)}{b_1(1-p)(1-s_hp) + b_2p} \quad \text{and} \quad g(p) = \frac{1}{\kappa}\cdot\frac{b_1(1-p)(1-s_hp)}{b_1(1-p)(1-s_hp) + b_2p}. \tag{3}$$

The general optimal control problem we want to investigate involves the least-squares functional J defined by

$$\hat{J}(u) = \frac{1}{2}\int_\Omega (1 - p(T,x))^2\, dx, \tag{4}$$

which models that one aims at steering the system as close as possible to the target state. In some sense, it stands for the research of a control strategy ensuring the persistence of infected mosquitoes at the time horizon T.

Of course, it is relevant from the biological point of view to impose several constraints on the control function u. Indeed, the production of *Wolbachia*-infected mosquitoes is limited, which imposes that the total number of mosquitoes released is bounded. Hence, the control function u is assumed to belong to the set

$$\mathcal{U}_{T,C,M} = \left\{ u \in L^\infty([0,T]\times\Omega), \quad 0 \le u \le M \text{ a.e. }, \int_0^T \int_\Omega u(t,x)\, dxdt \le C \right\}. \tag{5}$$

modeling an upper limit on the instantaneous number of *Wolbachia*-infected individuals released at time t, as well as on the total number of released mosquitoes.

We then deal with the following optimal control problem:

$$(\mathcal{P}_{\text{full}}) \qquad \boxed{\inf_{u\in\mathcal{U}_{T,C,M}} \hat{J}(u).}$$

Since this problem involves the minimization over function depending on time and space variables, it is difficult to study. Then, we will reduce it to a simpler one by assuming that the time distribution of the control function is given.

1.1. **Modeling of the optimal control problem.** In order to weaken the difficulty of Problem ($\mathcal{P}_{\text{full}}$), we introduce a simpler, although still relevant, problem by assuming that:

- releases are done periodically in time (for instance every week) and are impulses in time[1];
- at each release, the largest allowed amount of mosquitoes is released, corresponding to the maximal production capacity per week (which is relevant, according to the comparison principle).

As a consequence, we will be interested in determining the optimal way of releasing spatially the infected mosquitoes. Let us denote by $t_0 = 0 < t_1 < \ldots < t_N = T$, $t_i = i\Delta T$, the release times. Rewriting the L^1 constraint on the control as $\langle u, 1\rangle_{\mathcal{D}',\mathcal{D}((0,T)\times\Omega)} \leq C$, the control function reads

$$u(t,x) = \sum_{i=0}^{N-1} u_i(x)\delta_{\{t=t_i\}}, \qquad \text{with } \sum_{i=0}^{N-1}\int_\Omega u_i(x)\,dx \leq C,$$

where the pointwise constraint is modified into $0 \leq u_i(\cdot) \leq M$.

The new optimal design problem reads

$$(\mathcal{P}'_{\text{full}}) \quad \inf_{\mathbf{u}\in\mathcal{V}_{T,C,M}} \tilde{J}(\mathbf{u}), \quad \text{where } \mathbf{u} = (u_i)_{0\leq i\leq N-1}, \quad \tilde{J}(\mathbf{u}) = J\left(\sum_{i=0}^{N-1} u_i(\cdot)\delta_{\{t=t_i\}}\right)$$

and

$$\mathcal{V}_{T,C,M} = \Bigg\{ \mathbf{u} = (u_i(\cdot))_{0\leq i\leq N-1},$$
$$0 \leq u_i \leq M \text{ a.e. in } \Omega,\ i\in\{0,\ldots,N-1\},\ \sum_{i=0}^{N-1}\int_\Omega u_i(x)\,dx \leq C\Bigg\}.$$

It is possible to recast System (2) without source measure terms, coming from the specific form of the control functions. For the sake of simplicity, we provide here a naive formal analysis, but claim that this can be proven rigorously by using a standard variational analysis.

Let us approximate the Dirac measure at $t = t_i$ by the function $\frac{1}{\varepsilon}\mathbf{1}_{[t_i,t_i+\varepsilon]}$. Making the change of variable $t = t_i + \tau\epsilon$, and introducing $\tilde{p}$ given by $\tilde{p}(\tau,x) = p(t,x)$, one gets from system (2) that $\tilde{p}$ solves

$$\frac{\partial\tilde{p}}{\partial\tau} - \varepsilon\Delta\tilde{p} = \varepsilon f(\tilde{p}) + u_i g(\tilde{p}). \qquad \tau\in[0,1],\ x\in\Omega.$$

[1]We consider Dirac measures since at the time-level of the study (namely, some generations), the release can be considered as instantaneous.

Letting formally ε go to 0 and denoting, with a slight abuse of notation, still by $\tilde{p}$ the formal limit of the system above yields

$$\frac{\partial \tilde{p}}{\partial \tau}(\tau, x) = u_i(x) g(\tilde{p}(\tau, x)), \qquad \tau \in [0,1],\ x \in \Omega. \tag{6}$$

Let us denote G the anti-derivative of $\frac{1}{g}$ vanishing at 0, namely

$$G(p) = \int_0^p \frac{dq}{g(q)}.$$

Then, by a direct integration of (6) on $[0,1]$, we obtain

$$G(\tilde{p}(1,x)) = G(\tilde{p}(0,x)) + u_i(x), \qquad x \in \Omega.$$

Coming back on the function p yields

$$p(t_i^+, x) = G^{-1}(G(p(t_i^-, x)) + u_i(x)), \qquad x \in \Omega.$$

Hence we arrive at the system

$$\begin{cases} \dfrac{\partial p}{\partial t} - \Delta p = f(p), & t \in (0,T) \setminus \{t_i\}_{i \in \{1,\dots,N-1\}}, \quad x \in \Omega, \\ \partial_\nu p(t,x) = 0, & x \in \partial\Omega, \\ p(0^+, \cdot) = G^{-1}(u_0(\cdot)), & \\ p(t_i^+, \cdot) = G^{-1}\left(G(p(t_i^-, \cdot)) + u_i(\cdot)\right), & i \in \{1, \dots, N-1\} \end{cases} \tag{7}$$

and the optimization problem reads

$$\boxed{\inf_{\mathbf{u} \in \mathcal{V}_{T,C,M}} J(\mathbf{u}) \quad \text{with } J(\mathbf{u}) = \frac{1}{2}\int_\Omega (1 - p(T,x))^2\, dx}, \tag{$\mathcal{P}_{\text{reduced}}$}$$

where p is the solution of (7). In the next Section, we investigate the existence of solutions for this problem.

1.2. **Existence of minimizers.**

Theorem 1. *Problem* ($\mathcal{P}_{\text{reduced}}$) *has a solution.*

Proof. For the sake of readability, we only provide the proof in the case $N = 2$. Indeed, there is no additional difficulty to deal with the general case whose proof follows exactly the same lines. The proof is divided into several steps.

Let $u^n = \{u_i^n\}_{i \in \{1,\dots,N\}} \in (\mathcal{V}_{T,C,M})^{\mathbb{N}}$ be a minimizing sequence for Problem ($\mathcal{P}_{\text{reduced}}$).

Notice that, since u belongs to $\mathcal{V}_{T,C,M}$ and G^{-1} takes its value in $[0,1[$, we infer from the maximum principle that $0 \le p(t,\cdot) < 1$ for a.e. $t \in [0,T]$ so that one has for all $u \in \mathcal{V}_{T,C,M}$

$$0 \le J(u) \le \frac{|\Omega|}{2}.$$

It follows that $\inf_{u \in \mathcal{V}_{T,C,M}} J(u)$ belongs to $(0, \frac{|\Omega|}{2})$ and, in particular, is finite.

Step 1: *Convergence of the minimizing sequence.*
Let p^n be the solution to (7) associated to the control function u^n and let us

introduce

$$\begin{aligned} v_0^n(.) &= u_0^n(.) \\ v_1^n(.) &= G^{-1}(G(p^n(t_1^-,.)) + u_1^n(.)). \end{aligned}$$

By induction, one easily shows that v^n is uniformly bounded in L^∞. Since the class $\mathcal{V}_{T,C,M}$ is closed for the L^∞ weak-star topology, there exists $v^\infty \in \mathcal{V}_{T,C,M}$ such that, up to a subsequence, v^n converges weakly-star to v^∞ in L^∞. Here and in the sequel, we will denote similarly with a slight abuse of notation a given sequence and any subsequence.

Multiplying the main equation of (7) by p^n and integrating by parts, we infer from the above estimates the existence of a positive constant C such that

$$\frac{1}{2}\int_0^T\int_\Omega \partial_t(p^n(t,x)^2)dxdt + \int_0^T\int_\Omega |\nabla p^n(t,x)|^2 dxdt \leq C$$

for every $n \in \mathbb{N}$, which also reads

$$\frac{1}{2}\int_\Omega \left(\left[(p^n(t,x))^2)\right]_{t=0}^{t=t_1} + \left[(p^n(t,x))^2)\right]_{t=t_1}^{t=T} \right) dx + \int_0^T\int_\Omega |\nabla p^n(t,x)|^2 \, dxdt \leq C$$

for every $n \in \mathbb{N}$.

By using the pointwise bounds on p^n, it follows that p^n is uniformly bounded in $L^2([0,T], H^1(\Omega))$. Furthermore, by using (7), one gets that the sequence $\partial_t p^n$ is uniformly bounded in $L^2([0,T], W^{-1,1}(\Omega))$. According to the Aubin-Lions theorem (see [14]) we infer that p^n converges (up to a subsequence) to $p^\infty \in L^2([0,T], H^1(\Omega))$, strongly in $L^2([0,T], L^2(\Omega))$ and weakly in $L^2([0,T], H^1(\Omega))$. Passing to the limit in (7) yields that p^∞ is a weak solution to

$$\begin{cases} \partial_t p^\infty - \Delta p^\infty = f(p^\infty), & t \in (0,T), \quad x \in \Omega, \\ \partial_\nu p^\infty(t,x) = 0, & t \in (0,T), \quad x \in \partial\Omega, \end{cases} \tag{8}$$

It is standard that any solution to this bistable reaction-diffusion equation is continuous in time.

Introducing $u_0^\infty := G(p^\infty(0^+,.))$ and $u_1^\infty := G(v_1^\infty) - G(p^\infty(t_1^-,.))$, one shows that $p^\infty(t_1^-,.) = v_1^\infty(.)$ by passing to the limit as $n \to +\infty$ in the variational formulation on p^n, using adapted test-functions belonging to

$$V_1 = \left\{ q \in C^\infty([0,T[, C^\infty(\Omega) \cap C^0(\bar{\Omega})) \text{ whose support is contained in } [t_i, t_{i+1}[\right\}.$$

This is a consequence of the weak convergence of p^n in $H^1(\Omega)$ to p^∞. Notice, in particular, that $G(v_1^n)$ converges weakly star in L^∞ to $G(v_1^\infty)$, which is a consequence of the continuity and convexity[2] of G for $p \in [0,1)$.

Step 2: *Conclusion.*
Let us first show that u^∞ belongs to $\mathcal{V}_{T,C,M}$. Since the derivative of G is $1/g$ which is positive, G is increasing and therefore, one has $0 \leq u^\infty \leq m$ a.e. in Ω.
For the integral condition (namely, $\int_\Omega u \leq C$), let us distinguish between two cases:

Case 1: if $m|\Omega| \leq C$, the conclusion follows immediately.

---

[2]Indeed, one has $G''(p) = \kappa b^2 \dfrac{(1 - s_h p^2)}{((p-1)(s_h p - 1))^2}$. which is positive whenever p belongs to $[0,1]$.

Case 2: if $m|\Omega| > C$, let us use that G is, as aforementioned, lower semi-continuous for the weak-star topology of L^∞. Thus, we deduce that

$$\int_\Omega u^\infty = \int_\Omega G(v^\infty) \leq \liminf_{n\to+\infty} \int_\Omega G(v^n) = \liminf_{n\to+\infty} \int_\Omega u^n \leq C.$$

It follows that u^∞ belongs to $\mathcal{V}_{T,C,M}$ and one concludes by using the Fatou Lemma:

$$\begin{aligned} J(u^\infty) = \frac{1}{2}\int_\Omega (1-p^\infty(T,x))^2 dx &= \frac{1}{2}\int_\Omega \liminf_{n\to+\infty} (1-p^n(T,x))^2 dx \\ &\leq \liminf_{n\to+\infty} \frac{1}{2}\int_\Omega (1-p^n(T,x))^2 dx = \liminf_{n\to+\infty} J(u_n) = \inf_{u\in\mathcal{V}_{T,C,M}} J(u). \end{aligned}$$

We finally infer that u^∞ solves Problem $(\mathcal{P}_{\text{reduced}})$. □

Remark 1. *The uniqueness issue remains open, even for simple domain. It is likely that symmetries of the release domain play an important role.*

It is interesting to notice that, in a very particular case, we have an explicit expression of the minimizer for this problem.

Proposition 1. *Let $N \in \mathbb{N}^*$ and $M \leq \frac{C}{|\Omega|}$. Then $u = M$ is the unique solution of Problem $(\mathcal{P}_{\text{reduced}})$.*

Proof. It is a direct application of the comparison principle. Let u^* be a solution of Problem $(\mathcal{P}_{\text{reduced}})$. By contradiction, let us assume that u^* is not identically equal to M a.e. in Ω. Then, let t_i be a release time for which the associated control function u_i^* is not identically equal to M in Ω. Recall that $u_i^* \leq M$. Let us denote by $p*$ the solution of the problem (2) associated to the control function u^*. Let u^M be the control function defined by

$$u_i^M = M \quad \text{and} \quad u_j^M = u_j^* \quad \text{for all } j \in \{0,\dots,N-1\}\backslash\{i\}.$$

Let p^M be the solution of (2) associated to u^M identically. Since G^{-1} is an increasing function by the comparison principle we have for all time $t \in [0,T]$ and a.e. $x \in \Omega$,

$$0 < p^*(t,x) \leq p^M(t,x) < 1.$$

Evaluating this expression at time $t = T$, the expected conclusion follows by noting that the constant function equal to M on $(0,T)\times\Omega$ belongs to $\mathcal{U}_{T,C,M}$. □

1.3. **Computation of derivatives.** As a preliminary remark, we claim that for any element $\mathbf{u}$ of the set $\mathcal{V}_{T,C,M}$ and any admissible perturbation $\mathbf{h}$, the mapping $\mathcal{V}_{T,C,M} \ni \mathbf{u} \mapsto p \in L^2(0,T,H^1(\Omega))$, where p denotes the unique weak solution of (7), is differentiable in the sense of Gâteaux at $\mathbf{u}$ in the direction $\mathbf{h}$. Indeed, proving such a property is standard in calculus of variations and rests upon an application of the implicit function theorem. In the sequel, and with no confusion possible, we will denote by $\dot{p}$ the Gâteaux-differential of p at $\mathbf{u}$ in direction $\mathbf{h}$ and by $\langle dJ(\mathbf{u}), \mathbf{h}\rangle$ the Gâteaux-differential of J at $\mathbf{u}$ in direction $\mathbf{h}$, namely

$$\langle dJ(\mathbf{u}), \mathbf{h}\rangle = \lim_{\varepsilon\searrow 0} \frac{J(\mathbf{u}+\varepsilon\mathbf{h}) - J(\mathbf{u})}{\varepsilon}.$$

Let us make the cone of admissible perturbations precise. We call "admissible perturbation" any element of the tangent cone $\mathcal{T}_{\mathbf{u},\mathcal{V}_{T,C,M}}$ to the set $\mathcal{V}_{T,C,M}$ at $\mathbf{u}$.

Definition 1. *The cone $\mathcal{T}_{\mathbf{u},\mathcal{V}_{T,C,M}}$ is the set of N-tuples $\mathbf{h} = (h_0, \dots, h_{N-1}) \in (L^\infty(\Omega))^N$ such that, for any $i \in \{0, \dots N-1\}$ and for any sequence of positive real numbers ε_n decreasing to 0, there exists a sequence of functions $h_i^n \in L^\infty(0,T)$ converging to h_i as $n \to +\infty$, and $u_i + \varepsilon_n h_i^n \in \mathcal{V}_{T,C,M}$ for every $n \in \mathbb{N}$ (see e.g. [5]).*

Proposition 2. *Assume that $N = 1$. Let $\mathbf{u} = (u_0) \in \mathcal{V}_{T,C,M}$ and $\mathbf{h} = (h_0) \in \mathcal{T}_{\mathbf{u},\mathcal{V}_{T,C,M}}$. One has*

$$\langle dJ(\mathbf{u}), \mathbf{h}\rangle = \int_\Omega h(x)(G^{-1})'(u_0(x))q(0,x)\,dx,$$

where q is the unique solution of the backward problem

$$\begin{cases} -\partial_t q(t,x) - \Delta q(t,x) - f'(p(t,x))q(t,x) = 0, & (t,x) \in (0,T)\times\Omega, \\ \partial_n q(t,x) = 0, & (t,x) \in (0,T)\times\partial\Omega, \\ q(T,x) = p(T,x) - 1, & x \in \Omega. \end{cases}$$

Proof. By using the preliminary discussion, one has

$$\langle dJ(\mathbf{u}), \mathbf{h}\rangle = \int_\Omega \dot p(T,x)(p(T,x)-1)\,dx, \tag{9}$$

where $\dot p$ denotes the unique solution of the system

$$\begin{cases} \dfrac{\partial \dot p}{\partial t} - \Delta \dot p = f'(p)\dot p, & t \in (0,T), \quad x \in \Omega, \\ \partial_\nu \dot p(t,x) = 0, & x \in \partial\Omega, \\ \dot p(0^+,\cdot) = (G^{-1})'(u_0(\cdot))h. \end{cases} \tag{10}$$

Let us multiply the main equation of this system by q and then integrate by parts with respect to the variables t and x. By using in particular the Green formula, we get successively that

$$\begin{aligned} \int_0^T\int_\Omega q\frac{\partial \dot p}{\partial t}\,dxdt &= -\int_0^T\int_\Omega \dot p\frac{\partial q}{\partial t}\,dxdt + \int_\Omega q(T,x)\dot p(T,x)\,dx - \int_\Omega q(0,x)\dot p(0^+,x)\,dx, \\ -\int_0^T\int_\Omega q\Delta\dot p\,dxdt &= -\int_0^T\int_\Omega \dot p\Delta q\,dxdt, \end{aligned}$$

and therefore,

$$\langle dJ(\mathbf{u}), \mathbf{h}\rangle = \int_\Omega q(T,x)\dot p(T,x)\,dx = \int_\Omega q(0,x)\dot p(0^+,x)\,dx,$$

yielding the desired conclusion. □

Remark 2. *For practical purposes, it may be useful to notice that*

$$q(t,x) = \widetilde q(T-t,x), \qquad t \in [0,T],\ x \in \Omega,$$

where $\widetilde q$ denotes the solution of the initial boundary value problem

$$\begin{cases} \partial_t \widetilde q(t,x) - \Delta\widetilde q(t,x) - f'(p(T-t,x))\widetilde q(t,x) = 0, & (t,x) \in (0,T)\times\Omega, \\ \partial_n \widetilde q(t,x) = 0, & (t,x) \in (0,T)\times\partial\Omega, \\ \widetilde q(0,x) = p(T,x) - 1, & x \in \Omega. \end{cases}$$

2. A toy Problem

This section is devoted to investigating a simpler version of $(\mathcal{P}_{\text{full}})$ corresponding to the case $N = 1$ with $f = 0$. More precisely, let p be the solution of

$$\begin{cases} \dfrac{\partial p}{\partial t} - \Delta p = 0, & t \in (0,T), \quad x \in \Omega, \\ \partial_\nu p(t,x) = 0, & x \in \partial\Omega, \\ p(0^+,\cdot) = u_0(\cdot). \end{cases} \tag{11}$$

Then, the optimization toy problem reads

$$\boxed{\inf_{u_0 \in \mathcal{V}_{T,C,M}} \hat{J}(u_0) \quad \text{with } \hat{J}(u_0) = \frac{1}{2}\int_\Omega (1 - p(T,x))^2\, dx} \tag{$\mathcal{P}_{\text{toy}}$}$$

where $p \in C^0([0,T], L^2(\Omega))$ is the unique solution of Equation (11). Note that the equation (11) has to be understood in a weak sense, since $u_0 \in L^\infty(\Omega) \subset L^2(\Omega)$ (see for example [17, Section 10.7]).

For this simple problem, we are able to solve explicitely the optimization problem :

Theorem 2. *Problem* (11) *has a unique solution* u_0*, which is constant and equal to* $\min\left(1, M, \frac{C}{|\Omega|}\right)$.

Proof. First, note that Problem $(\mathcal{P}_{\text{toy}})$ has a solution. Indeed, it is standard that the mapping $L^2(\Omega) \ni u_0 \mapsto p \in C^0([0,T], L^2(\Omega))$ is continuous. Therefore, so is $\hat{J}$ by composition of continuous mappings. The conclusion follows by observing that $\mathcal{V}_{T,C,M}$ is a compact subset of $L^2(\Omega)$.

The proof relies on a well-adapted rewriting of the criterion $\hat{J}$. For that purpose, let us introduce the Neumann operator $-\Delta_N$ on Ω defined on

$$\mathcal{D}(-\Delta_N) = \{y \in H^2(\Omega) \mid \frac{\partial y}{\partial n}_{|\partial\Omega} = 0 \text{ and } \int_\Omega y(x)\, dx = 0\}.$$

According to the spectral theorem, there exists an orthonormal family $(\phi_j)_{j\geq 1}$ consisting of (real-valued) eigenfunctions of $-\Delta_N$, associated with the non-decreasing sequence positive eigenvalues $(\lambda_j)_{j\geq 1}$. Moreover, by setting $\lambda_0 = 0$ and $\phi_0 = \frac{1}{\sqrt{|\Omega|}}$, the sequence $(\phi_j)_{j\geq 0}$ is a Hilbert basis of $L^2(\Omega)$ and any solution p of (11) can be expanded in a unique way in $L^2(\Omega)$ as

$$p(t,x) = \sum_{j=0}^{+\infty} \langle p(0,\cdot), \phi_j\rangle_{L^2(\Omega)} e^{-\lambda_j t}\phi_j(x) = \sum_{j=0}^{+\infty} u_{0j} e^{-\lambda_j t}\phi_j(x), \tag{12}$$

with $u_{0j} = \langle u_0, \phi_j\rangle_{L^2(\Omega)}$. By expanding the square in the definition of $\hat{J}$, we then infer that

$$\begin{aligned} \hat{J}(u_0) &= \frac{|\Omega|}{2} - \int_\Omega p(T,x)\, dx + \frac{1}{2}\int_\Omega p(T,x)^2\, dx \\ &= \frac{|\Omega|}{2} - \sqrt{|\Omega|}u_{00} + \frac{1}{2}\sum_{j=0}^{+\infty} e^{-2\lambda_j T} u_{0j}^2 \\ &= \frac{|\Omega|}{2} - \int_\Omega u_0(x)\, dx + \frac{1}{2}\sum_{j=0}^{+\infty} e^{-2\lambda_j T}\left(\int_\Omega u_0(x)\phi_j(x)\, dx\right)^2. \end{aligned}$$

Let u be a solution of Problem (11) and $h \in \mathcal{T}_{u_0,\mathcal{V}_{T,C,M}}$. Then, one has

$$\begin{aligned}\langle d\hat{J}(u_0), h\rangle &= -\int_\Omega h(x)\,dx + \sum_{j=0}^{+\infty} e^{-2\lambda_j T}\left(\int_\Omega u_0(x)\phi_j(x)\,dx\right)\left(\int_\Omega h(x)\phi_j(x)\,dx\right)\\ &= \int_\Omega h(x)\psi(x)\,dx,\end{aligned}$$

where $\psi(x) = -1 + \sum_{j=0}^{+\infty} e^{-2\lambda_j T} u_{0j}\phi_j(x)$.

The first order optimality conditions reads

$$\langle d\hat{J}(u_0), h\rangle \geq 0, \qquad \forall h \in \mathcal{T}_{u_0,\mathcal{V}_{T,C,M}}. \tag{13}$$

The analysis of such optimality condition is standard in optimal control theory (see for example [9]) and yields the existence of a Lagrange multiplier $\xi \leq 0$ such that

- on $\{u_0 = M\}$, $\psi(x) \leq \xi$,
- on $\{u_0 = 0\}$, $\psi(x) \geq \xi$,
- on $\{0 < u_0 < M\}$, $\psi(x) = \xi$,
- $\xi\left(\int_\Omega u_0(x)\,dx - C\right) = 0$ (complementarity condition).

Let us investigate the optimality of constant functions. To this aim, notice that the functional $\hat{J}$ is strictly convex[3]. It follows that the optimality conditions (13) are at the same time necessary and sufficient and that Problem (11) has a unique solution.

Let u_0 be an admissible constant function for Problem ($\mathcal{P}_{\text{toy}}$). Then, $u_0 \in [0, M]$ whenever $M \leq C/|\Omega|$ and $u_0 \in [0, C/|\Omega|]$ elsewhere.

Furthermore, if u_0 is constant, then,

$$\psi(x) = -1 + u_0.$$

Let us now investigate each case separately. If $u_0 = 0$, then, from the complementarity condition, $\xi = 0$ and $\psi(x) = -1$ which is in contradiction with the optimality conditions above. Let us assume that $u_0 \neq 0$.

- If $u_0 = \frac{C}{|\Omega|}$, then this is admissible only if $C \leq M|\Omega|$. In this case we find $\psi(x) = \frac{-|\Omega|+C}{|\Omega|}$, and thus the optimality conditions are satisfied if and only if $|\Omega| \geq C$. All in all, $u_0 = \frac{C}{|\Omega|}$ is indeed a solution if, and only if, $\min(1, M)|\Omega| \geq C$.
- If $u_0 \neq \frac{C}{|\Omega|}$: then $\xi = 0$. Either $u_0 = M$, in which case the optimality conditions are satisfied only if $M \leq 1$, and this solution is admissible only if $M|\Omega| \leq C$; or $0 < u_0 < M$, in which case the optimality conditions hold only if $u_0 = 1$ (since $\psi \equiv \xi = 0$ in this case), which is admissible only if $M \geq 1$ and $|\Omega| \leq C$. All in all, $u_0 = \min(1, M)$ is a solution if and only if $\min(1, M)|\Omega| \leq C$.

The conclusion follows.

□

[3]The convexity results from the convexity of the square function combined with the linearity of $u_0 \mapsto p(T, \cdot)$. Furthermore,

$$\langle d^2\hat{J}(u_0), h, h\rangle = \sum_{j=0}^{+\infty} e^{-2\lambda_j T}\left(\int_\Omega h(x)\phi_j(x)\,dx\right)^2 \geq 0$$

and vanishes if, and only if, $\int_\Omega h(x)\phi_j(x)\,dx = 0$ for all j, meaning that $h = 0$ since $(\phi_j)_{j\geq 1}$ is a Hilbert basis of $L^2(\Omega)$. The strict convexity of $\hat{J}$ follows.

3. Gaussian Releases

From a practical point of view, not all controls $u \in \mathcal{V}_{T,C,M}$ correspond to a release that could actually be conducted, as for example the constant solution of the toy problem of the previous section. To guarantee a solution that could be implemented, we restrict here the admissible controls to more accurately model the way mosquitoes are released in practice.

We thus consider that there are $K \in \mathbb{N}$ simultaneous releases and that each one results in a Gaussian distribution of mosquitoes centered around the position of the release $x_k \in \Omega$ for $k = 1, ..., K$. Then, the feasible controls are of the form

$$u_K(x, x_1, ..., x_K) = \sum_{k=1}^{K} m \exp\left(-\frac{\|x - x_k\|^2}{\sigma^2}\right), \tag{14}$$

where the constants m and σ are chosen such that $u_K(\cdot, x_1, ..., x_K) \in \mathcal{V}_{T,C,M}$. In particular, we choose to saturate the constraint on the total number of mosquitoes released, i.e. we take $\int_\Omega u_K(x)dx = C$.

The goal is then to find the best position of the releases and the optimization problem becomes

$(\mathcal{P}_K)$

$$\boxed{\inf_{(x_1,...,x_K)\in\Omega^K} J_K(x_1, ..., x_K) \quad \text{with } J_K(x_1, ..., x_K) = \frac{1}{2}\int_\Omega (1 - p(T, x))^2\, dx},$$

where $p \in C^0([0, T], L^2(\Omega))$ is the unique solution of (7) with control $u_K(\cdot, x_1, ..., x_K)$.

Remark 3. *Since Ω is a bounded domain in $\mathbb{R}^2$, the question of the existence of a minimizer is trivial. But, the uniqueness is still a challenging problem.*

Proposition 3. *Let $(x_1, ..., x_K) \in \Omega^K$. For $k \in \{1, ..., K\}$, one has*

$$\frac{\partial J_K}{\partial x_k}(x_1, ..., x_K) = \int_\Omega (G^{-1})'(u_K(x))q(0, x)\frac{\partial u_K}{\partial x_k}(x, x_1, ..., x_K)\, dx,$$

where q is the unique solution of the backward problem

$$\begin{cases} -\partial_t q(t, x) - \Delta q(t, x) - f'(p(t, x))q(t, x) = 0, & (t, x) \in (0, T) \times \Omega, \\ \partial_n q(t, x) = 0, & (t, x) \in (0, T) \times \partial\Omega, \\ q(T, x) = p(T, x) - 1, & x \in \Omega. \end{cases}$$

Proof. It is an easy application of the chain rule. First, we notice that

$$J_K(x_1, ..., x_K) = J(u_K(x, x_1, ..., x_K)).$$

Next, using Proposition 2, we find thanks to the chain rule that for all $k \in \{1, ..., K\}$

$$\begin{aligned} \nabla J_K(x_1, ..., x_K) &= < dJ(u(x, x_1, ..., x_K)), \nabla u(x, x_1, ...x_K) > \\ &= \int_\Omega (G^{-1})'(u_K(x, x_1, ..., x_K)q(0, x)\nabla u_K(x, x, x_1, ..., x_K)dx. \end{aligned}$$

We deduce the result from the last equality. □

3.1. **Numerical Resolution.** We now present the computation of the numerical solution of $(\mathcal{P}_K)$. For this we use a direct method which consists in carrying out a discretization of Equation (7) and of the control in order to obtain a finite dimensional optimization problem with constraints. We can then compute an approximation of a local minimizer of $(\mathcal{P}_K)$ with a numerical optimization solver.

Our results were obtained with the finite element toolbox *FreeFem++* [6] which contains an implementation of the optimization routine *Ipopt* [20].

We therefore consider a finite element basis of functions $(\varphi_i)_i$ that allows us to discretize the control as $u_h(x, x_1, ..., x_K) = \sum_i u_i \varphi_i(x)$ and the proportion of infected mosquitoes as $p_h(t, x) = \sum_i p_i(t)\varphi_i(x)$, the finite element approximation of the solution of the PDE (7) with initial condition $G^{-1}(u_h(x, x_1, ..., x_K))$. The cost function can be computed with numerical integration as $J_h(x_1, ..., x_K) = \int_\Omega (1 - p_h(T, x))^2\, dx$. In addition, *Ipopt* requires the gradient of the cost function and thanks to Proposition 3 we have

$$\frac{\partial J_h}{\partial x_k} = \int_\Omega (G^{-1})'(u_h(x)) q_h(0, x) \frac{\partial u_h}{\partial x_k}(x, x_1, ..., x_K)\, dx$$

where $q_h(0, x)$ is the finite element approximation of the solution of the backwards PDE.

Remark 4. *Because of Proposition 1, we were interested in the case $M > \frac{C}{|\Omega|}$. In addition, we have fixed C such that the constant solution $u = \frac{C}{|\Omega|}$ leads to extinction (as T tends to $+\infty$) but there exists $R \in]0, \sqrt{\frac{C}{\pi M}}[$ such that the function $u(x) = M \times 1_{B(0,R)}(x)$ belongs to $\mathcal{V}_{T,C,M}$ and leads to invasion (as T tends to $+\infty$).*

We now present numerical simulations for the parameters given in Table 1. The birth and death rates are given per day, whereas the unit of the carrying capacity is per m^2 and the diffusion coefficient is given per m^2 per day. The numerical values are taken from [1] and references therein. We consider a square domain of 1 hectare, a final time of 200 days and we set the total amount of mosquitoes released such that $C < G(\theta)|\Omega|$. In Figure 1 we show the control $u_K(\cdot, x_1, ..., x_K)$ for $K = 3, 4, 5, 6$ releases and for each case the same total amount of mosquitoes is released. For the case of 6 releases we display in Figure 2 the time dynamics of the proportion of infected mosquitoes $p(t, \cdot)$. As expected, it leads to the total invasion of the domain.

Parameter	b_1	b_2	d_1	d_2	κ	D
Value	1.12	1.12	0.27	0.36	$6 \cdot 10^{-2}$	2.5

TABLE 1. Model parameters

4. Conclusion

We investigate in this work the optimization of the release of *Wolbachia*-infected mosquitoes into a host population in the aim to replace the wild population by a *Wolbachia*-infected population unable to transmit several diseases to human. To conduct this study, we first reduce the optimal problem under investigation by assuming that the time distribution is given. Then we obtain existence of a minimum for this latter problem. Finally, reducing again the control problem by considering that the releases are modelled by Gaussian distributions, some numerical computations are performed.

Optimisation strategies for release protocols of mosquitoes have been investigated by several authors [16, 4, 3]. However, in these papers, only the time optimization

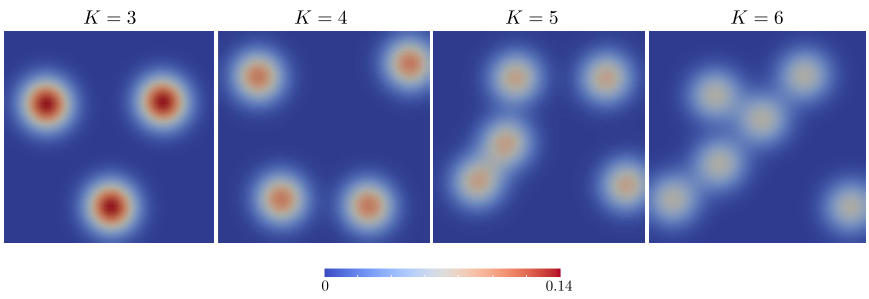

FIGURE 1. $u_K(\cdot, x_1, ..., x_K)$ for $K = 3, 4, 5, 6$ releases and $C = 0.017$.

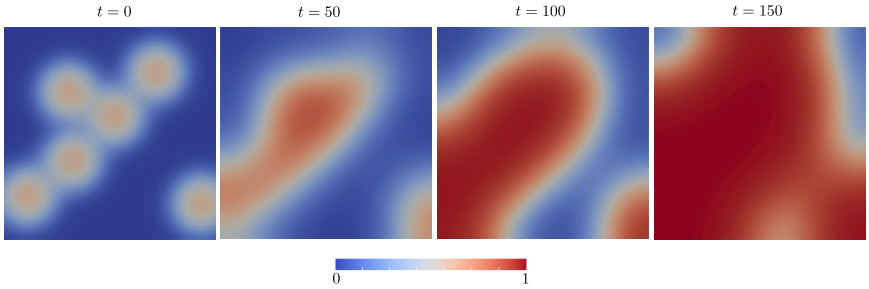

FIGURE 2. $p(t, \cdot)$ for $K = 6$ releases, $t = 0, 50, 100, 150$ days and $C = 0.017$.

of the releases is investigated. Up to our knowledge, this work is the first attempt in optimizing spatially the releases, which is of great interest for experiments in the field. The preliminary results obtained in this paper should be continued. In particular, the optimality conditions for the system $(\mathcal{P}_K)$ should be studied in a future work in the aim to find properties of the optimal solution. The numerical simulations should also be continued to have a better representation of what is observed in the field.

Appendix – Reduction of system (1)

For the sake of completness and for reader facility, we explain briefly in this appendix how to reduce system (1) to system (2). We will not provide all the details of this reduction but only the main steps. We refer to [15] and [1, Section 2.3] for the interested reader. The starting point is to introduce a small parameter $0 < \varepsilon \ll 1$ modelling the ratio of the fertility on the death rate. Indeed for mosquitoes population, the fertility is large compared to death rates. System (1) reads then

$$\begin{cases} \partial_t n_1^\varepsilon - D\Delta n_1^\varepsilon = \dfrac{b_1}{\varepsilon} n_1^\varepsilon (1 - s_h \dfrac{n_2^\varepsilon}{n_1^\varepsilon + n_2^\varepsilon})(1 - \dfrac{n_1^\varepsilon + n_2^\varepsilon}{\kappa}) - d_1 n_1^\varepsilon, \\ \partial_t n_2^\varepsilon - D\Delta n_2^\varepsilon = \dfrac{b_2}{\varepsilon} n_2^\varepsilon (1 - \dfrac{n_1^\varepsilon + n_2^\varepsilon}{\kappa}) - d_2 n_2^\varepsilon + u. \end{cases}$$

As $\varepsilon \to 0$, we expect from this system that $n_1^\varepsilon + n_2^\varepsilon \to \kappa$. Hence we introduce the quantity $n^\varepsilon = \frac{1}{\varepsilon}(1 - \frac{n_1^\varepsilon + n_2^\varepsilon}{\kappa})$ and denote $p^\varepsilon = \frac{n_2^\varepsilon}{n_1^\varepsilon + n_2^\varepsilon}$ the proportion of infected mosquitoes. From straightforward computations, we deduce the system satisfied by $(n^\varepsilon, p^\varepsilon)$:

$$\begin{cases} \partial_t n^\varepsilon - D\Delta n^\varepsilon &= \dfrac{1}{\varepsilon}\left((1 - \varepsilon n^\varepsilon) a(p^\varepsilon)(Z(p^\varepsilon) - n^\varepsilon) - \dfrac{u}{\kappa}\right), \\ \partial_t p^\varepsilon - D\Delta p^\varepsilon + \dfrac{2\varepsilon}{1 - \varepsilon n^\varepsilon} \nabla p^\varepsilon \cdot \nabla n^\varepsilon &= p^\varepsilon (1 - p^\varepsilon)\left(n^\varepsilon (b_2 - b_1(1 - s_h p^\varepsilon)) + d_1 - d_2\right) \\ &\quad + \dfrac{u(1 - p^\varepsilon)}{\kappa(1 - \varepsilon n^\varepsilon)}, \end{cases}$$

where we use the notations $a(p) = b_1(1-p)(1 - s_h p) + b_2 p > 0$ and $Z(p) = \frac{d_1(1-p) + d_2 p}{a(p)} > 0$. Assuming that the sequences $(n^\varepsilon)_\varepsilon$ and $(p^\varepsilon)_\varepsilon$ admit limits denoted n and p respectively, we deduce from the first equation that, formally,

$$n = Z(p) - \frac{u}{\kappa} a(p). \tag{15}$$

Passing into the limit into the equation satisfied by p, we get

$$\partial_t p - D\Delta p = p(1-p)(n(b_2 - b_1(1 - s_h p)) + d_1 - d_2) + \frac{u}{\kappa}(1 - p),$$

Injecting the expression of n (15) into this latter equation, we recover the equation

$$\partial_t p - D\Delta p = f(p) + u g(p),$$

with f and g defined in (3)

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