# Optimal mosquito release strategies for vector-borne disease control

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SORBONNE UNIVERSITÉ
CRÉATEURS DE FUTURS DEPUIS 1257

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SORBONNE UNIVERSITÉ

LJLL

École doctorale **École Doctorale Sciences Mathématiques de Paris Centre**

Unité de recherche **Laboratoire Jacques-Louis Lions**

Thèse présentée par **Jesús Bellver Arnau**

Soutenue le **14 décembre 2022**

En vue de l'obtention du grade de docteur de Sorbonne Université

Discipline **Mathématiques appliquées**

Spécialité **Contrôle Optimale**

# Optimal mosquito release strategies for vector-borne disease control

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**Mots clés :** contrôle optimal, contrôle vectoriel épidémique, moustiques, systèmes dynamiques, maladies à transmission vectorielle, wolbachia, remplacement de population des vecteurs, technique de l'insecte stérile.

**Keywords:** optimal control, epidemic vector control, mosquitoes, dynamical systems, vector-borne diseases, wolbachia, vector population replacement, sterile insect technique.

Cette thèse a été préparée au

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*A mis padres, Ana y Jesús,*
*a mi hermana, Ana,*
*y a Pepe.*

All models are wrong, but some are useful

George E.P. Box

## Optimal mosquito release strategies for vector-borne disease control

**Résumé**

Avec la hausse globale des maladies à vecteurs et l'expansion des habitats des moustiques dues au changement climatique, le contrôle des populations de moustiques est sans doute un des principaux défis pour la santé humaine dans les années à venir. Cette thèse est consacrée à la modélisation, l'analyse et la simulation de stratégies optimales de contrôle des moustiques et des maladies qu'ils transmettent en utilisant des lâchers de spécimens modifiés. Nous étudions d'abord les stratégies optimales de remplacement de population. Celles-ci consistent à remplacer de manière optimale la population sauvage par une population porteuse de la bactérie endosymbiotique *Wolbachia*, car il a été démontré que les moustiques porteurs de cette bactérie sont moins susceptibles de transmettre certains arbovirus. En considérant une limite de fécondité élevée, nous réduisons l'étude de la population de moustiques à une seule équation sur la proportion de moustiques infectés par *Wolbachia*. Nous étudions d'abord des stratégies optimisant une combinaison convexe du coût des lâchers et de la performance de la technique. Nous effectuons une analyse complète de ce problème, en prouvant une propriété de monotonie temporelle sur la proportion de moustiques infectés par *Wolbachia* et en utilisant une reformulation du problème basée sur un changement de variable approprié. Dans un deuxième temps, nous considérons l'optimisation spatiale des lâchers, en optimisant un seul lâcher instantané à l'instant initial maximisant la proportion finale de moustiques infectés par *Wolbachia* dans le domaine à un horizon temporel donné. Nous caractérisons complètement les solutions sous certaines hypothèses dans le cas non-diffusif. De plus, des simulations sont effectuées pour le cas avec diffusion. Enfin, nous étendons l'objet de l'étude aux humains. Nous considérons un modèle épidémiologique dans lequel les deux populations sont prises en compte ainsi que la dynamique d'une maladie vectorielle avec une transmission exclusivement homme-moustique et moustique-homme comme la dengue. Dans ce cadre, nous minimisons la quantité d'infections humaines pendant une épidémie en utilisant des lâchers instantanés de spécimens modifiés, représentés par des combinaisons linéaires de mesures de Dirac avec des coefficients positifs déterminant leurs intensités. Les stratégies optimales pour le remplacement de population et la technique de l'insecte stérile sont étudiées numériquement à l'aide d'algorithmes ad hoc, basés sur l'écriture de conditions d'optimalité au premier ordre caractérisant la meilleure combinaison de mesures de Dirac.

**Mots clés :** contrôle optimal, contrôle vectoriel épidémique, moustiques, systèmes dynamiques, maladies à transmission vectorielle, wolbachia, remplacement de population des vecteurs, technique de l'insecte stérile.

**Abstract**

With vector-borne diseases rising globally and mosquitoes expanding their habitats due to climate change, mosquito control is undoubtedly one of the main challenges for human health in the years to come. This thesis is devoted to the modeling, analysis and simulation of mosquito and mosquito-borne diseases optimal control strategies using modified vector releases. We first investigate optimal population replacement strategies. These consist in replacing optimally the wild population by a population carrying the endosymbiotic bacterium *Wolbachia*, since it has been shown that mosquitoes carrying this bacterium are less likely to transmit some arboviruses. By considering a high fecundity limit we reduce the study of the mosquito population to a single equation on the proportion of *Wolbachia*-infected mosquitoes. First, we study strategies optimizing a convex combination of both the cost of the releases and the performance of the technique. We fully analyse this problem, proving a time monotonicity property on the proportion of *Wolbachia*-infected mosquitoes and using a reformulation of the problem based on a suitable change of variable. Next, we consider the spatial optimization of the releases, optimizing a single instantaneous release at the initial time maximising the final proportion of *Wolbachia*-infected mosquitoes throughout the domain at a given time horizon. We fully characterize the solutions under some hypothesis in the non-diffusive case. Moreover, simulations are carried for the case with diffusion. Finally, we extend the focus of the study to humans. We consider an epidemiological model in which both populations are taken into account as well as the dynamics of a vector-borne disease with exclusively human-mosquito and mosquito-human transmission like dengue. In this setting, we minimise the amount of human infections during an outbreak using instantaneous releases of modified vectors, represented by linear combinations of Dirac measures with positive coefficients determining their intensity. Optimal strategies for both population replacement and the sterile insect technique are studied numerically using ad-hoc algorithms, based on writing first-order optimality conditions characterizing the best combination of Dirac measures.

**Keywords:** optimal control, epidemic vector control, mosquitoes, dynamical systems, vector-borne diseases, wolbachia, vector population replacement, sterile insect technique.

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# Agradecimientos

I'd like to start by apologising... This section may not be as well written or properly structured as the ones that follow it, for it has been, by far, the most difficult to write. So many feelings to condense in so little space (and in so many languages I do not master). Sorry for the mistakes that, for sure, you will find. I guess some things just cannot be expressed with words. The fact that this section has mostly been written looking through a translucent layer of tears has definitely not helped to make it more intelligible.

This is it. My PhD is done. As the last days of my time in this city slip through my fingers, I revisit all the little and big moments that led me where I am right now. The achievements and the failures. The breakthroughs and the moments I felt stuck. The laughs, the fun, the joy... and one or two tears. All of them lay now, clearly, in front of my eyes; and they all fit nicely, harmonically, one giving way to the other. But these moments were far from planned, far from inevitable. It has been the will and the kindness of many, many people what has allowed me to reach the finish line. Maybe you pointed out the right direction at some crossroad, maybe you helped me stand when I stumbled, or maybe you walked by my side for a while on this journey. This section tries to honor you, all of you, and set the record straight on the many things I received.

Tout d'abord, je veux commencer en remerciant mes directeurs de thèse: Luis Almeida et Yannick Privat. Merci pour faire confiance en moi. Luis, tu m'as conseillé et supporté même avant que je mettais les pieds sur le campus pour la première fois. Tu m'as présenté le sujet de ma thèse. Un sujet qui me passionne, qui m'a donné autant, et que, j'espère, continuera à le faire dans le futur. Merci aussi pour ta bonne humeur, qui a rendu beaucoup plus drôle et sympa ce chemin. Yannick, merci pour ta disponibilité, toujours prête à m'appeler quand je te partageais mes inquietudes sur un problème. Merci aussi pour ta patience quand je mettais du temps à comprendre tes raisonnements, merci pour ta guide et pour autant de bonnes idées. Je garderai toujours les après-midi face au tableau à Strasbourg qui m'ont fait sentir mathématicien pour la première fois. Merci aux deux pour votre soutien à distance pendant le Covid qui m'a aidé énormément à rester motivé pendant cette année aussi dur. J'espère qu'on ne soit qu'au début de notre relation, académique et personnel.

Je voudrais aussi remercier aux rapporteurs du manuscrit: Roland Herzog, José Tomás Lázaro et Alain Rapaport. Merci pour le temps dédié et le soin mis dans l'élaboration des rapports. Gracias Tomás por tu amabilidad y disponibilidad. Gracias tamién por presentarme a Fede y David; te debo una parte de todo lo que está por venir. Merci Alain pour tes commentaires, qui ont enrichi le Chapitre 3 beaucoup avant qu'il n'était un chapitre de cette thèse. J'adresse aussi mes remerciements à Benoît Perthame et Carlota Rebelo qui me font l'honneur de faire partie de mon jury de thèse.

Beyond her role as a member of the jury, I would like to thank specially Carlota, as well as Alessandro, for having been my "thesis godparents". You made me feel very welcomed during

my time in Lisbon. It is always a pleasure to discuss with you, whether it is or not about maths, and I hope we keep doing it in the future. Obrigadíssimo.

I'd like to thank also Ariela Briani and all the people at the FSMP, who gave me the opportunity to do my master in Jussieu in the first place with the PGSM scholarship, and then the awesome gift of pursuing this PhD, thanks to the cofund program. Your availability and dedication has smoothed every process, allowing me to focus on my research. I will be always thankful.

Je n'oublie pas François Graner, qui m'a fait découvrir, là en 2015, que la physique et les maths pouvaient être appliquées en biologie, en m'accueillant comme stagier, en m'ouvrant un nouveau monde de possibilités. Y gracias también a René Gato, por invitarme al taller de capacitación TIS en La Habana, por permitirme visitar las instalaciones del IPK y por hacerme conocer de primera mano las entrañas de tantos proyectos TIS y a la gente que está cada día sobre el terreno haciéndolos realidad. Fue un regalo impagable. Tu generosidad y entrega son un ejemplo para mí.

Pour finir cette partie, un chaleureux merci à Nicolas et Gwenaël, pour vos contributions au Chapitre 2.

Je passe maintenant à une partie un peu plus personnel, et bien plus difficile à écrire!

J'aimerais commencer cette partie en remerciant mes collègues de bureau: Emma, Nicolás [1], Eugenio, Mathieu et Fabrice. Merci pour rendre notre petit coin en 16-26 un endroit conviviale, drôle et productif! À ce sujet, merci aussi à notre bien-aimé canapé! Je remercie spécialement Emma, ma soeur de thèse, à qui je tiens autant. Merci pour les longues conversations chaque matin avant de travailler (ou au lieu de travailler...). À quel point elles vont me manquer!

Gracias a *La Muchachada*: Ramón, Claudia, Agustín, Ana, Emilio, Nicolás, Suney y Paula. Gracias por crear un espacio donde compartir opiniones, risas, juegos y creaciones culinarias en Español. Por hacerme apreciar nuestras diferencias, y lo que tenemos en común. Cuando os eche de menos, que lo haré a menudo, tendré montones de canciones para recordar esos buenos momentos. *¡Vamos Piratas!*

Gracias María por tu sentido del humor y por haber sabido escuchar, penas y alegrías. *Fantasía.*

*Shukran* Chourouk for the joy you spread and for those delightful musical afternoons. (I spent more time that I want to recognise trying to compile Arabic in LaTeX... and yet failed miserably...).

Mi volto adesso verso *Le ragazze*: Grazie Elena, per le piacevole discussioni culturale e linguistiche, e per farmi aspettare con gioia le domeniche. A Chiara, una aggiunta tardiva (ma indispensabile!) alla squadra. E grazie Noemi [2], per tante risate condivise.

Merci beaucoup aussi aux autres doctorants du labo: Antoine, Jules, Anatole, Juliette, Nga, Matthieu, Pierre, Lucas... pardonnez-moi pour ne pas citer tout le monde, la liste est longue. Vous avez tous contribué à faire de ces années une expérience formidable. Ah, et un grand merci à Robin pour m'offrir la plus importante source bibliographique pour cette thèse [160]! [3]

Vull fer un lloc ací per a donar-li les gràcies a Anna, pels cafés al Colegio i per les cerveses acompanyades de conversacions intenses. Espere que en vinguen moltes més a Barcelona. *Qu'est-ce que signifie "apprivoiser"? C'est une chose trop oubliée...*

Et pour finir (ou presque), merci à ce petit groupe d'amis, né entre notes de cours, examens et soirées au M2. Merci à Thomas, Giorgia, Naïla, Cyril, Noémie, Rémi, Lise, Élise et Camille. Merci pour les apéros sur les quais de Jussieu, pour les billards et pour tous les moments partagés.

1. a.k.a. *El profesor*
2. David Brava
3. [160] T. Nagata. "Les sciences naturelles de Tatsu Nagata: Le moustique.", *Seuil Jeunesse*, (2016).

Merci spécialement à Thomas et Giorgia, pour m'accompagner depuis tout le début de mes années à Paris. Vous m'êtes très chères. Là où je me trouve, vous aurez un "chez vous". Et un énorme merci à Naïla et Cyril pour avoir fait de son coin le centre officiel des retrouvailles et pour me faire sentir toujours aussi accueilli là-bas. Le nom "Rue des Bernardins" sentira pour moi toujours à raclette, jeux de société et bons souvenirs.

Para acabar quiero dar las gracias a mis padres y a mi hermana. Gracias, papás, por todo el esfuerzo, el sacrificio y el amor que habéis puesto en criarnos; para hacer de nosotros personas de éxito, personas felices, pero sobre todo, Personas. Gracias por haberme apoyado siempre en mis decisiones, aunque eso implicara distanciarme de vosotros. Gracias por decir, una y otra vez, "si això és lo que vols, saps que allí estarem". Habéis estado. Gracias Ana, por haber sido siempre el faro que iba alumbrando el camino, unos años por delante. Gracias por tu valentía. Por haberme llevado siempre contigo. Por apartar la maleza y por darme la mano para que yo también avanzara sin miedo. No nos la soltemos nunca. Te quiero. Os quiero.

Je pourrais encore continuer, me remonter plus en arrière, ou encore élargir le champ, mais le plus important a été dit. Juste une dernière chose avant de finir. Je veux aussi remercier Paris. Oui, oui, Paris. Ses quais et boulevards, ses places et monuments, ses musées et théâtres, sa lumière... Merci pour avoir été la toile de fond inégalée d'autant d'instants que je garderai, précieusement, à jamais. Tant que ma mémoire tient je fermerai mes yeux en revenant aux années passées dans cette ville, aux moments vécus en elle et aux gens qui les ont peuplé; et là je vais sourire, et là... là je vais pleurer! Merci!

# Funding

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement Nº 754362.

# Contents

# Introduction

## I Issues and challenges regarding mosquitoes

### I.1 Vector-borne disease burden

In the evolutionary arms race that pathogens [1] and hosts have been running for eons, perhaps one of the most curious ways microorganisms have found to reach our bodies is by hitchhiking inside the bodies of other life forms. *Vector-borne diseases* are diseases transmitted to humans by means of a necessary non-human animal intermediary, usually arthropods, transmitting the disease through their bite. The intermediary animal is called the *vector* of the disease. The list of known vector-borne diseases is long and includes some of the biggest human killers of all times. To name a few vector-borne diseases and its vectors: Bubonic Plague, which decimated Europe in the XIVth century, is transmitted by fleas, Lyme disease by ticks, Typhus by lice, the Sleeping sickness by Tsetse flies and Leishmaniasis by sandflies [154]. In this work we will focus on one particular vector and its associated vector-borne diseases: the mosquito.

Mosquitoes are, by far, the vectors responsible of transmitting the wider variety of diseases, and with the biggest toll on human health around the globe. The mosquitoes transmitting human diseases can be divided into two subfamilies: Anophelinae and Culicinae.

The first family includes the mosquitoes of the genus *Anopheles*. *Anopheles* mosquitoes are the culprits transmitting Malaria. Malaria is a severe disease caused by protozoa of the genus *Plasmodium*, it is known since ancient times and it is considered one of the infectious diseases responsible for more human deaths in history. Despite seeing a clearly descending trend in the last 15 years, Malaria remains as the seventh leading cause of death for children under 5 years old, and the fifth for children between 5 and 14 [119]. With the African region bearing, by far, the biggest burden in cases and deaths [124], as we can see in Figure 1. According to the World Health Organisation (WHO), there were 241 million cases and 627000 deaths by Malaria in 2020 alone. The African region representing 95% of cases and 96% of deaths. Children under 5 accounting for around 80% of all malaria deaths in the region [153].

On the other hand, the subfamily Culicinae includes *Aedes* and *Culex* mosquitoes. Several species of mosquitoes belonging to these genus transmit virus causing diseases like dengue fever, Zika, Chikungunya, West Nile fever, Yellow fever or japanese encephalitis amongst others. Amidst these diseases, dengue is the most prevalent one.

Dengue, in over 80% of cases, presents mild to no symptoms. Nevertheless, some cases can develop a direr version of the disease called severe dengue, which can produce intense bleeding and death. In spite of there not being specific treatment for severe dengue, with an early detection and proper medical care, fatality rates can get as low as 1%. Nevertheless, dengue is a cause of major concern in tropical and subtropical areas. Estimations suggest that 100 to 400 million

1. From greek: *pathos*, "passion, suffering" and *gen* "causing, producing".

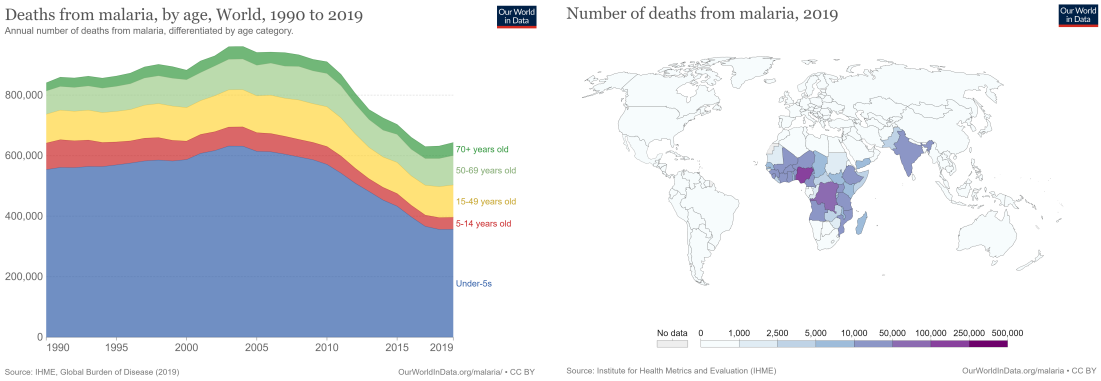


Figure 1 – Share of deaths from malaria by age group in the last three decades (left) and malaria death toll geographic distribution as of 2019 (right). Source of the image: [124]

infections of dengue occur each year [152], with Africa, South America, and especially South East Asia bearing most of them. The last decades have seen a dramatic increase in cases. Having almost doubled in the last thirty years [59] (See Figure 2).

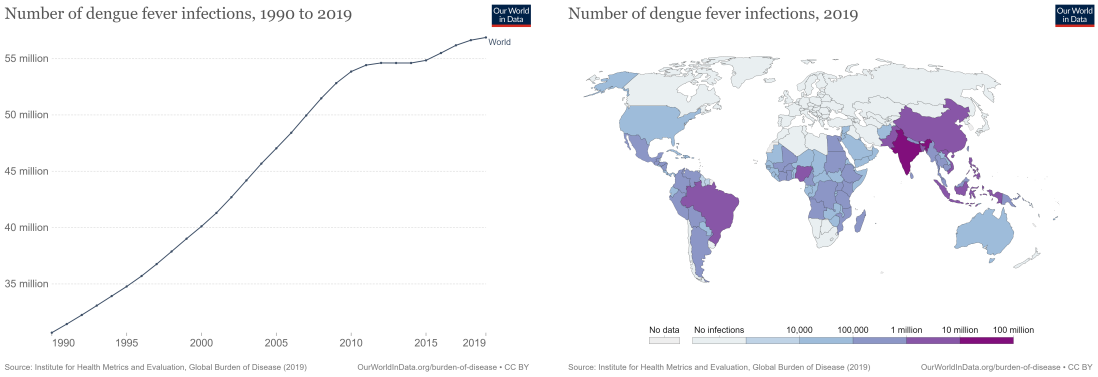


Figure 2 – Number of dengue fever infections' evolution in the last three decades (left) and its geographic distribution as of 2019 (right). Source of the data: [59]. Source of the image: [110]

No efficient vaccine has been found yet for any of these viruses, although, Valneva and Pfizer have promising vaccine candidates at Phase 3 of clinical trials for Chikungunya and Lyme disease [145, 114]. The only commercialized vaccine for dengue so far is Dengvaxia®. After the initial hype, governments and agencies took a step back and it is currently only recommended for children ranging 9 to 16 years old and only if they have been previously infected by one of the strains of dengue (dengue is, in fact, four different closely related virus strains DENV-1 to DENV-4), but is discouraged for other ages and for seronegative people since it has been shown to increase the risk of developing severe dengue in case of an infection [131, 141, 138]. Moreover, treatment for vector-borne diseases usually consists on alleviating the symptoms, since rarely the pathogen can be targeted directly. Therefore, prevention against these diseases relies heavily on controlling the vector.

On top of this, in recent years an expansion of the vector's habitat is taking place. In Europe,

for instance, dengue vector *Ae. albopictus* was first documented in Albania in the 1970s and it has not ceased to expand its distribution ever since, settling with special strength along the mediterranian coast [121]. Its current known distribution is depicted in Figure 3. To give two examples, in France, *Ae. albopictus* entered from Italy in 2004. Its advance has been steady and it has colonized great areas of the south and south-west since then. It has settled even in other areas detached from the main front like the Parisian region, probably following main human transportation routes [89]. This invasion process has been well studied and documented and has also sparkled the interest from a mathematical point of view [123]. Also in 2004, *Aedes albopictus* arrived in Spain, being firstly detected in the catalan town of San Cugat del Vallès [18]. Although initially attributed to the importation of used car tires, the real origin is not clear [122]. It has since expanded to other regions, specially southwards along the mediterranian coast. This, in combination with the presence of the common *Culex* mosquitoes has lead to West Nile fever outbreaks in the last years in Andalusia [90] and efforts from the government to try to contain their advance [91]. Although the epidemiological situation in Europe is not worrying for the moment, a project for controlling vector population based on the Sterile Insect Technique (see Section II.2) [142], is currently being developed in the Valencia region, where *Aedes albopictus* has a stronger presence.

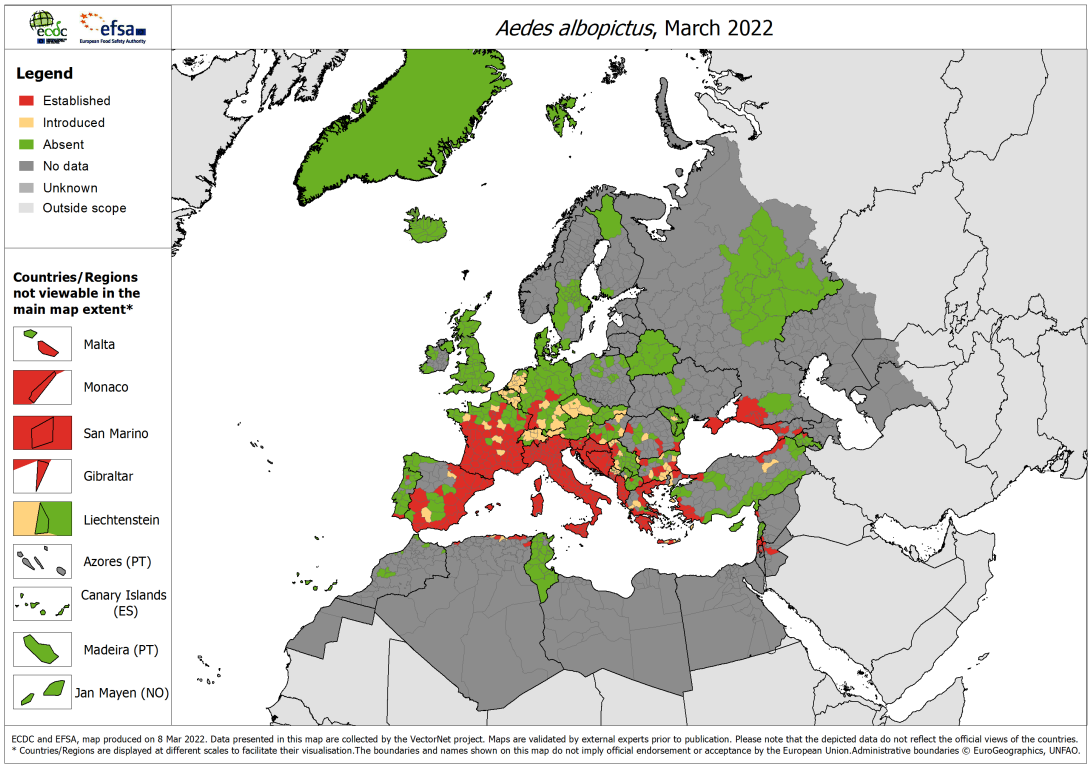


Figure 3 – *Aedes albopictus* geographic distribution in Europe as of March 2022. Source of the image: [50]

## I.2 Mosquito life cycle

Although details vary amongst species [40], mosquitoes undergo similar stages during their development. Their life cycle can be split into two clearly distinct phases: an aquatic phase composed of three stages, egg, larval and pupal, and an aerial phase as adults. In the aquatic phase mosquitoes are developing and sexually immature. After undergoing a metamorphose, they reach their aerial phase, where they mate and reproduce. This work does not focus on the modeling of the aquatic phase, which is a whole topic on its own. For the sake of completeness and as a starting point for the kind of models that will be discussed in this thesis, we quickly introduce the following model that can be found in [133].

$$\begin{cases} E' = b_E A - (h(L) + d_E)E, \\ L' = h(L)E - (\phi(L) + \tau_L + d_L)L, \\ P' = \tau_L L - (\tau_P + d_P)P, \\ A' = \tau_P P - d_A A. \end{cases} \tag{1}$$

This model is an example of *compartmental modeling*, a classical way to approach the modeling of population dynamics of a species. The model consists on a set of quantities or compartments that represent the abundance of, in this case, a certain life stage of the mosquito population, and which evolve according to ordinary differential equations. These equations can depend on the abundance of individuals in the compartment itself or in other compartments, creating a flow of individuals between compartments. All the parameters in system (1) are positive.

In (1), eggs are considered to be laid by adults at a certain rate $b_E$, and die at rate $d_E$. The eggs are considered to hatch at a rate depending on the amount of larvae present in the environment, $h(L)$, since larval density may stimulate or inhibit the hatching ability of the eggs through more than one mechanism simultaneously [48, 81]. After hatching, eggs become larvae. At this stage intra-specific competition for resources between larvae is a well documented fact affecting their development (and even their vector capacity as adults) [16, 19]. It is represented in this model, (1), by the term $\phi(L)L$. Larvae die at rate $d_L$ and progress to the pupal stage at rate $\tau_L$. Pupae, analogously die at rate $d_P$ and progress to the adult stage at rate $\tau_P$. At this stage mosquito reproduce, laying eggs and restarting the cycle.

Although model (1) is already fairly general, it is not the only way in which the life cycle of the mosquito can be modeled. Models can take into account disparities in male and female mosquito population, like having a different likelihood of reaching adulthood or having different dynamics, for instance, a different life expectancy. They can also take into consideration the resource availability in the environment by introducing a carrying capacity in the egg or adult stages (see II.2). As for model (1), more layers of complexity can be added to it. For instance, mosquito population presents a clear seasonality, specially in temperate climates [51, 68, 77, 139]. This is due to its complex dependence on external factors such as: temperature, rainfall and humidity, presence or lack of nutrients, length of the daylight (also known as photoperiod), etc. These factors vary periodically through the year. Incorporating periodicity into the parameters of system (1) can help to reproduce such variations, which can in turn help to predict disease outbreaks, which also present seasonal variations [116, 39, 97, 128].

Furthermore, some mosquito species present mechanisms to resist adverse conditions, such as desiccation or low temperatures during winters, which are not included in this simple model. These mechanisms include, at the egg stage, quiescence (dormancy responding directly to adverse conditions, ceasing as soon as good conditions return) and diapause (more complex and hormonally regulated, allowing to resist seasonal adverse conditions like winter), but also dormancy in the larval or adult stage [43].

## I.3 Epidemiology of Vector Borne Diseases

We turn the focus in this section to the adult stage of the mosquito. It is in this last stage that female mosquitoes acquire their blood feeding behaviour. Females use blood to obtain proteins, iron and other important substances for the egg formation [38]. Mosquitoes feed mostly on birds and mammals, and some, like *Ae. aegypti* or *Ae. albopictus*, feed almost exclusively on human blood [117]. Once they have had a blood meal containing a pathogen, it can develop in their bodies and reach the salivary glands, from where it can be transferred to a different human in a subsequent blood meal. The fact that anthropophilic mosquitoes are usually vectors of human diseases suggest a coevolution of host preference and pathogen-host interaction [136].

Compartmental models are widely spread to model disease transmission. A classical approach to modeling the phenomenon are the so called *SIR* models (Susceptible-Infectious-Recovered). The basic modeling approach is the following

$$\begin{aligned} S' &= bH - \frac{\beta}{H} IS - bS, \\ I' &= \frac{\beta}{H} IS - \sigma I - bI, \\ R' &= \sigma I - bR. \end{aligned} \tag{2}$$

In this model, $b$ stands for the birth (and death) rate, $\beta$ is proportional to the probability of transmission between an infectious and a susceptible and $\sigma$ stands for the rate at which people recover from disease. The total human population $H$, is considered to be constant. Transmission occurs when an infectious and a susceptible human encounter, this is modeled by humans in the susceptible compartment becoming infectious at a rate proportional to the product of the susceptible and the infectious population. This kind of models have its roots in the chemical law of mass action and consider random encounters between individuals in a well mixed population [63]. These models, yet being simple, capture the essence of disease transmission.

This model can be made gradually more complex. For instance an exposed compartment, $E$, can be added, i.e., a compartment of individuals that have the disease but are not able to transmit it yet, becoming a so called *SEIR* model. Many other tweaks can be done so that particular characteristics of each disease can be taken into account. To name a few: the presence of asymptomatic infectious people, a lack of recovery from disease or the ability to be reinfected.

For a vector-borne disease, such as dengue or malaria, the model has to be extended, for not only the human population must be considered, but also the mosquito one. The number of equations increases as a consequence. We introduce

$$\begin{aligned} S'_H &= b_H H - \frac{\beta}{H} I_M S_H - b_H S_H, \\ E'_H &= \frac{\beta}{H} I_M S_H - \gamma_H E_H - b_H E_H, \\ R'_H &= \sigma_H I - b_H R, \\ I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H, \\ S'_M &= f(M) - \frac{\beta}{H} S_M I_H - d_M S_M, \\ E'_M &= \frac{\beta}{H} S_M I_H - \gamma_M E_M - d_M E_M, \\ I'_M &= \gamma_M E_M - d_M I_M. \end{aligned} \tag{3}$$

Now the susceptible-infectious encounters occur between human and mosquitoes. Analog models to this one are common in the literature [17, 83].

Concerning this model several caveats should be addressed. First, transmission from human

to mosquito and mosquito to human are different phenomena, which do not occur necessarily with the same probability. Nevertheless, due to the difficulty in measuring the second one in lab conditions, $\beta$ is usually considered to be the same for both cases. Mosquitoes' lack of a recovered compartment comes from the fact that mosquitoes remain infectious during their short lifetime and do not recover from these diseases. Here, $f$ is a function that takes into account the growth of the mosquito population. We write it in a deliberately vague way to keep the model as general as possible for the moment. It is not unusual that this growth term does not only depend on the amount of female adult mosquitoes, represented here by $M$, but rather that it also takes into account, in one way or another, the aquatic phase of the mosquito life cycle. These models will play a role in chapter 3, when the control techniques we introduce in the following section are used in the context of epidemiology, where their potential to control disease becomes much more clear.

Dengue is a particular case worth singling out. As mentioned before, it presents 4 different strains than can infect individuals independently. Although this will not be treated in this thesis, models can take this into consideration at the cost of increasing the number of equations [76, 2]. It is also worth remarking that epidemiological models presented and studied in this work do not take into account vertical transmission of the arboviruses (the direct transmission of the pathogen from the mother to the offspring). The frequency of this phenomenon and its importance in transmission is still debated, although some studies suggest that it may play a key role in the establishment of endemicity in these viruses [54]. For completeness, a mathematical model tackling this question can be found in [1].

# II Vector Control: State of the Art

Vector control to prevent vector-borne diseases has a long history. It can be mainly split in two eras. Before the discovery of Dichlorodiphenyltrichloroethane (DDT), control was mainly done by environmental management: drainage of marsh and swamps, thus removing breeding sites, installation of mosquito screens in doors and windows as well as bed nets [150]. In fact, the drainage of stagnant water to prevent Malaria dates back to antiquity, although the nature of these diseases and their means of transmission were not properly understood [30, 150].

In the early 1940s, the discovery of DDT changed the panorama, and pesticides started to take the lead as the main tool to fight against vector-borne diseases. Big eradication campaigns were launched all around the world, such as the Global Malaria Eradication Programme (1955–1969) [101]. These campaigns relied heavily on generalized indoor residual spraying (spraying the interior of houses with insecticide periodically) but also aimed at raising public awareness and seeking community participation, resulting in the effective elimination of Malaria in several areas of the world like North America, the Caribbean, Western Europe and parts of Asia [150, 105]. The use of insecticides, nevertheless, presents a series of issues that must be taken into consideration. Insecticides are, in general, non-specific, i.e., they kill several insects, and not only those we want to target. This can carry with it a series of ecological problems. Moreover, pesticides can often be toxic for other animals too, including humans, and therefore must be handled and used carefully. For instance, the once globally used DDT was banned in most countries in the 1970s when its high toxicity for humans was discovered [144]. Pesticides present also a second type of problems: the development of resistance in mosquitoes due to mutations that are consequently selected. Resistance to different families of widely used insecticides has been observed around the world [96]. This requires the constant change in dose and pesticide type to maintain the effectiveness of the technique, and, more generally, to the need of incorporating specific insecticide resistance management in any proper vector control campaign [47].

In recent years, we might be entering in a new era of vector control thanks to the rise of the *rear and release* techniques [120]. These techniques consist on the mass production of mosquitoes with a certain modification in order to be released in the wild. The goal of the introduction of these modified mosquitoes being to alter the original population in a way that makes less likely the propagation of diseases, or the reduction of the population directly. Particularly, two techniques have gained traction in the mosquito control community: The so called *Wolbachia* method and Sterile Insect Technique (SIT).

There is no silver bullet when it comes to mosquito control. In order to mitigate, or even eradicate, vector-borne diseases and its dire consequences on human health, an integrated vector management approach must always be implemented. Collaboration with local communities and authorities, communication and education on healthy habits around mosquito, vector and disease surveillance and evidence-based decision making to rationally use all the tools at our disposal, are essential pieces of it [71]. It is precisely in the evidence-based decision making process that mathematical modeling, analysis and simulation (including the humble contributions of this thesis) finds its place in this fight. The addition of the rear and release techniques to the tool set can be a game changer in the years to come.

## II.1 Use of *Wolbachia*

*Wolbachia* is an endosymbiotic bacterium, i.e. a bacterium living inside the cells of the host, of the order Rickettsiales. *Wolbachia* infects a wide variety of arthropods and nematodes, presenting also very different effects and relationships with its hosts [149]. It was believed to be naturally present in around 20% of arthropods, although more recent analysis raise this figure up to 66% [66], which would make of *Wolbachia* the most prevalent intracellular bacteria genus. First discovered in the gonads of mosquito *Culex pipiens* almost a century ago [65], it was not until the 1990s that *Wolbachia* caught the attention of the scientific community because of its abundance and effects produced on its hosts. In insects, *Wolbachia* behaves mostly as a reproductive parasite, being transmitted vertically from the mother to the offspring. To improve its chances of reproduction *Wolbachia* alters, sometimes drastically, the phenotype of its hosts. Among these changes we find feminization (genetic males that develop as females), parthenogenesis (females that reproduce without male intervention), male killing (males die at the embryo stage) and, the most frequent, *Cytoplasmic Incompatibility* (CI) [149]. CI consists on the crossed infertility of an infected male and a non-infected female, see Table 1. Although it is not clear if *Wolbachia* is naturally present in *Aedes* mosquitoes [125], they can be artificially infected with particular strains that have been shown to produce CI on them [73, 129]. This alone, allows already to use the release of *Wolbachia*-infected mosquitoes as a control strategy. If only male mosquitoes are released, the overall effects and mathematical modeling of this strategy become the same as with the SIT (see Section II.2). This particular use of *Wolbachia* is a form of Incompatible Insect Technique (IIT). A proper sex separation in this technique is crucial since the accidental release of females can lead to a undesired population replacement, and once the population is replaced by a population carrying *Wolbachia* the technique would stop being effective [111]. But the main reason for its use in vector control is that *Wolbachia* has been shown to reduce the vector capacity of *Aedes* mosquitoes for transmitting several arboviruses like dengue, [95, 147], chinkugunya, [92], or zika, [37], by reducing the virus load in the saliva, [92, 23], but also by producing a malformation in the trunk of its hosts, preventing the normal blood meal of the mosquitoes [143]. More recent evidence points in the direction of *Wolbachia* being useful for other genus of mosquito, even for reducing Malaria transmission by *Anopheles* mosquitoes, which is caused by protozoa and not viruses [108].

Due to all the above, *Aedes* mosquitoes infected with *Wolbachia* have come to be a remark-

| ♂ \ ♀ | Infected | Non-infected |
|---|---|---|
| Infected | Infected | CI |
| Non-infected | Infected | Non-infected |

Table 1 – Offspring outcomes in a population with both *Wolbachia*-infected and non-infected mosquitoes.

able tool in the fight against mosquito-borne diseases. These features allow for a second use of *Wolbachia*-infected mosquito releases (the one that will be treated extensively in this thesis). By releasing both males and females, a self-sustained population of *Wolbachia*-infected mosquitoes can be established. This, combined with the CI, can lead to the replacement of the wild mosquito population by a new population carrying the bacterium, and less efficient in transmitting diseases. Indeed, several successful mass releases have been carried already in different locations in Australia [104, 127], Indonesia [137] or Brazil [56]. Thanks to these deployments we begin to have promising evidence of its ability to reduce dengue cases for real [70, 127]. As for the IIT we find also successful recent deployments in the literature, whether it is used alone (Australia, [21]) or in combination with the SIT (Thailand [75], Mexico [85] and China [159]). With results ranging from a 50% population reduction, to almost complete suppression. The main actor behind most of this rear and release programs is currently the World Mosquito Program, having active projects involving *Wolbachia* in twelve countries and territories [155].

**Non-spatial models.** Before moving on to more complex models, let us introduce the basics of vector control modeling using *Wolbachia* in the setting of population replacement. The introduction in an ecosystem of *Wolbachia*-infected mosquitoes (both males and females) is usually modeled as follows.

$$\begin{cases} M'(t) = b_M M(t)\left(1 - \dfrac{M(t)+W(t)}{K}\right)\left(1 - s_h \dfrac{W(t)}{M(t)+W(t)}\right) - d_M M(t), \\ W'(t) = b_W W(t)\left(1 - \dfrac{M(t)+W(t)}{K}\right) - d_W W(t) + u(t)\ ,\ t \in [0,T], \\ M(0) = K\left(1 - \dfrac{d_M}{b_M}\right)\ ,\ W(0) = 0. \end{cases} \tag{4}$$

Let us break down the expressions above. $M(t)$ stands for the density of wild mosquitoes, while $W(t)$ for the density of *Wolbachia*-infected mosquitoes. Both populations are modeled with a death term and a birth term following a logistic growth. This implies the growth of the mosquito population will slow down and eventually saturate at a certain value depending on $K$, called the *carrying capacity*. These terms model the limitation of the resources in an ecosystem and prevent the density from blowing up. The first equation presents also another term, $1 - s_h M/(M+W)$, taking into account the CI, where $0 < s_h \leqslant 1$ models how strict is this incompatibility. It is assumed that the wild population is at equilibrium and that no *Wolbachia*-infected mosquitoes are present in the wild at the beginning of the intervention. The model has different values for the birth and death rates in each population. This is because *Wolbachia* alters several parameters of the biology of mosquitoes. Different strains can have different effects

but, in general, *Wolbachia* infection lowers the birth rate, $b_W \leqslant b_M$, and increases the death rate $d_W \geqslant d_N$ of mosquitoes [78]. This must be taken into account when introducing *Wolbachia* in an ecosystem, since it can make *Wolbachia*-infected mosquitoes less competitive and thus harder to introduce [56]. *Wolbachia* can also alter other parameters related to the dynamics of dengue inside the mosquitoes (see Chapter 3). Finally, the function $u(\cdot)$ in the second equation represents the rate at which *Wolbachia*-infected mosquitoes are released into the ecosystem. This, in a mathematical setting, is called the *control function* and we will impose some natural constraints on it. For instance, the rate at which mosquitoes are released must be necessarily bounded, $0 \leqslant u(t) \leqslant U$ a.e., but also the total amount of mosquitoes at our disposal cannot be unlimited, thus, it is natural to introduce a bound on the integral of the control, $\int_0^T u(t)dt \leqslant C$. Therefore we will consider, in general, $u \in \mathcal{U}_{T,C,U}$, with

$$\mathcal{U}_{T,C,U} := \left\{ u \in L^\infty(0,T), 0 \leqslant u \leqslant U \text{ a.e. in } (0,T), \int_0^T u(t)dt \leqslant C \right\}. \tag{5}$$

Nonetheless, in this work, we will rarely work directly on system (4), but rather on a simplification of it. As shown in [10], system (4) can be simplified when the birth rate of the mosquitoes is assumed to be much higher than its death rate. This assumption is consistent with biological observations. Details of this passage can be found in Chapter 1 and in [10], but in a nutshell, by considering $b_M = b_M^0/\epsilon$ and $b_W = b_W^0/\epsilon$ and letting $\epsilon$ tend to 0, one can prove that $W(t)$, converges to $Kp(t)$ and $M(t)$ converges to $K(1-p(t))$, where $p(t)$ represents the proportion of *Wolbachia*-infected mosquitoes in the system. It is the solution to the following equation

$$\begin{cases} \frac{d}{dt}p(t) = f(p(t)) + u(t)g(p(t)), & t \in [0,T] \\ p(0) = 0. \end{cases} \tag{6}$$

Solutions of system (4) and the solution of equation (6) can be proven to be close to each other in the sense of the Gamma-convergence. In equation (6), $g(p)$ is a decreasing function and $f(p)$ is negative until a certain value $p = \theta$ and then positive, therefore the uncontroled system presents a bistable behaviour, consistent with the fact that, thanks to CI, *Wolbachia*-infected mosquitoes can invade a wild population if they are numerous enough. The particular expressions of $f(p)$ and $g(p)$ can be found in Chapter 1, (1.5).

There are several works in the literature tackling different control problems involving this equation. In [10] the authors consider the problem of steering system (4) from its initial equilibrium to the other non-trivial stable equilibrium of the system $(M^*, W^*) = (0, K(1 - d_W/b_W))$. In other words, they are interested in minimizing the distance, for a certain fixed time horizon $T$, between the final state of the system and the desired final state $(M^*, W^*)$ . In order to do this they pose the problem

$$\min_{u \in \mathcal{U}_{T,C,U}} \frac{1}{2} M(T)^2 + \frac{1}{2} \left( [W^* - W(T)]_+ \right)^2.$$

They show that, when translated to the simplified one-equation setting the problem becomes

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

In their work they prove that solutions are *bang-bang* (this means that $u^*(t)$ can only take the extreme values 0 and $U$) and that the best releasing protocol consists on a single phase release. In other words, all mosquitoes should be released at the highest rate possible and either at the

beginning or at the end. The factor determining when to release being the total amount of mosquitoes available. If the amount of available mosquitoes is enough to trigger a population replacement, mosquitoes should be released at the start to take advantage of CI, if not, at the end, since mosquitoes will die out as time passes. In mathematical terms, this threshold is given by $C$ being bigger or smaller than $\int_0^\theta \frac{M}{f(\nu)+Mg(\nu)}\,d\nu$.

A natural extension of these results consists in taking into account the cost of the releases in the functional to minimize. A first study of this question in a limited setting can be found in [3]. In this work the problem is simplified by assuming that the final state is fixed and set to $p(T) = \theta$. They prove that, in this context, the strategy minimizing the cost consists in one uninterrupted release, done whenever in the time window. Another generalization is done by considering the time window not fixed and including the final time in the functional to minimize. In this case the best strategy is carrying the release non-uninterruptedly and from the beginning. They also carry simulations on the 2D system (4), finding results in line with those of the 1D equation (6). Chapter 1 can be seen as further generalization of these results.

Works non focused on the study of equation (6) but also tackling the problem of the mosquito population replacement using *Wolbachia* are, for instance: [6], where some properties of optimal controls are shown, backed with numerical simulations, in a system similar to (4) but including not only adults but also eggs; [33], where the question of minimizing final time and costs is also tackled; [26], where a feedback control strategy guaranteeing the invasion while keeping the costs to a minimum is presented or [25] where general ideas for biological control of mosquitoes are established, in an attempt to establish 'model-free' feedback control principles. A similar optimal control approach for *Wolbachia*-infected mosquito releases, but applied to the context of the IIT can be found in [132]. Although, as previously mentioned and as the authors point out, mathematically speaking, the model studied in the case of the IIT is equivalent to an SIT model.

**Spatial models.** Although non-spatial models can describe the overall dynamics of a population, space plays a fundamental role when it comes to biological invasions. Hence, a natural extension of the models described is the addition of the space variable. Enriching the models in such a way can make arise new non-trivial strategies with no space-free equivalent. The natural spatial extension of model (4) can be written as follows,

$$\begin{cases} \partial_t M - D\Delta M = b_M M\left(1-\dfrac{M+W}{K(x)}\right)\left(1-s_h\dfrac{W}{M+MW}\right) - d_M M, \\ \partial_t W - D\Delta W = b_W W\left(1-\dfrac{M+W}{K(x)}\right) - d_W W + u, \quad t\in[0,T], \quad x\in\Omega, \\ M(0,x) = M^0(x), \quad W(0,x) = 0, \quad x\in\Omega, \\ \partial_\nu M(t,x) = \partial_\nu W(t,x) = 0, \quad x\in\partial\Omega, \end{cases} \tag{7}$$

where now the densities of the mosquito population depend on time, but also on space, $M = M(t,x)$, $W = W(t,x)$. The last line of the model means that no mosquitoes leave the domain we are considering for the problem. These boundary conditions can be straightforwardly altered without affecting the rest of the model if the problem studied requires so. In this model mosquitoes are considered to move in the landscape by diffusion, at diffusion rate $D$, which is the standard when modeling population movement. In addition, to write the model in all generality, the carrying capacity, $K(\cdot)$, does not need to be homogeneous in all the domain when the space is taken into consideration, which is almost always the case in field conditions. However, usually in the literature when diffusion is considered, the carrying capacity is considered constant in all the domain. This model has its own simplified version involving the proportion of *Wolbachia*-infected

mosquitoes, under the same assumptions on the birth rates.

$$\begin{cases} \partial_t p(t,x) - D\Delta p(t,x) = f(p(t,x)) + u(t,x)g(p(t,x)), & t \in [0,T], \quad x \in \Omega \\ p(0,x) = 0, \quad \forall x \in \Omega, \\ \partial_\nu p(t,x) = 0, \quad x \in \partial\Omega, \end{cases} \tag{8}$$

A formal derivation of this equation can be found in [134] and [46]. This equation is, nonetheless, only valid in case the carrying capacity is homogeneous, i.e., $K(x) = K$ for all $x \in \Omega$. When an inhomogeneous carrying capacity is considered an extra term needs to be added to take into account the gradient in the abundance of mosquitoes across the domain. In [98], a formal derivation of this equation is carried out. Approximating the total population of mosquitoes at first order by the carrying capacity, they arrive to the following expression

$$\begin{cases} \partial_t p(t,x) - D\Delta p(t,x) - 2D\dfrac{\nabla K(x)}{K(x)} \cdot \nabla p(t,x) = f(p(t,x)) + u(t,x)g(p(t,x)), \ (t,x) \in [0,T] \times \Omega, \\ p(0,x) = 0, \quad \forall x \in \Omega, \\ \partial_\nu p(t,x) = 0, \quad x \in \partial\Omega, \end{cases} \tag{9}$$

In Chapter 2 we study a problem where, in a first time, we set $D = 0$, i.e., diffusion is not considered, but with a non-homogeneous carrying capacity. Assuming $K(\cdot)$ to be constant, several problems have been addressed already in works preceding this thesis.

Since partial differential equations are much more difficult to study than ordinary ones a common approach to simplify the study of equation (8) is by posing the control problem on the initial datum of the equation. That is, consider one single instantaneous release at time $t = 0$, and then considering $u(t,x) = 0$. With $u(0,x) = u^0(x)$ and $u^0 \in \mathcal{U}_{0,C,U}$, where

$$\mathcal{U}_{0,C,U} := \left\{ 0 \leqslant u^0(x) \leqslant U \text{ a.e. in } \Omega, \int_\Omega u^0(x)dx \leqslant C \right\}. \tag{10}$$

In line with this we find, for instance, [46], where the problem

$$\min_{u^0 \in \mathcal{U}_{0,C,U}} \int_\Omega (1 - p(T,x))^2 \, dx,$$

is studied. In this work it is proven that spatially constant solutions are not always optimal, although they are always critical points. They also show that in case $C$ is small enough, spatially constant solutions are at least local minimizers. Lastly, they give numerical counterexamples on the optimality of constants. About this same problem, in [11], Gaussian releases are considered and their location is optimized numerically and in [135] they settle the existence and give estimates for a threshold on a radially symmetric initial data such that the invasion is guaranteed. They also quantify the uncertainty associated with the invasion in a more realistic scenario by studying a stochastic framework. In [99], they consider a closely related problem, $\max_{u^0 \in \mathcal{U}_{0,C,U}} \int_\Omega p(T,x)\, dx$, and prove the existence of solutions (even for $f(p)$ much more general than the one defined in (1.5)), and also give some conditions on the optimality of constants. In [86], the authors extend these results and give a characterization of singular controls.

Finally, regarding the study of traveling waves, in [29] conditions for the ignition of a traveling wave by means of a feedback control are studied, while in [98] they show that if the population gradient in an area is strong enough (due to an heterogeneous environment) invading fronts can be stopped and converge to stable ones.

**Epidemiological models.** Finally, *Wolbachia*-infected mosquito releases can be also modeled in an epidemiological framework. Incorporating the population dynamics introduced in (4) and the epidemiological model presented in (3) we can write

$$\begin{aligned}
S'_H &= bH - \frac{\beta_M}{H} I_M S_H - \frac{\beta_{WH}}{H} I_W S_H - b_H S_H,\\
E'_H &= \frac{\beta_M}{H} I_M S_H + \frac{\beta_{WH}}{H} I_W S_H - \gamma_H E_H - b_H E_H,\\
I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H,\\
S'_M &= b_M M \left(1 - \frac{M+W}{K}\right)\left(1 - s_h \frac{W}{M+W}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M,\\
E'_M &= \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M,\\
I'_M &= \gamma_M E_M - d_M I_M,\\
S'_W &= b_W W \left(1 - \frac{M+W}{K}\right) - \frac{\beta_{HW}}{H} S_W I_H - d_W S_W + u(t),\\
E'_W &= \frac{\beta_{HW}}{H} S_W I_H - \gamma_W E_W - d_W E_W,\\
I'_W &= \gamma_W E_W - d_W I_W.
\end{aligned} \tag{11}$$

Using *Wolbachia* in the context of population replacement implies the release of females. Thus the addition of these mosquitoes needs a new set of SEI compartments with different parameters, since infection with *Wolbachia* alters significantly different aspects of the biology of the mosquito. In particular, the most important effect in this context, $\beta_{HW}, \beta_{WH} < \beta_M$, that is, the probability of transmission between human and mosquito is significantly lower when mosquitoes have *Wolbachia* (a detailed explanation of this model will be done in Chapter 3). Other works like [69] use closely related models to asses the feasibility of *Wolbachia* use for dengue control. Also in [102] they tackle this question, with a more complex model where the aquatic phase and seasonality are also taken into consideration. A multi-strain model in interaction with *Wolbachia* can be found in [74].

Concerning optimal control problems, in [158], a similar model is used, although considering perfect pathogen blocking by *Wolbachia* ($\beta_{HW} = \beta_{WH} = 0$) and only bang-bang controls. In this work they tackle, mostly numerically, the problem of minimizing at the same time the cost of intervention, the final distance to a disease-free equilibrium state where *Wolbachia*-infected mosquitoes have invaded the population and the total amount of infections during the time horizon considered. In mathematical terms, this corresponds to

$$\min_{u\in\{0,U\}} A_1 \int_0^T u(t)\,dt + A_2 \int_0^T I_H^2(t)\,dt + A_3 \Psi(\mathbf{x}(T)). \tag{12}$$

Here, $A_i$, $i = 1, 2, 3$ are constants weighting the importance of each term, and $\Psi(\mathbf{x}(T))$ is a penalty term depending on the final state of the system, $\mathbf{x}(T)$.

## II.2 Sterile insect technique

The SIT consists on the massive release of male mosquitoes that have been previously sterilised (traditionally, in proportions of at least 10:1 with the wild male population [106]). This technique is much older than the use of *Wolbachia*, dating back to the 1950s, and it has been tested numerous times, also with other insect pests [41]. For instance, it was successfully used to eliminate the tsetse fly *Glossina austensi* from the Unguja island, in the Zanzibar archipelago [146] and the New World screwworm *Cochliomyia hominivorax* from Central America, the United

States and Lybia [64]. It is also currently being used with great success in the control of *Ceratitis Capitata* in the Mexican-Guatemalan border [49] and in the Valencian Region in Spain, where the need for aerial pesticide spraying was reduced by 90% [115]. This solid background has allowed the elaboration of detailed roadmaps to implement an SIT program [106].

Male mosquitoes are separated mostly by hand, which produces currently the bottleneck for the scaling up of the technique, although the process is also in the path for automatization. Trained workers can separate with high accuracy both sexes using specialized devices in the pupal stage since female pupae are bigger than male in *Aedes* and *Culex* mosquitoes [111]. For *Anopheles* on the other hand, the abdominal segment of pupae must be examined under the microscope to find morphological differences [58]. Other proposals for sex separation include taking advantage of behavioural differences at the adult stage (only females feed on blood). Blood meals with insecticide can be made available in a cage with unsorted mosquitoes). Finally the use of fluorescent transgenic markers only expressed in females at larval stage [35], or other genetic means, like producing a GM strain where only males are resistant to a certain chemical, allowing to separate sexes from the egg stage [156]. Then, sorted males are irradiated with X-rays or gamma rays in their late pupal or adult stage [64]. Optimizing the dose of radiation is key when it comes to the effectiveness of the technique, since higher radiation doses lead to higher sterility rates, but also to reduced competitiveness of the mosquitoes, which can be detrimental for the success of the technique [112]. Less commonly, males can also be sterilised using chemicals [41]. Sterile males then mate fertile females, producing non-viable eggs, thus reducing the population size. Female mosquitoes are generally considered to mate only once in their life time and use the stored sperm to fertilize their eggs, which enhances the performance of this technique. However, evidence of multiple matings in the wild has been found [31].

Successful releases were carried against *Culex* mosquitoes [113] in Florida in the 1960s and against *Anopheles* in El Salvador in the 1970s [148], to name a few. More recently, pilot field trials for *Aedes* have been tested in Italy [22], Reunion island [107], Cuba [57] and in the Valencian Region in Spain [142]. Most of these projects are in close collaboration with the main driver in the development of the SIT in the last decade: the Joint FAO/IAEA Programme [79].

A simple ODE model of the SIT can be written as follows

$$\begin{cases} M'(t) = b_M M(t)\left(1 - \dfrac{M(t)}{K}\right)\dfrac{M(t)}{M(t) + s_c M_S(t)} - d_M M(t), \\ M_S'(t) = u(t) - d_S M_S(t), \quad t \in [0,T], \\ M(0) = K\left(1 - \dfrac{d_M}{b_M}\right), \quad M_S(0) = 0. \end{cases} \tag{13}$$

This model captures the essential part of the effect on the population of the introduction of sterile mosquitoes and it is the model that will be studied in Chapter 3. The term $M/(M + s_c M_s)$ is proportional to the probability of a mating with a fertile male. $s_c \in (0,1]$ represents the mating competitiveness of the sterile mosquitoes, because female mosquitoes might tend to mate less frequently with sterile mosquitoes than with fertile ones. This is indeed a simplified model. In the literature, frequently, models contain the egg stage or they split the adult population in males and females to take into account a possible disparity in the number of mosquitoes that reach adulthood of each sex or that they have different lifespans or behaviours (sometimes they include both features at the same time). Also, in some models, Allee effects are considered in order to incorporate the effect of extinction of the population when it is reduced under a certain

threshold. A more complete system, studied in [132], is the following,

$$\begin{cases} E'(t) = b_E F(t)\left(1 - \dfrac{E(t)}{K}\right) - (d_E + \tau_E)E(t), \\ F'(t) = r\ \tau_E E(t)\dfrac{M(t)}{M(t) + s_c M_S(t)}\left(1 - e^{-\beta_S(M(t)+s_c M_S(t))}\right) - d_F F(t), \\ M'(t) = (1-r)\ \tau_E E(t) - d_M M(t), \\ M_S'(t) = u(t) - d_S M_S(t), \quad M_S(0) = 0, \quad t \in [0,T]. \end{cases} \tag{14}$$

In this model, the carrying capacity of the environment is considered to saturate egg population (as a proxy for a saturated aquatic phase population more generally speaking. Intraspecific competition occurs mostly at the larval stage.), rather than the adult one directly. Adults are considered to reach the adult state with a female to male proportion of $r$. When females and males are considered to reach adulthood with the same probability, $r = 1/2$, and that they have the same death rate, $d_M = d_F$, both equations can be added to obtain a single one for adults, as it has been considered in the other models presented so far. Lastly, the term $1 - e^{-\beta_S(M(t)+s_c M_S(t))}$ sets the Allee effect. The term accounts for the difficulty for females to find a partner when the male mosquito density is small. All works presented hereafter study some version of model (14).

Works having applied optimal control to the study of the SIT present similar approaches on the way of posing the problem. Usually there is an endpoint condition to be satisfied (namely, $F(T) \leqslant \epsilon$), and the functionals to minimize include the cost of the intervention, or the cost and the final time. Examples of this are [7] and [24]. In [7], an optimal feedback control strategy is described. [24] performs numerical simulations on the continuous strategy and gives suboptimal strategies considering impulsive releases. An impulsive release consists on considering the release to be instantaneous and it is presented as a discontinuity in the amount of sterile mosquitoes in the system. Also [27] considers impulsive releases and gives open and closed-loop feedback strategies minimizing the number of sterile males to be released periodically in order to reach elimination. In [132], the necessary conditions for reaching elimination using SIT (or IIT) are described for different kinds of release strategies: constant, instantaneous and periodic, and continuous. Finally, [28], broadens the scope of study by including migration of wild mosquitoes into the system. This is an important addition to the model since migrating mosquitoes from surrounding areas can repopulate areas that had been previously treated, disrupting the achievements.

SIT models also have their spatial counterparts including diffusion on the mosquito population. Similar questions to the ones posed in Section II.1 can be posed. As in II.1, the addition of space allows to study phenomena like invasion fronts. In [8] and [12] they study the phenomenon of wild mosquito reinvasion after mosquito have been eliminated. They show that buffer areas with permanent sterile mosquito releases above a certain threshold are effective for stopping a reinvasion front for any width of the buffer area considered. They also provide numerical simulations to illustrate this.

Lastly, in [9], they study the deployment technique known as *Rolling carpet*. This deployment technique consists on starting the treatment on one end of the terrain and progressively advancing towards the other end. In such a way that the treated area cannot be reinvaded since the remaining wild mosquitoes lay at the other side of the zone that is currently being treated. In [9] they compare the use of pesticides and that of the SIT for the rolling carpet deployment. They succeed in establishing travelling waves with negative speed (opposite speed to the sense in which the wild mosquito invasion would occur in the absence of treatment) for both cases, which ensures that treated areas will stay mosquito-free after the treatment.

Finally, models encompassing epidemiology and SIT can also be found, although optimal control approach in this setting is rare to the best of our knowledge. In [45] they study an

epidemiological model for Chikungunya while SIT releases are being performed. They compare the case of instantaneous periodical releases with a continuous and constant one. In [42] the model studied is for Zika. Nevertheless, in principle, these models could be used for modeling many other vector-borne diseases adjusting some parameter values.

### II.3 Other vector-based control techniques

For completeness, we mention that there are other vector-based control techniques which rely on the release of genetically modified mosquitoes. These techniques, in general, consist on introducing one or several modified genes into the mosquitoes' genome producing two kinds of effects:

- **Deletereous / Inmmune boosting effects:** In a similar spirit to the techniques already presented, one of the effects that these genes induce in mosquitoes is either boosting its immunity to disease or, on the contrary, killing the host when it gets infected. Other alternatives can be, for instance, preventing the females from flying or causing infertility in the mosquitoes [13, 82].
- **Gene drive:** The other characteristic these genes present is that they produce a so called *gene drive*. This means that the modifying gene has the ability of being passed to the next generation (except, of course, in the case of sterilizing genes) with more than a 50% chance (the usual proportion in Mendelian inheritance). Thus, this gene can be rapidly spread through the population [15, 13].

As in other fields of application the use of genetically modified organisms is highly controversial due to the fear on possible unforeseen outcomes of the introduction of new genetic material in ecosystems. Even more, in the case of gene drives. Thorough studies and trials in small isolated settings should be carried before considering the possibility of generalizing the use of these techniques [100].

## III Contributions of this thesis

In this thesis several problems regarding the optimal control of mosquito-borne diseases are studied, both analytically and numerically. Keeping in mind the goal of reducing the mosquito-borne disease burden, it aims at answering a variety of questions:

- How optimal strategies evolve when the cost of releasing mosquitoes is taken into account. If the material restrictions for carrying the releases are considerable, how should the releasing policies be adapted to still be competent?
- The spatial influence of an inhomogeneous environment in the optimal releasing strategies. Mosquitoes are not equally distributed in the environment, what is the best way to distribute mosquitoes in a release to maximize the efficacy of the techniques?
- How strategies evolve when the focus shifts from the mosquito population to the human population. The ultimate goal of controlling mosquito population is to prevent the spread of the diseases they transmit. In case one of these diseases is already circulating, how should be carried the deployments in order to minimise the amount of infections?

Our goal is to give qualitative answers to these questions, providing a better and deeper understanding of them, with the hope that this work can be the basis for future more quantitative and detailed studies of these topics.

The body of the manuscript is divided into three chapters. In the first two chapters we focus on the use of *Wolbachia* to achieve a population replacement. Although the ultimate goal in mind is always the control of vector-borne diseases, these chapters regard only the mosquito population.

It is implicit that by controlling the mosquito population effectively and efficiently the desired goal will follow. In the last chapter the focus of the study is switched. The problem studied concerns the human population in interaction with the mosquito one and optimal strategies are defined with respect to its effect on the reduction of the number of human cases of a disease. In this chapter both population replacement using *Wolbachia* and the sterile insect technique are studied and the optimal strategies arising for each one compared.

This manuscript is organized as follows:

— **Chapter 1: Optimal release strategies for mosquito population replacement.** In Chapter 1 we pose and study a problem to find optimal strategies for population replacement balancing the cost of the releases and its performance. The performance of the strategy is measured by the time required to achieve a previously set final proportion of *Wolbachia*-infected mosquitoes when the final time is considered to be free or as the distance to a full invasion state at the final time, when the final time is fixed. We also study the robustness of optimal strategies with respect to the convexity of the function chosen to model the cost of the mosquito releases. This chapter is taken from [4].

— **Chapter 2: Optimal initial time strategies for mosquito population replacement: influence of the carrying capacity on spatial releases** In Chapter 2 we study the optimal spatial distribution of a single initial release in an inhomogeneous environment, assuming that mosquitoes do not diffuse in the domain. We also explore numerically the case with diffusion. This chapter is a work in progress.

— **Chapter 3: Mosquito-borne disease outbreak control via instant vector releases.** In Chapter 3 the control problem is posed in an epidemiological model encompassing mosquitoes and humans. We study optimal instantaneous releases to minimize (or suppress when possible) the impact of an outbreak in the human population, studying both the use of *Wolbachia* and the SIT. This chapter is taken from [5].

We summarize hereafter, chapter by chapter, the main contributions of this thesis.

## Chapter 1: Optimal release strategies for mosquito population replacement

### Motivation

The goal of this chapter is to determine the optimal strategies for mosquito population replacement using *Wolbachia* according to a criterion that balances cost and performance. In this chapter we study the scalar equation (6). The chapter stems from [10], and generalizes the results obtained there, which can be seen as a particular case for one of the two families of problems studied (in particular, Family 2). We recall that, according to the notation used so far, $p(t)$ denotes the proportion of *Wolbachia*-infected mosquitoes.

In mathematical terms, the problem considered is the following:

$$\inf_{u\in\mathcal{U}_{T,C,U}} (1-\alpha)\int_0^T j_1(u(t))dt + \alpha j_2(T,p(T)). \tag{15}$$

In (15), $j_1$ is a function encompassing all the costs of mosquito releases: from production, to storage, transport or release. The particular choice for this function is non-obvious, we perform our study for a very general class of $j_1$ functions, namely: convex, linear and concave. We are interested in determining how robust are optimal strategies when cost functions with different convexities are considered. On the other hand, $j_2$ is a function modeling the performance of the intervention in some sense. $\alpha \in [0,1]$ is a parameter determining the relative importance of each term. A small value of $\alpha$ implies a bigger concern for cost saving, on the contrary a big value

of $\alpha$ means a bigger concern for the effectiveness of the technique. The control function belongs in $\mathcal{U}_{T,C,U}$, as defined in (5). We recall this means that both the rate at which mosquitoes can be released and the total amount of mosquitoes at our disposal are bounded. In practice we consider two different families of problems, each one associated with a particular choice for $j_2$.

For the first family of problems, we set a goal on the final proportion of mosquitoes to attain, $p(T) = p_T$ and we let the final time for our intervention, $T$, free. In this setting the function measuring the performance will be $j_2(T) = T$. A strategy would be considered more performant if it achieves a desired final proportion in less time than another one. The problem can be written in this case as

$$\begin{cases} \inf\limits_{\substack{u\in\mathcal{U}_{T,C,U}\\ T>0}} (1-\alpha)\displaystyle\int_0^T j_1(u(t))dt + \alpha T, \\ p' = f(p) + ug(p) \text{ in } (0,T),\ p(0) = 0\ ,\ p(T) = p_T\ , \end{cases} \tag{16}$$

where $p_T \in (0,1)$. For the second family, on the contrary, we fix the time horizon, $T$, in which the mosquito releases are going to be done. The performance in this case will be measured by how high is the level of population replacement achieved by the end of the intervention. We can formulate the problem in this case as

$$\begin{cases} \inf\limits_{u\in\mathcal{U}_{T,C,U}} (1-\alpha)\int_0^T j_1(u(t))dt + \alpha\left(1-p(T)\right)^2, \\ p' = f(p) + ug(p),\ p(0) = 0\ . \end{cases} \tag{17}$$

**Main Results**

We highlight here the main results and contributions presented in this chapter. Results in this chapter have been obtained by exploiting the optimality conditions resulting from the application of Pontryagin's Maximum Principle (PMP). The maximum principle is a well known result in control theory and we do not dive deep into its hypothesis and details. For further reading on the topic we refer to [61, 140]. The following theorems are taken from Chapter 1 (Theorems A and B, which are, in turn, simplified versions of the more technical Theorems 1.2 and 1.3 respectively). These theorems fully characterize the solutions to both problem families posed in (16) and (17). In particular, one can recover the results in [10] by setting $\alpha = 1$ in Theorem B.

The first theorem regarding Family 1, the case with the final time $T$ free, (16), reads

**Theorem A** (Family 1) *There exists $(T^*, u^*) \in \mathbb{R}_+ \times \mathcal{U}_{T,C,U}$ solving Problem (16). The overall behaviour of $u^*$ depends on the convexity of $j_1(\cdot)$, the value of $\alpha$ and the value of $C$.*

*In general, we distinguish the following cases:*

— *Case 1. $j_1$ is either linear or strictly concave. There exists a real parameter $\alpha^* \in [0,1)$ given by the parameters of the problem such that:*
  — *if $C$ is large enough: If $\alpha \in [\alpha^*, 1]$, then $u^* = U\mathbb{1}_{[0,T^*]}$. If $\alpha \in (0,\alpha^*)$, then $u^*$ is bang-bang with exactly one switch from $U$ to 0 at a time $t_s \in (0,T^*)$ determined by $\alpha$.*
  — *else, one has $u^* = U\mathbb{1}_{[0,C/U]}$.*

*In this case, the optimal time $T^*$ reads*

$$T^* = \int_0^{p_T} \frac{d\nu}{f(\nu) + u_p^*(\nu)g(\nu)} \quad \text{with } u_p^*(\nu) = U\mathbb{1}_{(0,p_s)}$$

*and*

$$p_s = \begin{cases} p(t_s) & \text{if } C \text{ is large enough,} \\ p(C/U) & \text{otherwise.} \end{cases}$$

— *Case 2. $j_1$ is convex. If $\alpha \in (0,1)$ singular controls may appear. The control $u^*$ is non-decreasing until $t^* \in (0,T^*)$ such that $p(t^*) = p^*$ and then non-increasing.*

*If $\alpha = 1$, the term with $j_1$ is no longer present and $u^* = U\mathbb{1}_{[0,\min\{T^*,C/U\}]}$.*

In order to prove this theorem, we first prove and then exploit the monotonicity of the $p$ associated to the optimal control $u^*$ in Lemma 1.1, and we introduce an adapted change of variables that allows us to drastically reduce the difficulty of the problem by transforming it into a problem of calculus of variations. To simplify the reasoning further, we solve first a simpler problem where no restriction on the total number of mosquitoes is considered (See Theorem 1.1). Solutions of this simpler problem that do respect the constraint $\int_0^T u(t)dt \leqslant C$ will also be solutions of the constrained problem.

We prove that optimal strategies depend on the convexity of the cost function, $j_1$. In case this function is concave or linear, solutions are bang-bang. Solutions start with $u^* = M$ and switch at most once, depending on the value of $C$ and $\alpha$. In case $j_1$ is a convex function, we characterize the singular controls solving the problem. The particular shape of these solutions is also dependent on $C$ and $\alpha$, as well as other parameters of the problem. Nonetheless, they all share a common property of being non-decreasing prior to $p(t) = p^*$ and non-increasing afterwards. With $p^*$ being explicitly known and verifying $p^* < \theta$. In Figure 4 we see can see an illustration of the kind of solutions obtained depending on the convexity of $j_1$.

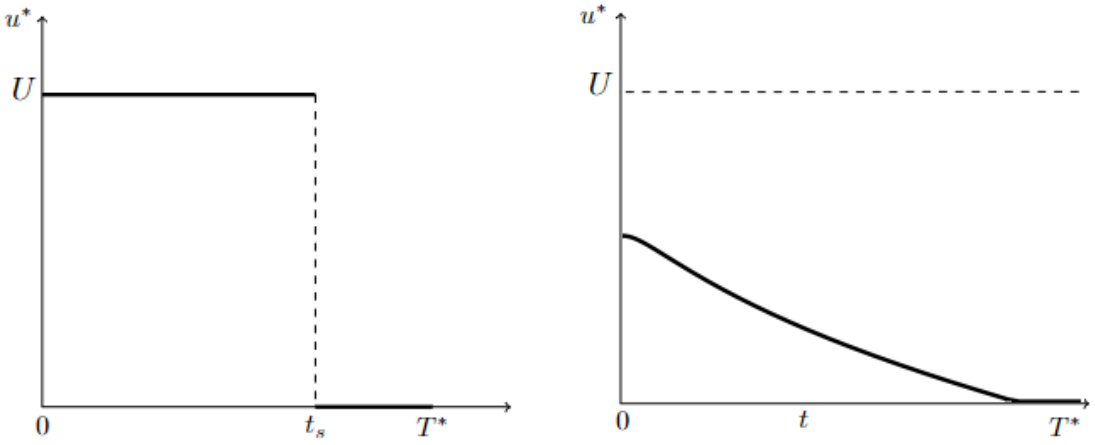


Figure 4 – Example of a bang-bang (left) and a singular control (right) arising as solutions of (16) for $j_1$ concave and convex respectively.

In the case of Family 2, where the final state, $p(T)$, is free, (17), the result reads

**Theorem B** (Family 2) *There exists $u^* \in \mathcal{U}_{T,C,U}$ solving Problem (17). In addition, there exists an interval $(t^-,t^+)$ such that, outside of it $u^* = 0$ and the state $p_{u^*}$ associated to $u^*$ is constant. Inside $(t^-,t^+)$, $p_{u^*}$ is increasing and the behaviour of $u^*$ depends on the convexity of $j_1(\cdot)$, the value of $\alpha$ and the values of $C$ and $T$. We distinguish between the following cases:*

— *Case 1. $j_1$ is either linear or strictly concave. The solution is $u^* = U\mathbb{1}_{[t^-,t_s]}$, with $t_s \leqslant t^+$ the switching time.*

— *Case 2. $j_1$ is convex. If $\alpha \in (0,1)$ singular controls may appear. The control $u^*$ is non-decreasing until $t^* \in (t^-,t^+)$ such that $p(t^*) = p^*$ and then non-increasing.*

*If $\alpha = 1$, then $u^* = U\mathbb{1}_{[t^-,t_s]}$, with $t_s$ defined as in the concave and linear case.*

To prove this theorem we follow a similar path. We also prove a similar monotonicity property on $p(t)$, allowing us to study a calculus of variations problem in a certain subinterval of the time window considered (Lemma 1.2). Then, we show that $u^*(t) = 0$ outside of this interval. To characterise the solutions we reduce once again the complexity of the problem by breaking it down into two different ones. First we characterize the optimal strategy for $\alpha = 0$ and an arbitrary final state fixed (Theorem 1.4) and then we treat the full problem as a one dimensional one where the variable to be optimized is, precisely, this final state.

For both families, in order to establish the existence of solutions for the concave case, one cannot apply the standard reasonings in calculus of variations, since the functional studied is not lower semicontinuous. We approach the problem in an innovative way, by investigating the optimality conditions for a finite dimension auxiliary problem. This reasoning allows us to obtain existence, but also to characterize the solutions, establishing they are bang-bang.

Note how optimal strategies described in Theorem B are, overall, very similar to those presented in Theorem A. In conclusion, in this chapter we prove a robustness property on the optimal controls, in the sense that solutions are similar for both families of problems.

Results obtained in this work can be translated into general guidelines for real releasing policies when we restrict ourselves to the cases where $p(T) > \theta$. This restriction being natural in practical applications, since, while in this case the system tends naturally to $p(T) = 1$, in case $p(T) \leqslant \theta$ the invasion of *Wolbachia*-infected mosquitoes will not occur without further intervention. In order to understand these guidelines, first we need to understand the meaning of the convexity/concavity of function $j_1$ in this problem. Function $j_1$ can be seen as aggregating all costs of mosquito production transport and release. In other words, it is a measure of the cost per mosquito per unit of time. The second derivative of this function is a measure of the marginal increase in the cost per mosquito as production is scaled up. For instance, the simplest scenario, $j_1(u) = u$, means that costs are proportional to production: Releasing mosquitoes twice as fast over a period of time implies costs twice as high. This might not always be the case, economies of scale usually lead to a decrease in the marginal cost of production per unit, so $j_1$ can be expected to be concave: As more mosquitoes are released, the extra cost per mosquito is reduced. Nonetheless, opposite effects can occur. Scaling up production can come with unforeseen consequences in management, storage capacity or logistics, therefore, in some cases the marginal cost of production can quickly increase, justifying the need for a convex $j_1$.

In a nutshell, if we know $p$ at any given time, which can be done by setting up mosquito traps to measure the *Wolbachia*-infected mosquitoes in the wild (a common practice in any field implementation of any vector control technique), our results yield:

— If $j_1$ is either linear or strictly concave, and so mosquito production costs are decreasingly expensive or stay constant, the optimal releasing strategy is bang-bang. We act as soon and as fast as possible, until the critical proportion $p = \theta$ is surpassed. This means optimal controls are $u^* = M$ from the beginning, and with one switch, at most, after $p(t) = \theta$. See figure 1.2.

— If $j_1$ is strictly convex, and thus mosquito production is increasingly expensive, solutions are more complex due to the appearance of singular controls. Nevertheless, we can conclude that in this case efforts must also be concentrated at the beginning, since the optimal control is non-decreasing until $p(t) = p^*$ and non-increasing afterwards, with $p^* < \theta$. Therefore efforts can be relaxed after the proportion $p(t) = p^*$ is achieved. See figure 1.3.

**Perspectives**

The natural continuation of this work would be the addition of spatial dimensions to the problem. An adequate spatial distribution of the releases can be key for the success of these

techniques and it is not obvious that homogeneous releases should always be the optimal solution. In fact, in [46] the contrary is proven. This should be even more the case when mosquito distribution in the environment in non-homogeneous. Nonetheless, the complexity of the problem when space is added invites to simplify it by posing less ambitious questions. In the next chapter space is introduced, but we restrict ourselves to the family 2 of problems, with $T$ fixed, and with $\alpha = 1$, that is, we do not optimize the cost of the releases, but only its performance in a non-homogeneous environment.

## Chapter 2: Optimal initial time strategies for mosquito population replacement: influence of the carrying capacity on spatial releases

### Motivation

The spatial distribution of the mosquito releases is a specially relevant aspect of the deployments. In this chapter we approach the question of how to optimize the spatial distribution of an instantaneous release at $t = 0$ when the distribution of wild mosquitoes in the environment is inhomogeneous. As introduced in section II.1, this is modeled by considering the carrying capacity of the environment to be not necessarily constant, but a function of the space variable, $K(x)$, $x \in \Omega$.

In order to deduce the equation studied in this chapter, we first consider an equation analogous to (8) but, in principle, without diffusion ($D = 0$). This case is a toy model lacking of realism, nonetheless, it is of interest from a mathematical point of view. It must be seen as a first step towards the study of the full model with diffusion, which we also tackle numerically. To highlight the spatial dependency of the carrying capacity and in order to facilitate the exposition we extract $K(x)$ from the definition of $g$, therefore in this chapter $g$ is defined by (2.6) [2]. Thus, the equation we are interested in reads

$$\begin{cases} \partial_t p(t,x) = f(p(t,x)) + \frac{u(t,x)}{K(x)} g(p(t,x)), \quad t \in [0,T], \quad x \in \Omega \\ p(0,x) = 0, \quad \forall x \in \Omega. \end{cases} \tag{18}$$

The goal in mind is to minimize the distance of the final state to the state of full *Wolbachia* invasion in the population across the domain, thus, the problem we consider at first is

$$\min_{u \in \mathcal{U}_{T,C,U}} \int_0^T \int_\Omega \left(1 - p(T,x)\right)^2 \, dx \tag{19}$$

where $\mathcal{U}_{T,C,U}$ in this chapter is defined analogously to (5) but taking into account the space. That is,

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

As mentioned, in this chapter we focus in optimizing a single instantaneous release at time $t = 0$. In other words, we study problem (19) when the time distribution of the releases is set to $u(t,x) = u_0(x)\delta(t)$.

$$\min_{p_0 \in \mathcal{P}_{0,C,U}} \int_\Omega \left(1 - p(T,x)\right)^2 \, dx, \tag{20}$$

2. Although $f$ may also seem different from the one defined in (1.5), these changes are purely cosmetic.

where

$$\mathcal{P}_{0,C,U} = \left\{ p_0 \in L^\infty(\Omega), \quad 0 \leqslant p_0 \leqslant G^{-1}\left(\frac{U}{K(x)}\right) \text{ a.e.}, \quad \int_\Omega K(x)G(p_0(x))\,dx \leqslant C \right\}.$$

and

$$\begin{cases} \partial_t p(t,x) = f(p(t,x)), \quad t \in [0,T], \\ p(0,x) = p_0(x), \quad x \in \Omega. \end{cases} \tag{21}$$

Finally, we also take a look at the case with diffusion with Neumann boundary conditions (modeling that mosquitoes cannot leave the domain) from a numerical point of view. In this case, the problem is still the same, (20), but the equation studied is

$$\begin{cases} \partial_t p(t,x) - D\Delta p(t,x) - 2D\frac{\nabla K(x)}{K(x)} \cdot \nabla p = f(p(t,x)) - D\frac{\Delta K}{K}\psi(p), \quad t \in [0,T] \\ p(0,x) = p_0(x), \quad x \in \Omega, \\ \partial_\nu p(t,x) = 0, \quad x \in \partial\Omega. \end{cases} \tag{22}$$

with $\psi(p) := p(1-p)\frac{b_W^0 - b_M^0(1-s_h p)}{b_M^0(1-p)(1-s_h p)+b_W^0 p}$. The deduction of this equation from a two-species model like system (7) when an inhomogeneous carrying capacity is considered can be found in Chapter 2, and more detailed in [98].

**Main results**

We present here the main results contained in Chapter 2 of this manuscript. In this chapter we first characterise the solutions with the help of a function we define, namely

$$w_T(p_0) := -g(p_0(x))(1-p(T,x))\exp\left(\int_0^T f'(p(s,x))\,ds\right).$$

Exploiting the first and second order optimality conditions we prove that there exists a $\lambda^* \geqslant 0$ such that the optimal solution to problem (20), $p_0^*(x)$, satisfies

— On $\{p_0^* = p_U(x) := G^{-1}\left(\frac{U}{K(x)}\right)\}$, we have $w_T \leqslant -\frac{\lambda^*}{K(x)}$,
— On $\{p_0^* = 0\}$, $w_T \geqslant -\frac{\lambda^*}{K(x)}$,
— On $\{0 < p_0^* < p_U\}$, $w_T = -\frac{\lambda^*}{K(x)}$, and in this set, each minimum satisfies the condition $\frac{\partial w_T}{\partial p_0} \geqslant 0$.

In the light of this result it becomes clear that the monotonicity of $w_T$ plays a fundamental role in the characterization of solutions. Next, we show that, under certain hypothesis on the parameters of the problem, there exists a $T_0 > 0$, that we compute explicitly, such that

— If $T \leqslant T_0$, then $w_T$ is monotonically increasing
— If $T > T_0$, then $w_T$ is unimodal, first decreasing, then increasing.

We explore numerically the regions of the parameter space satisfying this hypothesis in Appendix B.

To conclude, we prove two theorems characterizing the solutions of problem (20). In case $T \leqslant T_0$, we solve explicitly the problem, fully characterizing the solution. Here we present a simplified version of Theorem 2.1.

**Theorem C** ($T \leqslant T_0$) *Assume $T \leqslant T_0$ and $0 < C < U|\Omega|$. Then there exists a unique*

$p_0^* \in \mathcal{P}_{0,C,U}$, *that solves problem* (20). *It is given by*

$$p_0^*(x) = \begin{cases} 0 & \text{if } -\frac{\lambda^*}{K(x)} \leqslant w_T(0), \\ p_U(x) := G^{-1}\left(\frac{U}{K(x)}\right) & \text{if } -\frac{\lambda^*}{K(x)} \geqslant w_T(p_U(x)), \\ w_T^{-1}\left(-\frac{\lambda^*}{K(x)}\right) & \text{if } -\frac{\lambda^*}{K(x)} \in (w_T(0), w_T(p_U(x))), \end{cases}$$

*for any* $\lambda^* \geqslant 0$ *such that the associated* $p_0^*(x)$ *satisfies* $\int_\Omega K(x)G(p_0^*(x))\,dx = C$.

In case $T > T_0$ we prove that either the solution can be determined in an analogous way to the previous case, or, in case it cannot, thanks to the solution of an auxiliary problem that we define, the original problem (20) can be reduced to a one dimensional problem. Note that this reduction can be done whether the original problem was posed for $\Omega \subset \mathbb{R}$ or $\Omega \subset \mathbb{R}^2$. Next theorem is a simplified version of Theorem 2.2.

**Theorem D** ($T > T_0$) *Assume* $T > T_0$ *and* $0 < C < U|\Omega|$. *Under some conditions on the birth and death rates of mosquitoes, there exists at least one* $p_0^* \in \mathcal{P}_{0,C,U}$ *that solves problem* (20). *Defining*

$$\tilde{p}_\lambda(x) = \begin{cases} 0 & \text{if } -\frac{\lambda}{K(x)} < \min\limits_{p_0 \in (0, p_U(x))} w_T(p_0), \\ p_U(x) & \text{if } -\frac{\lambda}{K(x)} \geqslant w_T(p_U(x)), \\ w_T^{-1}\left(-\frac{\lambda}{K(x)}\right) & \text{if } -\frac{\lambda}{K(x)} \in \left[\min\limits_{p_0 \in (0, p_U(x))} w_T(p_0), w_T(p_U(x))\right), \end{cases}$$

*there exist* $\lambda_1 \geqslant \lambda_0 \geqslant 0$ *and at least one* $\lambda^* \in [\lambda_0, \lambda_1]$ *such that either* $p_0^*(x) = \tilde{p}_{\lambda^*}(x)$ *for all* $x \in \Omega$, *or, under some circumstances, the following holds:*

— *For each* $\lambda \in [\lambda_0, \lambda_1]$, *we introduce* $\chi_\lambda^*$, *a characteristic function solving*

$$\min_{0 \leqslant \chi_\lambda \leqslant 1} \int_{\tilde{\Omega}_\lambda} K(x)^2(1 - p(T,x))^2 \chi_\lambda(x) + K(x)^2(1 - \chi_\lambda(x))dx,$$

*under the constraint*

$$\int_{\tilde{\Omega}_\lambda} K(x)G\left(\tilde{p}_\lambda(x)\right)\chi_\lambda(x)dx \leqslant C - \int_{\Omega \setminus \tilde{\Omega}_\lambda} K(x)G\left(\tilde{p}_\lambda(x)\right)dx,$$

*with* $\tilde{\Omega}_\lambda \subset \Omega$ *a certain subdomain given by the parameters of the problem. Here,* $p(\cdot, x)$ *solves* (21), *and has* $\tilde{p}_\lambda(x)$ *as its initial condition. There exists at least one* $\lambda^* \in [\lambda_0, \lambda_1]$, *such that* $p_0^*$ *can be described as*

$$p_0^*(x) = \begin{cases} \tilde{p}_{\lambda^*}^*(x), & \text{if } x \in \Omega \setminus \tilde{\Omega}_{\lambda^*}, \\ \tilde{p}_{\lambda^*}^*(x)\chi_{\lambda^*}^*, & \text{if } x \in \tilde{\Omega}_{\lambda^*}, \end{cases}$$

— *Considering* $p_0^*(x)$ *as the initial condition of* $p(\cdot, x)$, $\lambda^*$ *is a solution of the one-dimensional problem*

$$\min_{\lambda \in [\lambda_0, \lambda_1]} \int_\Omega (1 - p(T,x))^2\,dx.$$

We also implement an ad hoc numerical algorithm to visualize optimal solutions by exploiting Theorem 2.1 and 2.2. Finally, we study numerically the problem with diffusion. Implementing a numerical algorithm in GEKKO (see [20]). The equation studied in this case is equation (22).

In (5) we show a selection of the solutions obtained in the simulations of this chapter in different settings.

An important property found is that the associated releases to the solutions of problem (20), i.e., $u_0^*(x) = K(x)G\left(p_0^*(x)\right)$ are non-decreasing when $K(x)$ increases in most cases. This implies that, in general, where the initial concentration of mosquitoes is higher, releases should be more intense too. We prove that this is the case, at least, for $T \leqslant T_0$ and the case $T > T_0$ when some conditions are met. This monotonicity breaks when diffusion is considered, giving raise to more complex behaviours such as the formation of invasive fronts.

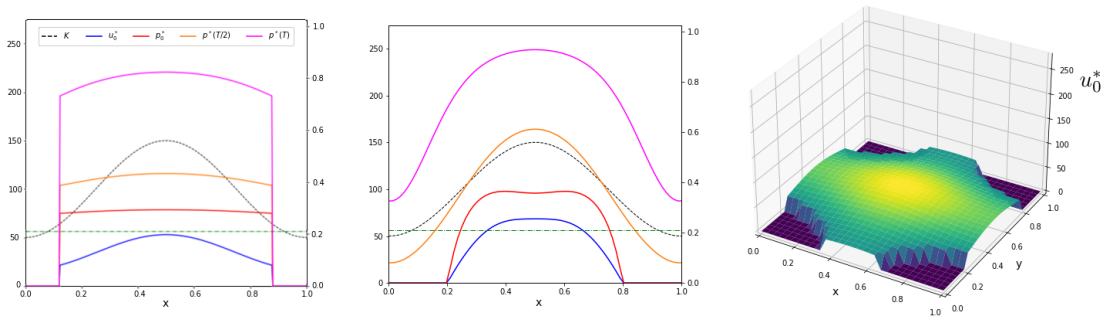


Figure 5 – Results of the simulations for a sinusoidal carrying capacity, modeling a higher concentration of mosquitoes in the center of the domain. From left to right: results in 1D, results in 1D with diffusion and results in 2D. In all simulations $T = 25$, $C = 30$.

**Perspectives**

This work has, at least, three clear lines of research in which it could be extended.

— First, not restricting the study to an instantaneous release, but rather to the original problem (19) with a continuous $u(t, x)$. This is a work in progress, not included in this thesis.

— Second, a more ambitious goal could be the study of several instantaneous releases. Usually, in the field, releases are scheduled, for example, weekly. This can be modeled by a control function composed of a series of instantaneous releases, equally separated in time, $u(t) = \sum_{i=1}^{n} u_i(x)\delta(t - t_i)$ with $t_i = (i-1)\frac{T}{n}$ and $i = 1, \ldots, n$. Even when diffusion is not considered we expect this to be a very hard question to tackle in a non-numerical way.

— Lastly, the diffusive case could be studied from a theoretical point of view. A complete understanding of solutions in this case is undoubtedly the most important research line to follow. Although the passage from ordinary differential equations to partial differential equations adds a lot of complexity to the problem, a starting point could be to try to obtain results analogous to those in [46] on the optimality of the solutions for the non-diffusive case when diffusion is added. Numerically, it can be studied by simulating the system for small final times and diffusion rates. At the time of writing this thesis, these questions are currently being developed, for this chapter is a work in progress.

## Chapter 3: Vector-borne disease outbreak control via instant vector releases

### Motivation

In this chapter we introduce, study and simulate an epidemiological system consisting of mosquitoes and humans. We are interested in minimizing the amount of infections occurring in a human population during an outbreak of a disease transmitted by mosquitoes by applying vector-based control techniques. We investigate optimal ways to carry releases of *Wolbachia*-infected (see Section II.1) and sterile male mosquitoes (see Section II.2), we compare the results of both techniques and analyze their differences. In order to do so, we combine models for population dynamics and epidemiological models. For the population replacement the system has already been introduced in (11). In practice, we won't work directly on this system given its complexity, but rather on a simplified one. In a nutshell, by assuming a high birth rate in the mosquito population, we perform the analogous passage from system (4) to the scalar equation (6) but applied to system (11) (see Chapter 3 for more details), obtaining

$$\begin{aligned}
S'_H &= bH - \frac{\beta_M}{H} I_M S_H - \frac{\beta_{WH}}{H} I_W S_H - b_H S_H, \\
E'_H &= \frac{\beta_M}{H} I_M S_H + \frac{\beta_{WH}}{H} I_W S_H - \gamma_H E_H - b_H E_H, \\
I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H, \\
E'_M &= \frac{\beta_M}{H}(K(1-p) - E_M - I_M) I_H - \gamma_M E_M - d_M E_M, \\
I'_M &= \gamma_M E_M - d_M I_M, \\
E'_W &= \frac{\beta_{HW}}{H}(Kp - E_W - I_W) I_H - \gamma_W E_W - d_W E_W, \\
I'_W &= \gamma_W E_W - d_W I_W, \\
p' &= f(p) + ug(p).
\end{aligned} \tag{23}$$

where the equations for the susceptible mosquitoes take the much simpler form $S_M = K(1-p)$ and $S_W = Kp$.

A similar thing can be done to bring together models (13) and (3). This model is simpler, since the sterile mosquitoes released do not need to be considered from an epidemiological point of view. Since only females bite, the released males are unable to spread the disease. We obtain the following system

$$\begin{aligned}
S'_H &= b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H, \\
E'_H &= \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H, \\
I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H, \\
S'_M &= b_M M \left(1 - \frac{M}{K}\right) \frac{M}{M + s_c M_S} - \frac{\beta_M}{H} S_M I_H - d_M S_M, \\
E'_M &= \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M, \\
I'_M &= \gamma_M E_M - d_M I_M, \\
M'_S &= u - d_S M_S.
\end{aligned} \tag{24}$$

The problem we are interested in is

$$\min_{u \in \mathcal{S}} \int_0^T I_H(t)dt, \text{ subject to } \int_0^T u(t)dt = C, \tag{25}$$

with $\mathcal{S}$ being a set of admissible controls that we will specify. That is, minimising the amount of infected humans during an outbreak (of duration $T$), provided that we have at our disposal $C$ mosquitoes and that all will be released. We estimate the duration of an outbreak in the system by performing a simulation where a few infected humans are introduced in a fully susceptible population.

Systems with this amount of equations are needed in order to properly take into account the dynamics of disease in the population. In exchange, they are very hard to study, especially from a theoretical point of view. Our approach in this chapter will be to consider the mosquito releases to be instantaneous. This means that we consider that the time it takes to deploy a release is very small in comparison to the time horizon considered. This facilitates the study of the system, since it becomes a finite dimensional problem. Indeed, we are assuming that our control function is of the form $u(t) = \sum_{i=1}^{n} c_i \delta(t - t_i)$, and the constraint reads now

$$\int_0^T u(t)dt = \left\langle \sum_{i=1}^{n} c_i \delta(t - t_i), 1 \right\rangle_{\mathcal{M}([0,T]),\mathcal{C}^0([0,T])} = \sum_{i=1}^{n} c_i = C.$$

Therefore, the control variables will be the times at which the releases are carried, $t_i$, and the amount of mosquitoes released each time, $c_i$. The problem can be then stated as follows

$$\min_{\substack{0 \leqslant t_i \leqslant T \\ c_i \geqslant 0}} \int_0^T I_H(t)dt, \text{ subject to } \sum_{i=1}^{n} c_i = C, \quad i = 1, \dots, n. \tag{26}$$

without loss of generality, we impose $t_1 \leqslant \cdots \leqslant t_n$. This modifies systems (24) and (11) by transforming the equation where the control appears into differential equations with discontinuities. In proposition 3.1 of chapter 3 we show how this assumption modifies the dynamics of $M_S(t)$, system (3.8), and $p(t)$, equation (3.11). Note that there is work to provide a well-posed framework, existence and regularity results to optimal control problems with measurement type data. This work has been developed in several articles such as [87, 88, 93, 94, 151]. In this chapter, we will apply such techniques to particular epidemiological systems. We provide a detailed proof of formulas for determining the control sensitivity of various quantities of interest, so that this work is self-contained.

**Main Results**

We extract the main contributions of Chapter 3. Results of this chapter are mostly numeric. We draft the numerical algorithm implemented with the aim of solving problem (26) for systems (24) and (23). Two different kinds of variables need to be determined: the release times, $t_i$ and the amount of mosquitoes released at each release, $c_i$. For the release times we compute the derivative of the criterion with respect to each $t_i$, $\delta_{t_i} J(t)$ analytically (See 3.4 for more details). At each step, we fix the amount of mosquitoes released, $(c_i)_{1 \leqslant i \leqslant n}$, and we update the control according to the derivatives we computed, taking into account the restriction $0 \leqslant t_1 \leqslant \cdots \leqslant t_n \leqslant T$. In other words, at a given step $k$, we update the control $u_k = \sum_i c_i \delta(t - t_i)$, according to

$$u_{k+1} = \Pi_{\mathcal{T}} \left( u_k - \varepsilon_t \nabla_t J(u_k) \right), \text{ where } \quad \nabla_t J(u) = \left( \delta_{t_1} J(u), \dots, \delta_{t_n} J(u) \right),$$

and where $\Pi_{\mathcal{T}}$ denotes the projection onto the set of controls $\{ 0 \leqslant t_1 \leqslant \cdots \leqslant t_n \}$. In order to optimize the $c_i$ we implemented an Uzawa algorithm with an augmented Lagrangian. The

functional considered was

$$L(u,\lambda) = \int_0^T I_H(t)dt + \lambda\left(\sum_{i=1}^{n} c_i - C\right) + \frac{\rho}{2}\left(\sum_{i=1}^{n} c_i - C\right)^2. \tag{27}$$

The functional is extended in order to handle the constraint $\sum_{i=1}^{n} c_i = C$. In (27). $\lambda$, is a non-negative real number, and its value is computed iteratively along with $u$. The idea behind the Uzawa algorithm is to transform the constrained minimization problem into an unconstrained one, where the new functional is minimized with respect to $u$, and maximized with respect to $\lambda$ (see [72] for details). The second term added in (27) is introduced only to accelerate the convergence of the algorithm. This is achieved for a certain range of values of the parameter $\rho$.

One step at a time, we approach the target saddle point of $L(u,\lambda)$ by updating the control according to

$$\begin{aligned} u_{k+1} &= u_k - \varepsilon_c\left(\nabla_c J(u_k) + \lambda_k + \rho\left(\textstyle\sum_{i=1}^{n} c_i - C\right)\right), \\ \lambda_{k+1} &= \max\left(\lambda_k + \rho\left(\textstyle\sum_{i=1}^{n} c_i - C\right), 0\right). \end{aligned}$$

Here, $\nabla_c J(u)$ is analogous to $\nabla_t J(u)$ but the derivatives have been computed with respect to the $c_i$. We represent a schematic version of the algorithm in Figure 6.

We sum up here the results of applying this algorithm to solve the problem considered for each of the techniques. In the case of the SIT, results depend not only on the amount of mosquitoes released, but also on the number of releases considered. Results for 10 and 20 releases can be seen in figures 3.1 and 3.2 respectively. The reduction in the amount of infections is greater when more mosquitoes are released, which was expected, but also when the same amount of mosquitoes is spread over more releases. In all cases the releases are distinct (there is not any case where $t_i = t_{i+1}$). This is due to the fact that since mosquito population decays exponentially two releases combined will sustain a sterile population for a shorter time than two separate releases. Nevertheless, this trend does not continue indefinitely. After approximately twenty releases, the further reduction in the number of cases becomes very small when more releases are considered.

Optimal strategies can be summed up as follows:

— In case we have at our disposal few mosquitoes, or in case we do not consider enough releases, the optimal strategy is focused on the *mitigation* of the outbreak. Mosquitoes are released spaced around the peak of the epidemic. Biologically speaking, if a sterile population cannot be sustained (in other words, if a wild population, cannot be kept low) in a consistent manner during the whole time window considered, then mosquitoes should be released when most of the transmissions are happening, that is, around the peak of the epidemic. An example of this is the upper row in Figure 7.

— In case we have enough mosquitoes and we consider enough releases, these start shifting to the beginning of the time window, eventually reaching $t_1 = 0$. The optimal strategy shifts towards the *suppression* of the outbreak. Releases are concentrated at the beginning but nevertheless small releases keep being carried out over an extended period of time. The idea being to prevent the outbreak to gain traction in the first place by reducing drastically from the start the amount of wild mosquitoes. Later, the small releases allow to prevent the wild mosquitoes from repopulating the system, thus, preventing the appearance of a new outbreak later. An example of this kind of solution is the lower row of Figure 7. The shift to the left can be clearly seen when 20 releases are considered (bottom right graph).

In the case of the *Wolbachia* releases, solutions do not present such rich behaviours. For any initial amount of releases considered, all collapse into one single release containing all the mosquitoes combined. Two clear distinct strategies appear as a function of the amount of mosquitoes at our disposal. The value splitting the two regimes is $C = G(\theta)$, which is, ex-

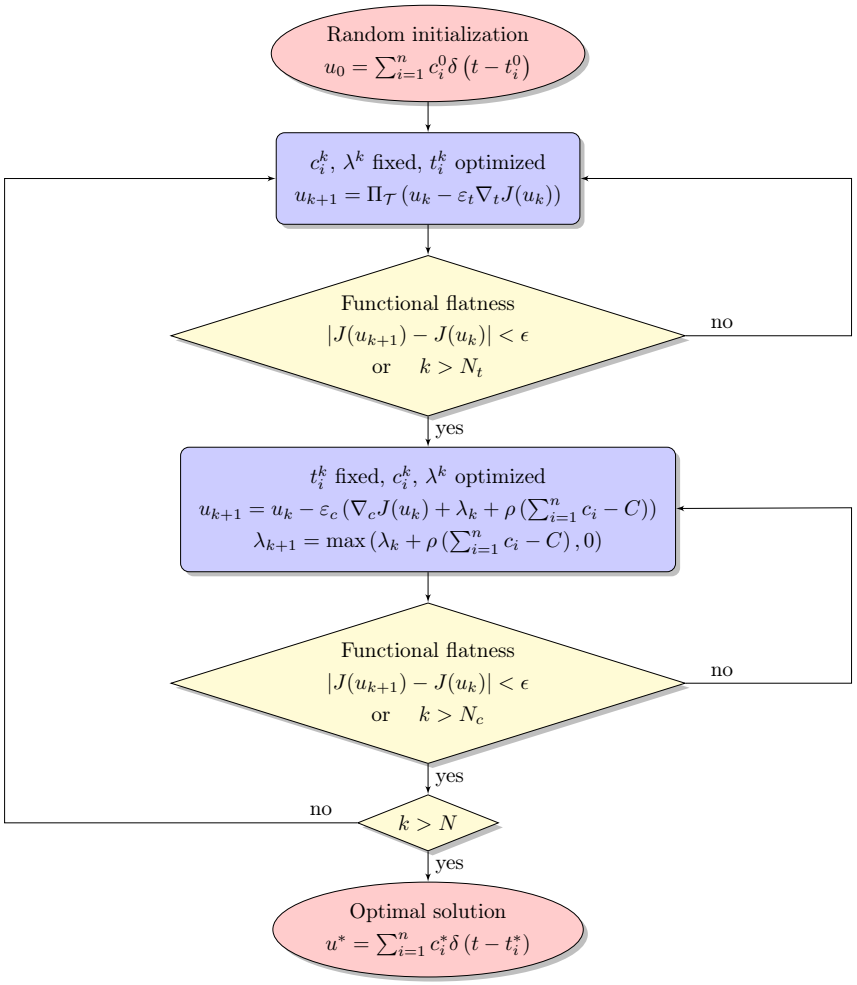


Figure 6 – Schematic representation of the Algorithm implemented in Chapter 3 to solve problem (26).

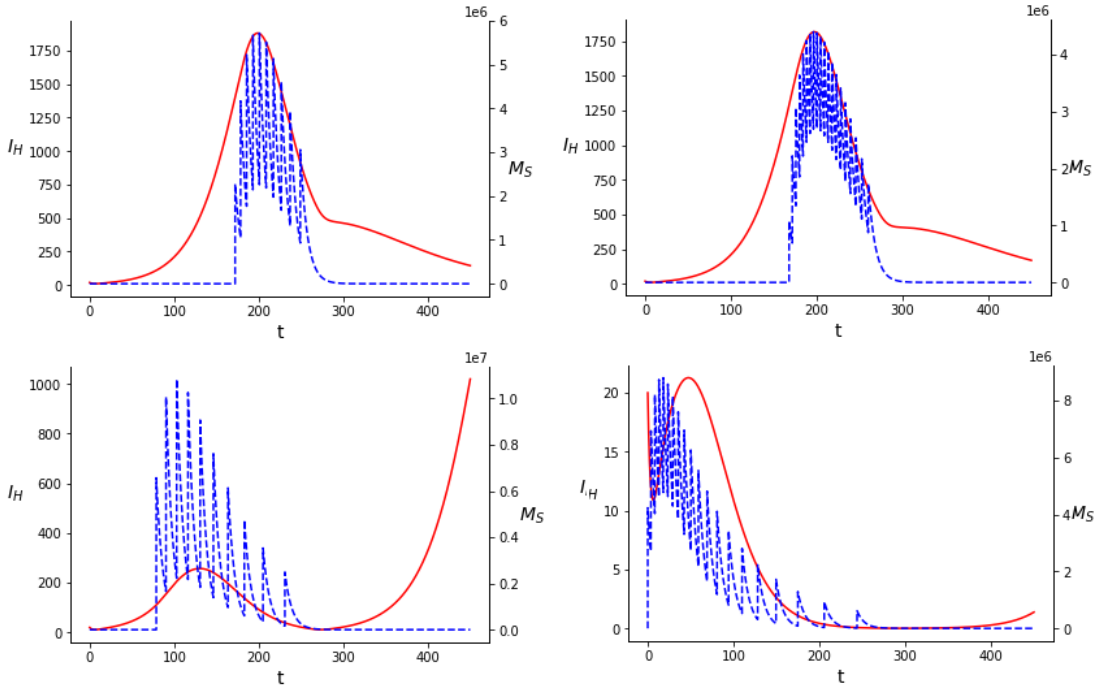


Figure 7 – Evolution on optimal strategies for the SIT when the amount of mosquitoes to release is increased, from $C = 3 \cdot 10^7$ (left column) to $C = 6 \cdot 10^7$ (right column). In the upper and lower rows, 10 and 20 releases are considered respectively. The dashed blue line corresponds to the amount of sterile mosquitoes in the system. The amount of infectious humans, $I_H^*$, is shown in red. Notice the change in scale in the left axis of the bottom row due to the reduction in the amount of human infections.

actly, the amount of mosquitoes necessary to increase in one single release the *Wolbachia*-infected mosquito proportion from $p = 0$ to $p = \theta$. We recall that $p$ evolves according to $p' = f(p)$ and that $\theta$ is the single zero of $f(p)$ in $(0, 1)$. We also recall that if $p \in (0, \theta)$, $f(p) < 0$ and thus the proportion of *Wobachia*-infected mosquitoes decreases back to $p = 0$ after a certain time. On the other hand, if $p \in (\theta, 1)$, $f(p) > 0$ and thus the proportion of *Wobachia*-infected mosquitoes increases naturally ($p \to 1$ when $t \to \infty$), producing a population replacement without further intervention. Therefore, if $C > G(\theta)$ there are enough mosquitoes to trigger a population replacement in one single release, while if $C < G(\theta)$ there are not. This fact produces the threshold for $C$ splitting two different strategies:

— In case we cannot trigger a population replacement the optimal strategy consists again in the mitigation of the disease outbreak. *Wobachia*-infected mosquitoes are released before reaching the peak of the epidemic in order to maximize the proportion of *Wolbachia*-infected mosquitoes while most of the transmissions are happening, resulting in a dampening in the infection curve.

— In case there are enough *Wolbachia*-infected mosquitoes to trigger the population replacement, the optimal strategy is to act as soon as possible. Since $p$ will increase without further intervention, there is no advantage in delaying the release, so there is the highest proportion of *Wolbachia*-infected mosquitoes from the beginning.

This switch in behaviour can be seen in figure 8.

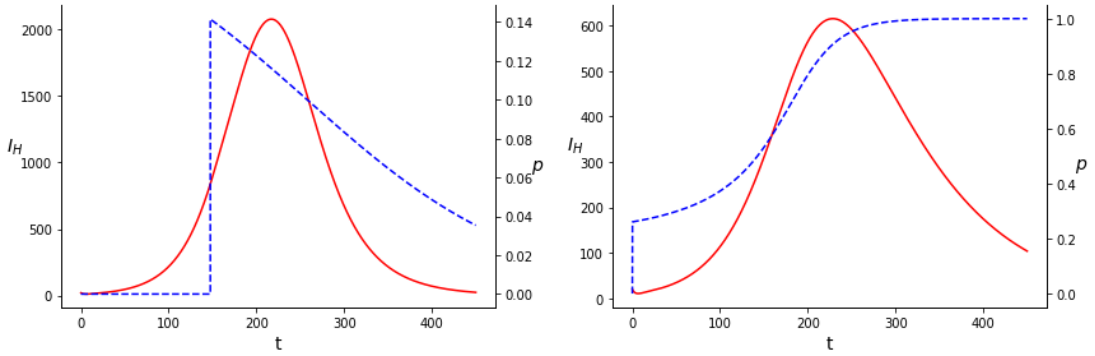


Figure 8 – Switch of optimal strategy for the *Wolbachia* method when $C$ is increased from $C < G(\theta)$ (left) to $C > G(\theta)$ (right). The proportion of *Wolbachia* infected mosquitoes corresponds to the dashed blue line and should be read with the axis to the right of each graphic. The amount of infected humans, $I_H^*$, is depicted in red and its axis is on the left. Notice how the scale for the human infections is considerably bigger in the left graphic.

Finally, we also explore the case where only the times of the releases are optimized but the amount of mosquitoes to release at each time is fixed. We compare the reduction in the number of cases obtained with this simpler strategy with the more refined one. This problem is simpler to solve but also more in line with current applications.

**Perspectives**

To the best of our knowledge, literature is not rich in works similar to this. This work opens a broad range of interesting questions worth investigating in future works. A non-exhaustive list includes:

— In practice, mosquitoes are produced in relatively fixed amounts weekly. Given that the duration of an outbreak can be a considerable number of weeks, it would be interesting to look at $C$ as a function of time. For instance, increasing in a linear way, $C(t) = C_0 + C_1 t$, or with discrete increases as a step function, $C(t) = C_0 \left\lceil \frac{t}{7} \right\rceil$, with time measured in days.

— In the case of the SIT, results vary significantly with the number of releases considered when this one is low, but the improvements dampen as the number of releases increase. It can be useful to properly study the improvement of results as a function of the number of releases considered for different values of $C$. That is, calling $u_n^*$ the optimal strategy for $n$ releases, explore numerically the function $\mathcal{J}(n) := J(u_n^*) - J(u_{n-1}^*)$. The value of this function would give an idea of how worth it is to consider a bigger number of releases.

— Also in the SIT case, results depend on the time window considered, since mosquitoes can reproduce again in treated areas when the treatment is stopped. A very interesting question would be: How does the optimal strategy evolve as $T$ increases? In other words, how do optimal strategies evolve when we do not restrict ourselves to the duration of a particular outbreak but instead we want to minimize the infections for, a priori, unbounded periods of time?

Chapter 1

# Optimal release strategies for mosquito population replacement

This chapter is the subject of L. Almeida, J. Bellver Arnau and Y. Privat. "*Optimal Control Strategies for Bistable ODE Equations: Application to Mosquito Population Replacement*", published in *Applied Mathematics & Optimization* [4].

## 1.1 Introduction

### 1.1.1 Around *Wolbachia* control strategies

Around 700 000 people die annually due to mosquito-transmitted diseases [154]. In particular, mosquitoes of the genus Aedes, such as *Aedes Aegypti* and *Aedes Albopictus* can transmit several arboviruses as Dengue, Chikungunya, Yellow fever or Zika [60, 109]. 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 [32]. As no antiviral treatment nor efficient vaccine are known for Dengue, the current method for preventing its transmission relies mainly on targeting the vector, i.e. the mosquito [15, 14, 67]. As introduced in section II.1 of the Introduction of this thesis, it has been shown that the presence of the bacterium *Wolbachia* [65] in these mosquitoes reduces their vector capacity (capability of transmission of the associated disease) for the aforementioned arboviruses [147, 92, 143, 95]. The bacterium is transmitted from the mother to the offspring. Furthermore, there is a phenomenon called *Cytoplasmatic Incompatibility* (CI) [129, 73], which produces cross sterility between *Wolbachia*-infected males and uninfected females. These two key phenomena make the introduction of mosquitoes infected with *Wolbachia* a promising control strategy to prevent Dengue transmission.

In this chapter we explore several ways of modeling optimal release strategies, in the spirit of [10], where a simpler approach involving a least squares functional was presented. We enrich the model of [10] by introducing and analyzing two relevant families of problems.

In a nutshell, we will first consider two families of functionals that are convex combinations of a term accounting for the cost of the mosquitoes used and

— either a growing function of the time horizon, let free, but fixing the final proportion of *Wolbachia*-infected mosquitoes.

— or a penalization (more precisely a decreasing function) of the final proportion of *Wolbachia*-infected mosquitoes at the final time of the experiment. Note that the horizon of time will be considered fixed in this case.

This will lead us to introduce two large families of relevant optimization problems in order to model this issue. Analyzing them will allow us to discuss optimal strategies of mosquito releasing and also the robustness of the properties of the solutions with respect to the modeling choices (in particular the choice of the functional we optimize).

Nevertheless, the results presented in this chapter are not restricted to this particular problem. In Remark 1.2 we state the conditions under which our results are applicable to other control problems with bistable equations.

### 1.1.2 Issues concerning modeling of control strategy

To study these issues, let us consider the same model as in [10] for modeling two interacting mosquito populations: a *Wolbachia*-free population $M$, and a *Wolbachia* carrying one, $W$. The resulting system reads

$$\begin{cases} \frac{dM(t)}{dt} = b_M M(t)\left(1 - s_h \frac{W(t)}{M(t)+W(t)}\right)\left(1 - \frac{M(t)+W(t)}{K}\right) - d_M M(t), \\ \frac{dW(t)}{dt} = b_W W(t)\left(1 - \frac{M(t)+W(t)}{K}\right) - d_W W(t) + u(t)\ , t > 0, \\ M(0) = M^0\ , W(0) = W^0, \end{cases} \tag{1.1}$$

where

— the parameter $s_h \in [0,1]$ is the cytoplasmic incompatibility (CI) rate [1].

— The other parameters $(b_i, d_i)$ for $i \in \{M, W\}$ are positive and denote respectively the intrinsic mortality and intrinsic birth rates. Moreover, we assume that $b_i > d_i$, $i = M, W$.

— $K > 0$ denotes the environmental carrying capacity. Note that the term $(1 - s_h \frac{W}{M+W})$ models the CI.

— $u(\cdot) \in L^\infty(\mathbb{R}_+)$ plays the role of a control function that we will use to act upon the system. This control function represents the rate at which *Wolbachia*-infected mosquitoes are introduced into the population.

System (1.1) for modeling mosquito population dynamics with *Wolbachia* has been first introduced in [52, 53]. We also mention [69] where this model is coupled with an epidemiological one.

The aim of this technique is to replace the wild population by a population of *Wolbachia*-infected mosquitoes. To understand mathematically this question, it is important to recall that, under the additional assumption

$$1 - s_h < \frac{d_M b_W}{d_W b_M} < 1 \tag{1.2}$$

satisfied in practice [10], System (1.1) has four non-negative steady states, among which two which are locally asymptotically stable, namely:

$$\bar{\mathbf{M}} = (M^*, 0) := \left(K\left(1 - \frac{d_M}{b_M}\right), 0\right) \quad \text{and} \quad \bar{\mathbf{W}} = (0, W^*) := \left(0, K\left(1 - \frac{d_W}{b_W}\right)\right).$$

Observe that $\bar{\mathbf{M}}$ corresponds to a mosquito population without *Wolbachia*-infected individuals whereas $\bar{\mathbf{W}}$ corresponds to a mosquito population composed exclusively of infected individuals.

1. Indeed, when $s_h = 1$, CI is perfect, whereas when $s_h = 0$ there is no CI

Note that the two remaining steady-states are unstable: they correspond to the whole population extinction and a coexistence state.

Hence, the optimal control issue related to the mosquito population replacement problem can be recast as:

*Starting from the equilibrium $\bar{\mathbf{M}}$, how to design a control steering the system as close as possible to the equilibrium state $\bar{\mathbf{W}}$, minimizing at the same time the cost of the releases?*

Of course, although this is the general objective we wish to pursue, the previous formulation remains imprecise and it is necessary to clarify what is meant by "the cost of release" and the set in which it is relevant to choose the control function.

Following [6] and [10], we will impose several biological constraints on the control function $u$: the rate at which mosquitoes can instantaneously be released will be assumed bounded above by some positive constant $U$, and so will be the total amount of released infected mosquitoes up to the final time $T$. The set of admissible control functions $u(\cdot)$ thus reads

$$\mathcal{U}_{T,C,U} := \left\{ u \in L^\infty(0,T), 0 \leqslant u \leqslant U \text{ a.e. in } (0,T), \int_0^T u(t)dt \leqslant C \right\}. \tag{1.3}$$

As shown in [10], System (1.1) can be reduced to a single equation under the hypothesis of high birth rates, i.e. considering $b_M = b_M^0/\varepsilon$, $b_W = b_W^0/\varepsilon$ and letting $\varepsilon$ decrease to 0. In this frame, the proportion $W/(M+W)$ of *Wolbachia*-infected mosquitoes in the population, uniformly converges to $p$, the solution of a simple scalar ODE, namely

$$\begin{cases} \frac{dp}{dt}(t) = f(p(t)) + u(t)g(p(t)), & t \in (0,T) \\ p(0) = 0, \end{cases} \tag{1.4}$$

where

$$f(p) = p(1-p)\frac{d_M b_W^0 - d_W b_M^0(1-s_h p)}{b_M^0(1-p)(1-s_h p) + b_W^0 p} \quad \text{and} \quad g(p) = \frac{1}{K}\frac{b_M^0(1-p)(1-s_h p)}{b_M^0(1-p)(1-s_h p) + b_W^0 p}. \tag{1.5}$$

We remark that $f(0) = f(1) = 0$ and, under assumption (1.2), there exists a single root of $f$ strictly between 0 and 1 at $p = \theta = \frac{1}{s_h}\left(1 - \frac{d_M b_W^0}{d_W b_M^0}\right)$. The function $p \mapsto g(p)$ is non-negative, strictly decreasing in $[0,1]$ and such that $g(1) = 0$.

In the absence of a control function, the equation on $p$ simplifies into $\frac{dp}{dt} = f(p)$. This is a bistable system, with an unstable equilibrium at $p = \theta$ and two stable equilibria at $p = 0$ and $p = 1$. Notice that the derivative of the function $f/g$ has a unique zero $p^*$ in $(0,\theta)$ defined by

$$p^* = \frac{1}{s_h}\left(1 - \sqrt{\frac{d_M b_W^0}{d_W b_M^0}}\right), \tag{1.6}$$

which will be useful in the following.

In [10], the control problem

$$\inf_{u \in \mathcal{U}_{T,C,U}} J(u), \quad \text{with } J(u) = \frac{1}{2}M(T)^2 + \frac{1}{2}\left[(W^* - W(T))_+\right]^2. \tag{1.7}$$

related to the aforementioned system (1.1), is considered. Denoting by $J^\varepsilon(u)$ the criterion $J(u)$ where the birth rates $b_M$ and $b_W$ have been respectively replaced by $b_{1,\varepsilon} = b_M^0/\varepsilon$ and $b_{2,\varepsilon} = b_W^0/\varepsilon$,

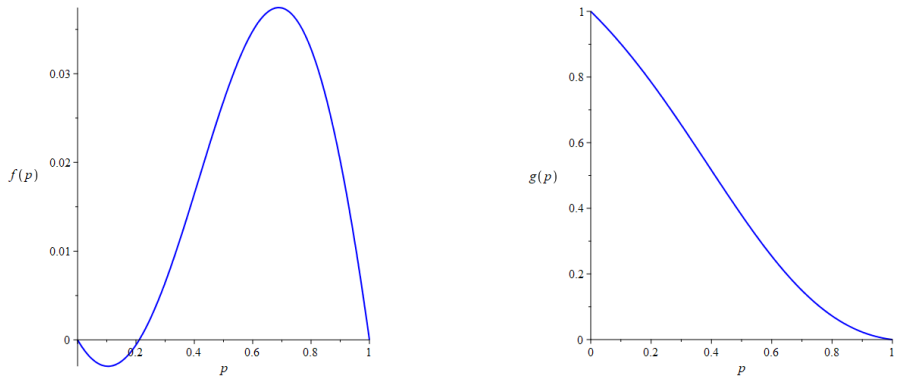


Figure 1.1 – Plots of $p \mapsto f(p)$ (left) and $p \mapsto g(p)$ (right) for the values of the parameters in Table 1.1. In this case $\theta \approx 0.211$.

with $\varepsilon > 0$, a $\Gamma$-convergence type result is proven [10, Proposition 2]. More precisely, any solution $u_\varepsilon$ of Problem (1.7) with birth rates $b_{1,\varepsilon}$ and $b_{2,\varepsilon}$ converges weakly-star in $L^\infty(0,T)$ to a solution of the reduced problem (1.4). Moreover,

$$\lim_{\varepsilon \to 0} \inf_{u \in \mathcal{U}_{T,C,U}} J^\varepsilon(u) = \inf_{u \in \mathcal{U}_{T,C,U}} J^0(u),$$

where

$$J^0(u) = \lim_{\varepsilon \to 0} J^\varepsilon(u) = K(1 - p(T))^2 \tag{1.8}$$

and $p$ is the solution of (1.4) associated to the control function choice $u(\cdot)$. The arguments exposed in [10] can be adapted easily to our problem. Since the solutions of both the full problem (1.7) and the minimization of $J^0$ given by (1.8) will be close in the sense above, it is relevant to investigate the later, which is easier to study both analytically and numerically.

We now introduce the two families of optimal control problems we will consider in the following sections. Although the model (1.4) driving the evolution of the *Wolbachia*-infected mosquitoes density is the same as in [10], we will enrich it by introducing and analyzing new families of problems in which

— the horizon of time can be let free;
— the cost of producing *Wolbachia*-infected mosquitoes can be included. Since such a cost is not so easy to take into account, we will write it in a rather general way

$$\int_0^T j_1(u(t))\, dt \tag{1.9}$$

where $j_1 : \mathbb{R} \to \mathbb{R}$ denotes a increasing function such that $j_1(0) = 0$.

To take the time of the experiment and the final state into account in the cost functional, we will use a function $j_2 : \mathbb{R}_+ \times [0,1] \ni (T,p)) \mapsto j_2(T,p) \in \mathbb{R}$.

Let us now present the two families of problems we will deal with. We will be led to make

the following assumptions, in accordance with the modelling above:

$$\begin{cases} j_1(\cdot) \text{ is a non-negative increasing function such that } j_1(0) = 0, \\ \text{two times differentiable, either strictly concave, linear or strictly convex on } (0,T). \\ \\ j_2(\cdot) \text{ is a non-negative function of class } \mathcal{C}^1, \text{ strictly increasing} \\ \text{w.r.t. its first variable and strictly decreasing w.r.t. its second variable.} \\ \text{Moreover, for all } p \in [0,1], \lim\limits_{T\to+\infty} j_2(T,p) = +\infty. \end{cases} \tag{$\mathcal{H}$.1}$$

Family 1

A first way of modeling optimal strategy for releasing *Wolbachia*-infected mosquitoes consists in minimizing a convex combination of the time horizon, denoted $T$, which is considered free and the cost of producing and releasing the mosquitoes defined by (1.9), by imposing a target value on the final density of *Wolbachia*-infected mosquitoes. This leads to introduce the following optimal control problem

$$\begin{cases} \inf\limits_{\substack{u\in\mathcal{U}_{T,C,U} \\ T>0}} J_\alpha(T,u), \\ p' = f(p) + ug(p) \text{ in } (0,T),\ p(0) = 0\ ,\ p(T) = p_T\ , \end{cases} \tag{$\mathcal{P}^{1,\alpha}_{p_T,C,U}$}$$

where $p_T \in (0,1)$ is given and $J_\alpha(u)$ is defined by

$$J_\alpha(T,u) = (1-\alpha)\int_0^T j_1(u(t))dt + \alpha j_2(T,p(T)), \tag{1.10}$$

where $\alpha \in [0,1]$, $j_1(\cdot)$ and $j_2(\cdot)$ satisfy ($\mathcal{H}$.1) and $\mathcal{U}_{T,C,U}$ is given by (1.3). The function $(T,p) \mapsto j_2(T,p)$ aims at penalizing the time used in our case. Once the existence of solutions is established, it will be fixed to be $j_2(T,p(T)) = T$. In what follows, we will not tackle the case where $\alpha = 0$ since in that case, existence may not be guaranteed. More precisely, it is rather easy to show that in that case, Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$ has no solution whenever $p_T > \theta$.

Family 2

Another possible way of modeling optimal strategy for releasing *Wolbachia*-infected mosquitoes consists in minimizing a convex combination of the final distance from $p(T)$ to the state of total invasion $p = 1$ and the cost of producing and releasing the mosquitoes defined by (1.9). In that case, we fix the horizon of time $T$ and let $p(T)$ free. This leads to consider the problem

$$\begin{cases} \inf\limits_{u\in\mathcal{U}_{T,C,U}} J_\alpha(u), \\ p' = f(p) + ug(p),\ p(0) = 0\ , \end{cases} \tag{$\mathcal{P}^{2,\alpha}_{T,C,U}$}$$

where $\alpha \in [0,1]$, $j_1(\cdot)$ and $j_2(\cdot)$ satisfy ($\mathcal{H}$.1) and $\mathcal{U}_{T,C,U}$ is given by (1.3). The main difference here with respect to the previous case is the fact that the time horizon $T$ is fixed, $p(T)$ is free and that $j_2(T,p(T))$ now represents a function penalizing the final distance to a certain final state (typically, the state of total invasion $p = 1$). Since $T$ in this family is fixed, abusing of the

notation we will write $J_\alpha(u)$ instead of $J_\alpha(T,u)$, but $J_\alpha(u)$ will still be defined by (1.10). After establishing the existence of solutions to this problem we will fix $j_2(T,p(T)) = (1-p(T))^2$ as in (1.8). A study of similar problems in a much more limited setting can be found in [3].

### 1.1.3 Main results

Let us state here briefly the main results of this chapter. These results will be further detailed in sections 1.2.2 and 1.3.1 respectively. In this section, in order to avoid too much technicality, we provide simplified statements of the main contributions of this chapter. Let us fix $U > 0$ and $C > 0$, and let us consider $j_1(\cdot)$ satisfying the hypothesis stated above in ($\mathcal{H}$.1).

Our first result regards Family 1. In accordance with the biological modelling considerations above, let us assume hereafter that $j_2(T,p_T) = T$ and that the final proportion of mosquitoes in the populations is fixed $p(T) = p_T < 1$. The following result is a simplified and less precise version of Theorem 1.2.

**Theorem A** (Family 1) *There exists $(T^*,u^*) \in \mathbb{R}_+ \times \mathcal{U}_{T,C,U}$ solving Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$. The overall behaviour of $u^*$ depends on the convexity of $j_1(\cdot)$, the value of $\alpha$ and the value of $C$.*

*In general, we distinguish the following cases:*

— *Case 1. $j_1$ is either linear or strictly concave. There exists a real parameter $\alpha^* \in [0,1)$ given by the parameters of the problem such that:*
  — *if $C$ is large enough: If $\alpha \in [\alpha^*,1]$, then $u^* = U\mathbb{1}_{[0,T^*]}$. If $\alpha \in (0,\alpha^*)$, then $u^*$ is bang-bang with exactly one switch from $U$ to 0 at a time $t_s \in (0,T^*)$ determined by $\alpha$.*
  — *else, one has $u^* = U\mathbb{1}_{[0,C/U]}$.*

  *In this case, the optimal time $T^*$ reads*

$$T^* = \int_0^{p_T} \frac{d\nu}{f(\nu) + u_p^*(\nu)g(\nu)} \quad \text{with } u_p^*(\nu) = U\mathbb{1}_{(0,p_s)}$$

  *and*

$$p_s = \begin{cases} p(t_s) & \text{if } C \text{ is large enough,} \\ p(C/U) & \text{otherwise.} \end{cases}$$

— *Case 2. $j_1$ is convex. If $\alpha \in (0,1)$ singular controls may appear. The control $u^*$ is non-decreasing until $t^* \in (0,T^*)$ such that $p(t^*) = p^*$ and then non-increasing.*

*If $\alpha = 1$, the term with $j_1$ is no longer present and $u^* = U\mathbb{1}_{[0,\min\{T^*,C/U\}]}$.*

**Remark 1.1.** We remark that in case $j_1$ is either linear or strictly concave the controls are always bang-bang (and the case $\alpha = 1$ is similar to $\alpha < 1$) while when $j_1$ is convex, singular controls may appear when $\alpha < 1$ while for $\alpha = 1$ the control is still bang-bang.

For our second result, regarding Family 2 let us assume hereafter that $j_2(T,p_T) = (1-p_T)^2$ and that the time horizon $T > 0$ is fixed. The following result is a simplified and less precise version of Theorem 1.3.

**Theorem B** (Family 2) *There exists $u^* \in \mathcal{U}_{T,C,U}$ solving Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$. In addition, there exists an interval $(t^-,t^+)$ such that, outside of it $u^* = 0$ and the state $p_{u^*}$ associated to $u^*$ is constant. Inside $(t^-,t^+)$, $p_{u^*}$ is increasing and the behaviour of $u^*$ depends on the convexity of $j_1(\cdot)$, the value of $\alpha$ and the values of $C$ and $T$. We distinguish between the following cases:*

— *Case 1. $j_1$ is either linear or strictly concave. The solution is $u^* = U\mathbb{1}_{[t^-,t_s]}$, with $t_s \leqslant t^+$ the switching time.*

— *Case 2. $j_1$ is convex. If $\alpha \in (0,1)$ singular controls may appear. The control $u^*$ is non-decreasing until $t^* \in (t^-, t^+)$ such that $p(t^*) = p^*$ and then non-increasing.*

*If $\alpha = 1$, then $u^* = U\mathbb{1}_{[t^-,t_s]}$, with $t_s$ defined as in the concave and linear case.*

**Remark 1.2.** The use of bistable ODEs is widely spread to model a great variety of phenomena from biology, to physics and economy. Examples of systems with a bistable behaviour can be found in population dynamics, exploitation of natural resources, cell division, cancer modeling, apoptosis, chemical reactions or mechanical systems. Therefore, these results may be interesting outside of the particular context in which they have been presented.

In order to be able to apply Theorems A and B, $f, g \in \mathcal{C}^1([0,1])$ for the system considered must satisfy two conditions:

— **Bistability:** $p \mapsto f(p)$ must satisfy that $f(0) = f(1) = 0$, and that there exists a unique $\theta \in (0,1)$ such that $f(\theta) = 0$, $f(p) < 0$ for $p \in (0,\theta)$ and $f(p) > 0$ for $p \in (\theta, 1)$.

— **Increasingly costly to control:** $p \mapsto g(p)$ must be non-negative, strictly decreasing in $[0,1]$ and such that $g(1) = 0$. This means that as the state of the system gets closer to the steady state $p = 1$ it becomes increasingly harder to push.

Moreover, function $p \mapsto (f/g)(p)$ must satisfy two additional conditions, namely:

— **Unimodality**: $p \mapsto (f/g)(p)$ must be unimodal, that is, strictly decreasing for $p \in (0, p^*)$ and strictly increasing afterwards. With $0 < p^* < \theta$.

— $\lim_{p\to 1}(f/g)(p) = +\infty$.

### 1.1.4 Biological interpretation of our results and final comments

From a biological point of view, this problem is studied with more generality than what is strictly necessary. Only a certain subset of parameters is interesting for real field releases. In order to give a biological interpretation we restrict ourselves to the case where $p(T) > \theta$ so that the system in the long term tends to $p = 1$ without further action. Otherwise, once the releases ended the system would return to the initial condition after a certain time meaning that the installation of the *Wolbachia*-infected mosquito population would have failed. Independently of the family considered, with this restriction, our results yield:

— If $j_1$ is either linear or strictly concave, the optimal releasing strategy is bang-bang. Starting with $u^* = U$ and switching at most once, only after the critical proportion, $p(t) = \theta$, is surpassed.

— If $j_1$ is strictly convex, the possible appearance of singular solutions makes the analysis more intricate. In any case, solutions attain their maximal value at $t = t^*$ such that $p(t^*) = p^*$. Either $u^*$ has a global maximum at $t^*$ or there exists an open interval $I$ where $u^*(t) = U$ and $t^*$ belongs to $I$, although in the first case the value of the maximum attained at that point is not always straightforward to determine.

The function $j_1$ aggregates all the costs of the mosquito production, transport and release. Its convexity represents the marginal increase of the cost per mosquito. A concave function means that producing mosquitoes becomes proportionally less expensive as we scale up the production, while a convex function implies the opposite; the rate at which the costs increase grows as we increase the mosquito production. Finally, a linear $j_1$ means that the cost of production is scale-independent, directly proportional to the number of mosquitoes produced.

Since in a real case some of the parameters may be very difficult to determine beforehand, this interpretation gives us some guidelines to implement a sensible feedback strategy in the field. In order to do this, we would have to measure the proportion of infected mosquitoes using traps and adapt the amount of mosquitoes we release in consequence. We have shown that under a broad set of circumstances the best strategy is to act as soon as possible, and as fast as possible, at least until the critical value $p(t) = \theta$ is attained. An exception to this rule being the case

when the production of mosquitoes is increasingly expensive. Nevertheless, in this context, the effort must also be concentrated soon, when the proportion of mosquitoes is $p(t) \approx p^*$, which allows to reduce the amount of mosquitoes used before reaching $p(t) = \theta$.

## 1.2 Analysis of Family 1 problems

### 1.2.1 A first result: optimization without constraint on the number of mosquitoes used.

This section is devoted to studying the case where the time horizon $T$ is free and no constraint is imposed on the total number of mosquitoes used. In other words, we will deal with the optimal control problem

$$\begin{cases} \inf\limits_{\substack{u\in\mathcal{V}_{T,U}\\ T>0}} J_\alpha(T,u), \\ p' = f(p) + ug(p) \text{ in } (0,T),\ p(0) = 0\ ,\ p(T) = p_T\ , \end{cases} \tag{$\mathcal{Q}^{1,\alpha}_{p_T,U}$}$$

where $J_\alpha(T,u)$ is defined by

$$J_\alpha(T,u) = (1-\alpha)\int_0^T j_1(u(t))dt + \alpha T, \tag{1.11}$$

where $\alpha \in [0,1]$, $j_1(\cdot)$ satisfies $(\mathcal{H}.1)$ and $\mathcal{V}_{T,U}$ is given by

$$\mathcal{V}_{T,U} := \{u \in L^\infty(0,T), 0 \leqslant u \leqslant U \text{ a.e. in } (0,T)\}. \tag{1.12}$$

In what follows, it will be convenient to introduce the following notations:

$$m^*(p_T) := \max_{p\in[0,p_T]}\left(-\frac{f(p)}{g(p)}\right) > 0 \quad \text{and} \quad m_*(p_T) = \min_{p\in[0,p_T]}\left(-\frac{f(p)}{g(p)}\right) \leqslant 0. \tag{1.13}$$

for $p_T \in (0,1)$. Note that, as long as $p \mapsto (f/g)(p)$ satisfies the conditions of Remark 1.2, these quantities are unique.

Let us introduce the mapping $F_0$ defined by

$$v \mapsto F_0(v) := \frac{(1-\alpha)(vj_1'(v) - j_1(v)) - \alpha}{(1-\alpha)j_1'(v)}. \tag{1.14}$$

For the sake of notational simplicity, we do not underline the dependence of $F$ with respect to $\alpha$. A straightforward computation shows that $F_0$ is increasing (resp. decreasing) whenever $j_1$ is strictly convex (resp. strictly concave).

**Theorem 1.1.** *Let us assume that $\alpha \in (0,1]$, $p_T \in (0,1)$, (1.2) is true, and $j_1(\cdot)$ satisfies the first assumption of $(\mathcal{H}.1)$. Let us assume that $U > m^*(p_T)$. Then, there exists a pair $(T^*,u^*) \in \mathbb{R}_+ \times \mathcal{V}_{T,U}$ solving Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$. Moreover, let us distinguish between two cases:*

— *The case where $j_1$ is either linear or strictly concave. Let us introduce the real parameter $\alpha^* \in [0,1)$ given by*

$$\alpha^* = \frac{-m_* j_1(U)/U}{1 - m_* j_1(U)/U}. \tag{1.15}$$

*In this case, if $\alpha \in [\alpha^*,1]$, then $u^* = U\mathbb{1}_{[0,T^*]}$ and if $\alpha \in (0,\alpha^*)$, then $u^*$ is bang-bang*

*with exactly one switch from $U$ to 0 at $t_s \in (0, T^*)$ such that*

$$t_s = \int_0^{p_s} \frac{d\nu}{f(\nu) + Ug(\nu)} \quad \text{where } p_s \text{ is implicitly determined by } -\frac{f(p_s)}{g(p_s)} = \frac{-\alpha U}{(1-\alpha) j_1(U)}.$$

*The optimal time $T^*$ is given by*

$$T^* = \int_0^{p_T} \frac{d\nu}{f(\nu) + u_p^*(\nu) g(\nu)} \quad \text{with } u_p^*(\nu) = U \mathbb{1}_{(0,p_s)},$$

*with the convention that $p_s = p_T$ if $\alpha \in [\alpha^*, 1]$.*

— *The case where $j_1$ is convex. In this case, define $u_p^*$ as*

$$u_p^* : [0, p_T] \ni p_t \mapsto \max\{\min\{U, F_0^{-1}(-f(p_t)/g(p_t))\}, 0\}$$

*If $\alpha \in (0, 1)$ the optimal time $T^*$ and control $u^*$ read*

$$T^* = \int_0^{p_T} \frac{d\nu}{f(\nu) + u_p^*(\nu) g(\nu)} \quad \text{and} \quad \forall t \in [0, T^*], \qquad u^*(t) = u_p^*(p_t)$$

*where $p_t$ denotes the unique solution in $[0, p_T]$ of the equation $t = \int_0^{p_t} \frac{d\nu}{f(\nu) + u_p^*(\nu) g(\nu)}$. If $\alpha = 1$ the same holds with $u_p^* = U \mathbb{1}_{[0,p_T]}$.*

*If $\alpha = 1$ the same holds with $u_p^* = U \mathbb{1}_{[0,p_T]}$.*

**Remark 1.3.** A reasonable concern in the definition of $v \mapsto F_0(v)$ is its behavior in case $j_1'(0) = \infty$ or $j_1'(0) = 0$ like in the functions $u \mapsto j_1(u) := \sqrt{u}$ and $u \mapsto j_1(u) := u^2$. We can check, taking limits, that in these cases the reasoning is still valid and that the results obtained hold. The limit reads

$$\lim_{v \to 0} F_0(v) = \lim_{v \to 0} v - \frac{j_1(v)}{j_1'(v)} - \frac{\alpha}{(1-\alpha) j_1'(v)}$$

— If $j_1'(0) = \infty$, we obtain $\lim_{v \to 0} F_0(v) = 0$. In this case, $j_1(\cdot)$ must be concave and therefore $F_0(\cdot)$ decreasing, thus $F_0(v) < 0$ for all $v \in (0, U]$. Looking at the maximization conditions, (1.24), we see that this is consistent with the results.

— If $j_1'(0) = 0$ we can apply l'Hôpital's rule to find $\lim_{v \to 0} \frac{j_1(v)}{j_1'(v)} = \lim_{v \to 0} \frac{j_1'(v)}{j_1''(v)} = 0$ and therefore $\lim_{v \to 0} F_0(v) = -\infty$. This implies that we can never have $F(0) \geqslant 0$ and thus $u^* > 0$ for all $t \in (0, T^*)$.

For the sake of simplicity we showed this for $F_0(\cdot)$ but this remark will still be valid for the functions $F_\lambda(\cdot)$ we will introduce in 1.20.

Let us comment and illustrate the result above, by describing the behaviour of the solutions of Family 1, classified with respect to the convexity of $j_1(\cdot)$ and pointing out the limit values of $\alpha$ separating the different regimes.

Exploiting Theorem 1.2, we know that in the concave and linear cases, solutions are necessarily bang-bang. Either $u^* = U \mathbb{1}_{[0,T^*]}$ or with one switch from $U$ to 0 occurring at time $t_s = \int_0^{p_s} \frac{d\nu}{f(\nu) + Ug(\nu)}$ with $p_s$ solving $-\frac{f(p_s)}{g(p_s)} = \frac{-\alpha U}{(1-\alpha) j_1(U)}$. This happens if and only if $\alpha < \alpha^*$. The value of $\alpha$ separating both regimes is $\alpha^* = \frac{-m_* j_1(U)/U}{1 - m_* j_1(U)/U}$. The existence and uniqueness of such a $p_s$ is guaranteed under the hypothesis of Remark 1.2, and not exclusively for the $f$ and $g$ of this particular problem.

The convex case has a richer set of behaviours than the other ones. As an example, on Fig. 1.3 solutions are plotted for the particular choice $j_1(u) = e^{u/11} - 1$. This function is not intended to

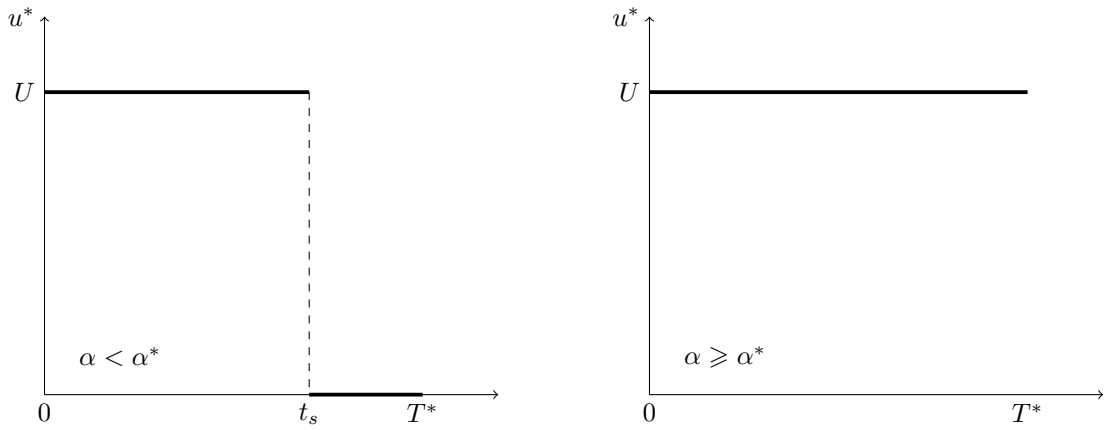


Figure 1.2 – Control functions $u^*$ solving problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$ in the linear and concave case.

| Category | Parameter | Name | Value |
|---|---|---|---|
| Optimization | $p_T$ | Final state | 0.99 |
| | $U$ | Maximal instantaneous release rate | 10 |
| Biology | $b^0_M$ | Normalized wild birth rate | 1 |
| | $b^0_W$ | Normalized infected birth rate | 0.9 |
| | $d_M$ | Wild death rate | 0.27 |
| | $d_W$ | Infected death rate | 0.3 |
| | $K$ | Normalized carrying capacity | 1 |
| | $s_h$ | Cytoplasmatic incompatibility level | 0.9 |

Table 1.1 – Parameter values used to plot the solutions to problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$

represent any realistic scenario but to illustrate the variety of possible solutions. The parameters considered for these simulations are given in Table 1.1, using the biological parameters considered in [10]. To obtain this plot, one needs to compute the function $F_0^{-1}$ which has been done by using the nonlinear system solver of the software Python.

The key factors to understand the behaviour of $u^*$ in the convex case are the relative positions of $F_0(0)$ and $F_0(U)$ with respect to $m_*$ and $m^*$. We begin by excluding the case $F_0(0) \geqslant m^*$ because for all $p_T \in (0,1)$, $F_0(0) \leqslant 0 < m^*$. Let us introduce

$$\alpha_0 := \frac{-m_* j_1'(0)}{1 - m_* j_1'(0)}, \tag{1.16}$$

$$\alpha_1 := \frac{U j_1'(U) - j_1(U) - m^* j_1'(U)}{1 + U j_1'(U) - j_1(U) - m^* j_1'(U)}, \tag{1.17}$$

$$\alpha_2 := \frac{U j_1'(U) - j_1(U) - m_* j_1'(U)}{1 + U j_1'(U) - j_1(U) - m_* j_1'(U)}. \tag{1.18}$$

These values are the thresholds separating the different regimes of the solutions. As an example, we deduce the value of $\alpha_1$. If $U \geqslant F_0^{-1}(m^*)$ then

$$u_p^* : [0, p_T] \ni p_t \mapsto \max\{\min\{U, F_0^{-1}(-f/g(p_t))\}, 0\} = \max\{F_0^{-1}(-f/g(p_t)), 0\}.$$

Instead, if $U < F_0^{-1}(m^*)$, there will be an interval of positive measure in which $u_p^* = U$. Since $F_0$ depends on $\alpha$, we can compute the smallest value of $\alpha$ for which the inequality $U \geqslant F_0^{-1}(m^*)$ holds:

$$F_0(U) := \frac{(1-\alpha)(Uj_1'(U) - j_1(U)) - \alpha}{(1-\alpha)j_1'(U)} \geqslant m^* \Leftrightarrow \alpha \geqslant \frac{Uj_1'(U) - j_1(U) - m^* j_1'(U)}{1 + Uj_1'(U) - j_1(U) - m^* j_1'(U)} := \alpha_1$$

Here we assumed $Uj_1'(U) - j_1(U) - m^* j_1'(U) \geqslant 0$, otherwise one can check that it is impossible to have $F_0(U) \geqslant m^*$. Doing a similar reasoning, one can see that we have similar equivalencies between $F_0(0) \leqslant m_*$ and $\alpha \geqslant \alpha_0$ and between $F_0(U) \leqslant m_*$ and $\alpha \geqslant \alpha_2$.

We conclude that the behaviors of the solution with respect to $\alpha$ are the following:

— If $\alpha \geqslant \alpha_0$, then $u^* > 0$ for a.e. $t \in (0, T^*)$, whereas if $\alpha < \alpha_0$ then there is an interval at the end in which $u^* = 0$.

— If $\alpha \leqslant \alpha_1$, then $u^* < U$ for a.e. $t \in (0, T^*)$.

— If $\alpha_1 < \alpha < \alpha_2$ an interval in which $u^* = U$ appears.

— Finally if $\alpha \geqslant \alpha_2$, $u^* = U$ for a.e. $t \in (0, T^*)$.

We recall that the function $x \mapsto \frac{x}{1+x}$ maps $[0, \infty)$ into $[0, 1)$. This implies that $(\alpha_0, \alpha_2) \in [0, 1)^2$ and that if $Uj_1'(U) - j_1(U) - m^* j_1'(U) \geqslant 0$, $\alpha_1 \in [0, 1)$ too. For the purpose of the discussion, in case $Uj_1'(U) - j_1(U) - m^* j_1'(U) < 0$ we can consider that $\alpha \geqslant \alpha_1$ always. Finally, since $x \mapsto \frac{x}{1+x}$ is increasing one only needs to compare the numerators of the expressions of $\alpha_0$, $\alpha_1$ and $\alpha_2$ in order to compare their values. Computing this we obtain that $\alpha_2 \geqslant \alpha_0$ and $\alpha_2 \geqslant \alpha_1$. Nevertheless, in a general setting the relative position between $\alpha_1$ and $\alpha_0$ is not fixed.

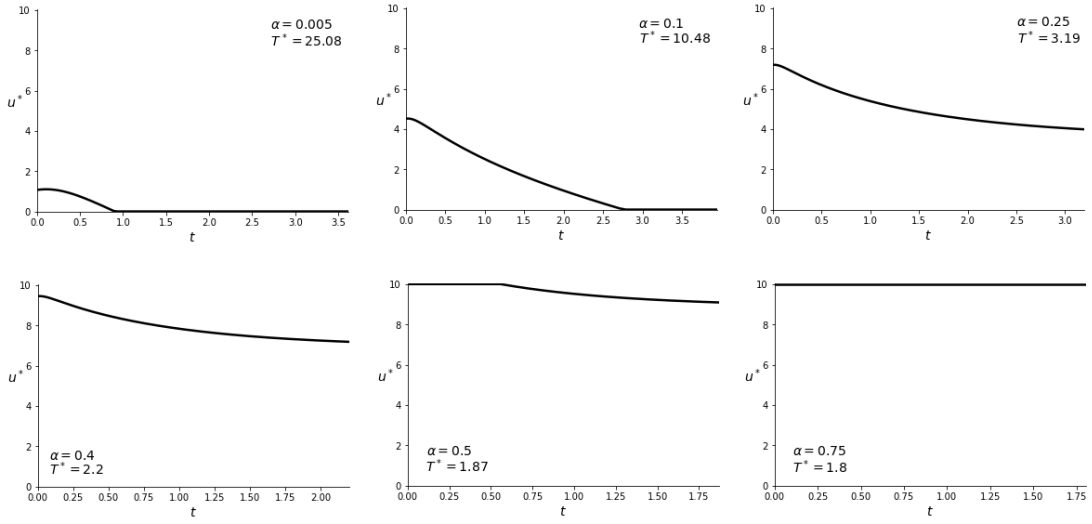


Figure 1.3 – Control functions $(T^*, u^*)$ solving problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ with $j_1(u) = e^{u/11} - 1$ as $\alpha$ increases, from left to right and from top to bottom. The values of $\alpha_0$, $\alpha_1$ and $\alpha_2$ obtained are $\alpha_0 \approx 0.15$, $\alpha_1 \approx 0.44$ and $\alpha_2 \approx 0.55$. For the sake of clarity, for $\alpha = 0.005$ and $\alpha = 0.1$, $u^*$ has not been represented in all its domain. Note that $u^* = 0$ in the rest of the domain.

### 1.2.2 Description of solutions

The following result characterizes the solutions to Family 1 problems.

Let us introduce

$$C^{p_T}(U) = \int_0^{p_T} \frac{U}{f(\nu) + Ug(\nu)} d\nu. \tag{1.19}$$

In this section we will assume, in accordance with the modeling issues discussed in Section 1.1.2, that $j_2(T, p_T) = T$. Therefore, (1.11) becomes

$$J_\alpha(T, u) = (1-\alpha) \int_0^T j_1(u(t))dt + \alpha T.$$

For $\alpha \in (0,1)$, let us also introduce the mapping

$$v \mapsto F_\lambda(v) := \frac{(1-\alpha)(vj_1'(v) - j_1(v)) - \alpha}{(1-\alpha)j_1'(v) - \lambda}, \tag{1.20}$$

where $\lambda \in \mathbb{R}_-$ is a constant depending on the parameters of the problem, and the quantity

$$C_{\mathcal{Q}} := \int_0^{T^*_{\mathcal{Q}}} u^*_{\mathcal{Q}}(t)dt, \tag{1.21}$$

with $\left(T^*_{\mathcal{Q}}, u^*_{\mathcal{Q}}\right)$ being the solution to the unconstrained case that has been treated in Theorem 1.1. Therefore, $C_{\mathcal{Q}}$ is the cost associated with this solution.

Nevertheless, we remark that existence properties for the optimal control problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$, studied in Section A, are established in a more general setting, without prescribing explicitly the function $j_2$.

**Theorem 1.2** (Family 1)**.** *Let us assume that $\alpha \in (0,1]$, $p_T \in (0,1)$, (1.2) is true, and $j_1(\cdot)$ satisfies the assumptions of $(\mathcal{H}.1)$. Let us assume that $U > m^*(p_T)$ and*

$$C > C^{p_T}(U) \text{ if } p_T \leqslant \theta \qquad \text{and} \qquad C > C^{\theta}(U) \text{ otherwise.}$$

*Then, there exists a pair $(T^*, u^*) \in \mathbb{R}_+ \times \mathcal{U}_{T,C,U}$ solving Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$. Moreover, let us distinguish two cases:*

— *Case where $j_1$ is either linear or strictly concave. The optimal time and control are given by*

$$u^* = U\mathbb{1}_{[0,\min\{C_{\mathcal{Q}},C\}/U]} \quad \text{and} \quad T^* = \frac{\min\{C_{\mathcal{Q}}, C\}}{U} + \int_{p_s}^{p_T} \frac{d\nu}{f(\nu)},$$

*with $p_s$ solving $C^{p_s}(U) = \min\{C_{\mathcal{Q}}, C\}$.*

— *Case where $j_1$ is convex. Let $u^*_p$ be defined by*

$$u^*_p : [0, p_T] \ni p_t \mapsto \max\left\{\min\left\{U, F_\lambda^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right)\right\}, 0\right\}$$

*If $\alpha \in (0,1)$ the optimal time $T^*$ and control $u^*$ are given by*

$$T^* = \int_0^{p_T} \frac{d\nu}{f(\nu) + u^*_p(\nu)g(\nu)} \quad \text{and} \quad \forall t \in [0, T^*], \qquad u^*(t) = u^*_p(p_t)$$

*where $p_t$ denotes the unique solution in $[0, p_T]$ of the equation $t = \int_0^{p_t} \frac{d\nu}{f(\nu)+u^*_p(\nu)g(\nu)}$ and $\lambda$ is a Lagrange multiplier such that $\lambda = 0$ if, and only if, $C_{\mathcal{Q}} \leqslant C$.*

*If $\alpha = 1$ then $u^* = U\mathbb{1}_{[0,\min\{C^{p_T}(U),C\}/U]}$.*

**Remark 1.4.** In case $C_{\mathcal{Q}} > C$, we have that $\lambda < 0$. Moreover, this value $\lambda$ is implicitly determined by the equation $\int_0^{p_T} u_p^*(\nu)/(f(\nu)+u_p^*(\nu)g(\nu))d\nu = C$.

**Remark 1.5.** For $p_T \leqslant \theta$ and $C = C^{p_T}$ we still have existence of solutions, and indeed $u^* = U\mathbb{1}_{[0,T^*]}$ with $T^* = \int_0^{p_T} \frac{d\nu}{f(\nu)+Ug(\nu)} = \frac{C}{U}$. For the sake of clarity we exclude this case from the statement of the theorem, but it will be briefly discussed in the proof.

### 1.2.3 Proof of Theorem 1.1

The existence of solutions for Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$ follows from an immediate adaptation of Proposition A.3 and is left to the reader. Our approach is based on an adequate change of variable. In order to make this proof easier to follow, let us distinguish several steps.

**Step 1: a change of variable for recasting the optimal control problem.**

To introduce the adequate change of variable, we need the following result.

**Lemma 1.1.** *Let $(T^*, u^*) \in \mathbb{R}_+ \times \mathcal{V}_{T,U}$ solve Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$ and let $\alpha > 0$. Let us introduce $p_{u^*}$ solving*

$$\begin{cases} p'_{u^*} = f(p_{u^*}) + u^* g(p_{u^*}) & \text{in } (0,T^*) \\ p_{u^*}(0) = 0, \end{cases}$$

*then one has $p'_{u^*}(t) > 0$ for all $t \in (0,T^*)$.*

*Proof.* Let us argue by contradiction, assuming the existence of $0 \leqslant t_1 < t_2 \leqslant T$ such that $p_{u^*}(t_2) \leqslant p_{u^*}(t_1)$. Looking at the functional $J_\alpha$ we are minimizing, we claim that $T^*$ is the smallest time at which $p_{u^*}(T^*) = p_T$. Indeed, since $\alpha > 0$, if there exists $T < T^*$ such that $p_{u^*}(T) = p_T$, the pair $(T, u^*|_{(0,T)})$ is admissible for Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$, and moreover, $J_\alpha(T, u^*|_{(0,T)}) < J_\alpha(T^*, u^*)$ which contradicts the minimality of $(T^*, u^*)$.

Let us first assume that $p_{u^*}(t_2) < p_{u^*}(t_1)$. Therefore, since $p_{u^*}(T) = p_T$, we infer by continuity the existence of $t_3 \in (t_2, T^*)$ such that $p_{u^*}(t_3) = p_{u^*}(t_1)$. Let us define $\tilde{u}$ as

$$\tilde{u}(t) = \begin{cases} u^*(t) & t \in (0,t_1), \\ u^*(t+t_3-t_1) & t \in (t_1,\tilde{T}) \end{cases}$$

where $\tilde{T} = T^* - t_3 + t_1$. We proceed by direct comparison between the cost of both controls, obtaining

$$J_\alpha(T^*,u^*) - J_\alpha(\tilde{T},\tilde{u}) \quad = \quad (1-\alpha)\int_{t_1}^{t_3} j_1(u^*(t))dt + \alpha(t_3-t_1) \ > 0,$$

which contradicts the optimality of $(T^*, u^*)$. The remaining case where $p_{u^*}(t_1) = p_{u^*}(t_2)$ can be treated similarly, by choosing $t_3 = t_2$. □

Let us now exploit this lemma in order to perform a useful change of variables that will allow us to reformulate Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$. Given that $u \in \mathcal{V}_{T,U}$ solving Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$ satisfies the necessary conditions $p(0) = 0$, $p(T) = p_T$ and $p'(t) = f(p(t)) + u(t)g(p(t)) > 0$ for all $t \in (0,T)$. Therefore, $p$ defines a bijection from $(0,T)$ onto $(0,p_T)$. Denoting by $p^{-1} : [0,p_T] \to [0,T]$ its inverse, one has

$$p(t) = p_t \Leftrightarrow t = p^{-1}(p_t) = \int_0^{p_t} (p^{-1})'(\nu)d\nu = \int_0^{p_t} \frac{d\nu}{p'(p^{-1}(\nu))}$$

which leads to define the change of variable

$$t = \int_0^{p_t} \frac{d\nu}{f(\nu) + u(p^{-1}(\nu))g(\nu)}.$$

Introducing the function $p_t \mapsto u_p(p_t)$ defined by $u_p(p_t) := u(p^{-1}(p_t)) = u(t)$, one can easily infer that Problem $(\mathcal{Q}^{1,\alpha}_{p_T,U})$ is equivalent to

$$\inf_{u \in \hat{\mathcal{V}}_{p_T,U}} \hat{J}_{p,\alpha}(u_p), \qquad (\widehat{\mathcal{Q}}^{1,\alpha}_{p_T,U})$$

where $\hat{J}_{p,\alpha}(u_p)$ is defined by

$$\hat{J}_{p,\alpha}(u_p) = \int_0^{p_T} \frac{(1-\alpha)j_1(u_p(\nu)) + \alpha}{f(\nu) + u_p(\nu)g(\nu)} d\nu, \tag{1.22}$$

and $\hat{\mathcal{V}}_{p_T,U}$, is given by

$$\hat{\mathcal{V}}_{p_T,U} := \{u_p \in L^\infty(0, p_T), 0 \leqslant u_p \leqslant U \text{ a.e.}\}.$$

To recover the solution of $(\mathcal{Q}^{1,\alpha}_{p_T,U})$ from the solution of $(\widehat{\mathcal{Q}}^{1,\alpha}_{p_T,U})$, it suffices to undo the change of variable by setting $u(\cdot) = u_p(p(\cdot))$.

Note that, according to Lemma 1.1, the space $\hat{\mathcal{V}}_{p_T,U}$ is bigger than the space where solutions actually belong. The appropriate space is the range of $\mathcal{V}_{T,U}$, defined in (1.12), by the change of variable above, that is

$$\mathcal{W} := \{u_p \in L^\infty(0, p_T), f(p_t) + u_p(p_t)g(p_t) > 0 \text{ a.e.}\}.$$

It is notable that, as can be observed in Figure 1.4, one has

$$u_p \in \mathcal{W} \Leftrightarrow -f/g(\cdot) < u_p(\cdot) \leqslant U \text{ a.e. on } (0, \min\{p_T, \theta\}) \text{ and } 0 \leqslant u_p(\cdot) \leqslant U \text{ a.e. on } (\min\{p_T, \theta\}, p_T).$$

It follows from the definition of $\mathcal{W}$ that

$$\inf_{u \in \hat{\mathcal{V}}_{p_T,U}} \hat{J}_{p,\alpha}(u_p) \leqslant \inf_{u \in \mathcal{W}} \hat{J}_{p,\alpha}(u_p)$$

To solve the optimization problem in the right-hand side, we will solve Problem $(\widehat{\mathcal{Q}}^{1,\alpha}_{p_T,U})$, and check *a posteriori* that its solution $u_p^* \in \hat{\mathcal{V}}_{p_T,U}$ satisfies $u_p^* \in \mathcal{W}$ so that we will infer that

$$\inf_{u \in \mathcal{W}} \hat{J}_{p,\alpha}(u) = \inf_{u \in \hat{\mathcal{V}}_{p_T,U}} \hat{J}_{p,\alpha}(u) = \hat{J}_{p,\alpha}(u_p^*).$$

**Step 2: first-order optimality conditions through the Pontryagin Maximum Principle.**

Let us introduce, with a slight abuse of notation, the function $t$ given by

$$t(p_t) = \int_0^{p_t} \frac{d\nu}{f(\nu) + u_p(\nu)g(\nu)}.$$

Let $\bar{U} = [0, U]$. It is standard to derive optimality conditions for this problem [2] and one gets

$$\text{for a.e. } p_t, \quad u_p^*(p_t) \quad \in \quad \arg\max_{v \in \bar{U}} -\frac{(1-\alpha)j_1(v) + \alpha}{f(p_t) + vg(p_t)}. \tag{1.23}$$

The case $\alpha = 1$ is obvious and leads to $u^*(\cdot) = U$ on $[0, T^*]$, after applying the inverse change of variable.

Let us now assume that $\alpha \in (0, 1)$. It is standard to introduce the switching function [3] $\psi$ defined by

$$\psi(v) = -\frac{f(p_t)(1-\alpha)j_1'(v) + g(p_t)\left((1-\alpha)\left(vj_1'(v) - j_1(v)\right) - \alpha\right)}{\left(f(p_t) + vg(p_t)\right)^2},$$

and the maximization condition (1.23) yields

$$\begin{cases} \psi(0) \leqslant 0 \text{ on } \{u_p^* = 0\}, \\ \psi(u_p^*) = 0 \text{ on } \{0 < u_p^* < U\}, \\ \psi(U) \geqslant 0 \text{ on } \{u_p^* = U\}, \end{cases}$$

these equalities and inequalities being understood up to a null Lebesgue measure set. These functions allows us to write the aforementioned optimality conditions as

$$\begin{cases} F_0(0) \geqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = 0\}, \\ F_0(u_p^*) = -\frac{f(p_t)}{g(p_t)} \text{ on } \{0 < u_p^* < U\}, \\ F_0(U) \leqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = U\}, \end{cases} \tag{1.24}$$

where $F_0$ is given by (1.14).

Since the derivative of $F_0$ writes

$$F_0'(v) = (1-\alpha)j_1''(v)\frac{(1-\alpha)j_1(v) + \alpha}{\left((1-\alpha)j_1'(v)\right)^2},$$

this function shares the sign of $j_1''(v)$.

**Step 3: analysis of the first-order optimality conditions.**

Before discussing the different cases, it is useful to recall the behaviour of the function $p_t \mapsto -\frac{f(p_t)}{g(p_t)}$, represented in Figure 1.4. This function has two roots at $p_t = 0$ and $p_t = \theta$, is strictly positive between them and strictly negative after $p_t = \theta$, with a maximum at $p_t = p^*$ as defined in (1.6) and such that $\lim_{p_t \to 1} f(p_t)/g(p_t) = -\infty$ (See Remark 1.2). Another property that will be useful thereafter is that $p_t \mapsto f(p_t)/g(p_t)$ is not constant on any set of positive measure.

We conclude the proof looking each case separately:

2. Indeed, one way consists in applying the Pontryagin Maximum Principle (PMP). Introducing the Hamiltonian $\mathcal{H}$ of the system, defined by

$$\begin{array}{rccl} \mathcal{H}: & (0,1) \times \mathbb{R}_+ \times \mathbb{R} \times \{0,-1\} \times \bar{U} & \to & \mathbb{R} \\ & (p_t, t, \tau, q^0, u_p) & \mapsto & \frac{\tau + q^0((1-\alpha)j_1(u_p) + \alpha)}{f(p_t) + u_p g(p_t)}. \end{array}$$

where $\tau$ is the conjugated variable of $t$ and satisfies $\tau' = -\partial_t \mathcal{H} = 0$ and therefore, $\tau$ is constant. Furthermore the transversality condition on $\tau$ yields $\tau = 0$. The instantaneous maximization condition reads $u_p^*(p_t) \in \arg\max_{v \in \bar{U}} \mathcal{H}(p_t, t, \tau, q^0, v)$. Finally, since $(\tau, q^0)$ is nontrivial, one has $q^0 = -1$.

3. Indeed, according to the PMP, the switching function is given by $\psi := \partial_{u_p} \mathcal{H}(p_t, t, \tau, v)$.

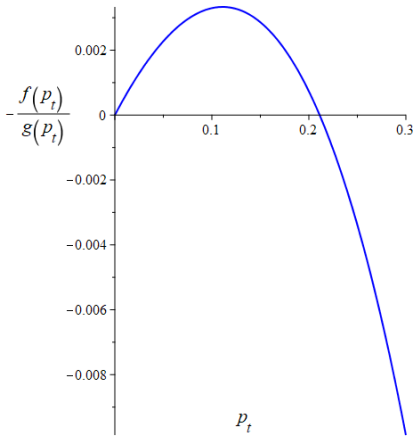


Figure 1.4 – Function $p_t \mapsto -\frac{f(p_t)}{g(p_t)}$ represented between $p_t = 0$ and $p_t = 0.3$ for the parameters at table 1.1.

— If $j_1''(\cdot) = 0$ then $F_0$ is constant, so that $F_0(0) = F_0(U)$ and $u_p^*$ is necessarily *bang-bang*, equal to 0 or $U$ a.e. in $(0, p_T)$ because $F_0(u_p^*) = -\frac{f(p_t)}{g(p_t)}$ cannot be constant. Looking at conditions (1.24) we see that if $F_0(0) \leqslant m_*$ the solution is $u_p^* = U\mathbb{1}_{[0,p_T]}$, since only the condition $F_0(U) \leqslant -\frac{f(p_t)}{g(p_t)}$ can be satisfied. On the other hand, if $F_0(0) > m_*$ then $u_p^*$ has one switch from $U$ to 0. We conclude by computing

$$F_0(0) = \frac{-\alpha}{(1-\alpha)j_1'(0)} \leqslant m_* \iff \alpha \geqslant -m_* \frac{j_1'(0)}{1 - m_* j_1'(0)} = \alpha^*$$

and noticing that $j_1'(0) = j_1(U)/U$.

— If $j_1''(\cdot) < 0$, then $F$ is decreasing. We introduce the function $\Psi$ we are maximizing, given by

$$\Psi(v) := -\frac{(1-\alpha)j_1(v) + \alpha}{f(p_t) + vg(p_t)}$$

and we recall that $\Psi' = \psi$. To show that $u_p^*$ is *bang-bang*, let us use (1.23). For a given $p_t \in (0, p_T)$, let $N(v)$ be the numerator of $\psi(v)$. If there exists $v_0 \in (0, U)$ maximizing $\Psi(\cdot)$, then $f(p_t) + v_0 g(p_t) > 0$ according to Lemma 1.1. Moreover, $\psi(v_0) = N(v_0) = 0$ since $v_0$ is a critical point of $\Psi$ and $\Psi''(v_0) = \psi'(v_0) \leqslant 0$. We compute

$$\psi'(v_0) = \frac{N'(v_0)\left(f(p_t) + vg(p_t)\right)^2 - N(v_0)2\left(f(p_t) + vg(p_t)\right)g(p_t)}{\left(f(p_t) + vg(p_t)\right)^4} = \frac{N'(v_0)}{\left(f(p_t) + v_0 g(p_t)\right)^2}.$$

which has the same sign as $N'(v_0)$, and

$$N'(v_0) = -(1-\alpha)j_1''(v_0)\left(f(p_t) + v_0 g(p_t)\right).$$

Therefore, one has $\Psi''(v_0) > 0$ leading to a contradiction with the maximality of $v_0$. It follows that the points $v_0 \in (0, U)$ satisfying $F_0(v_0) = -\frac{f(p_t)}{g(p_t)}$ cannot maximize $\Psi$, which shows that any solution is *bang-bang*.

A straightforward computation shows that

$$\Psi(U) - \Psi(0) = -\frac{(1-\alpha)j_1(U)f(p_t) - \alpha U g(p_t)}{f(p_t)(f(p_t) + Ug(p_t))}.$$

According to the optimality conditions (1.23), and because of the variations of $-f/g$, one sees that if $u_p^*$ has a switching point, then it necessarily occurs strictly after $\theta$ since $F_0(0) < 0$.
Hence, from the expression of $\Psi(U) - \Psi(0)$, we get that any switching point $p_s$ solves the equation

$$-\frac{f(p_s)}{g(p_s)} = \frac{-\alpha U}{(1-\alpha)j_1(U)}$$

and we can compute that the smallest value of $\alpha$ for which this equation has a solution is the one such that $m_* = \frac{-\alpha U}{(1-\alpha)j_1(U)}$ which allows us to recover $\alpha^*$.

— If $j_1''(\cdot) > 0$, then $F_0(\cdot)$ is increasing, and the three conditions (1.24) are mutually exclusive and are thus both necessary and sufficient. The function $p_t \mapsto -\frac{f(p_t)}{g(p_t)}$ is increasing until $p^*$, defined in (1.6), and then decreasing (See the unimodality condition in Remark 1.2). Since $F_0$ defines a bijection, the optimality conditions (1.24) rewrite

$$\begin{cases} 0 \geqslant F_0^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right) \text{ on } \{u_p^* = 0\}, \\ u_p^* = F_0^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right) \text{ on } \{0 < u_p^* < U\}, \\ U \leqslant F_0^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right) \text{ on } \{u_p^* = U\}. \end{cases}$$

The expected expression of $u^*$ follows then easily.

In order to finish the proof, we have to check that the solution $u_p^* \in \hat{\mathcal{V}}_{p_T,U}$ belongs to $\mathcal{W}$. This two spaces only differ for $p_t \in [0, \theta)$. We have that $F_0(0) = \frac{-\alpha}{(1-\alpha)j_1'(0)} \leqslant 0$. This implies that $u_p^* \neq 0$ in $(0, \theta)$, because the optimality condition $0 \geqslant F_0^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right)$ cannot be satisfied in any open interval inside $(0, \theta)$. In the concave and linear case, since the solution is bang-bang, this also means that $u_p^* = U$ in $(0, \theta)$, therefore $f(p_t) + u_p^*(p_t)g(p_t) > 0$ in $p_t \in (0, \theta)$. In the convex case, we need to prove that $f(p_t) + u_p^*(p_t)g(p_t) > 0$ also in case the solution is a singular control. In that case, $u_p^*$ satisfies the equation $u_p^* = F_0^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right)$. Now $F_0(\cdot)$ is increasing, and so is $F_0^{-1}(\cdot)$, therefore

$$F_0^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right) > -\frac{f(p_t)}{g(p_t)} \Leftrightarrow -\frac{f(p_t)}{g(p_t)} > F_0\left(-\frac{f(p_t)}{g(p_t)}\right) \text{ for } p_t \in (0, \theta).$$

This is true if, and only if $v > F_0(v)$ for $v \in (0, m^*]$. We have that

$$v > F_0(v) \Leftrightarrow v > \frac{(1-\alpha)(vj_1'(v) - j_1(v)) - \alpha}{(1-\alpha)j_1'(v)} \Leftrightarrow 0 > -\frac{(1-\alpha)j_1(v) + \alpha}{(1-\alpha)j_1'(v)}.$$

All the terms in the last fraction are positive, yielding that $f(p_t) + u_p^*(p_t)g(p_t) > 0$ for all $p_t \in (0, \theta)$, which ends the proof.

### 1.2.4 Proof of Theorem 1.2

Let us first recall that existence of solutions for Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ has been proved in Proposition A.3.

**Step 1: derivation of the first-order optimality conditions.**

By mimicking the reasoning in the first step of the proof of Theorem 1.1, one shows that the conclusion of Lemma 1.1 still holds true in that case, in other words, the optimal state $p_{u^*}$ is increasing in $[0, T^*]$. This allow us to reformulate Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ by defining the change of variable

$$t : p_t \mapsto \int_0^{p_t} \frac{d\nu}{f(\nu) + u(p^{-1}(\nu))g(\nu)},$$

introducing the function $p_t \mapsto u_p(p_t)$ defined by $u_p(p_t) := u(p^{-1}(p_t)) = u(t)$, so that Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ is equivalent to

$$\inf_{u \in \hat{\mathcal{U}}_{p_T,C,U}} \hat{J}_{p,\alpha}(u_p), \qquad (\hat{\mathcal{P}}^{1,\alpha}_{p_T,C,U})$$

where $\hat{J}_{p,\alpha}(u_p)$ is defined by (1.22) and $\hat{\mathcal{U}}_{p_T,C,U}$ is given by

$$\hat{\mathcal{U}}_{p_T,C,U} := \left\{ u_p \in L^\infty\left([0,p_T]\right), 0 \leqslant u_p \leqslant U \text{ a.e. }, \int_0^{p_T} \frac{u_p(\nu)}{f(\nu) + u_p(\nu)g(\nu)} d\nu \leqslant C \right\}.$$

To recover the solution of $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ from the solution of $(\hat{\mathcal{P}}^{1,\alpha}_{p_T,C,U})$, it suffices to undo the variable change by setting $u(\cdot) = u_p(p(\cdot))$. Note that, as pointed out in the step 1 of Section 1.2.3, we are solving the problem in $\hat{\mathcal{U}}_{p_T,C,U}$, a bigger space than the range of $\mathcal{U}_{T,C,U}$ by the change of variable introduced in Lemma 1.1. This range is $\hat{\mathcal{W}} = \mathcal{W} \cap \hat{\mathcal{U}}_{p_T,C,U}$. As we have seen before, solutions to Problems $(\hat{\mathcal{P}}^{1,\alpha}_{p_T,C,U})$ and

$$\inf_{u \in \hat{\mathcal{W}}} \hat{J}_{p,\alpha}(u_p), \tag{1.25}$$

coincide as long as the solutions to Problem $(\hat{\mathcal{P}}^{1,\alpha}_{p_T,C,U})$ satisfy $f(p_t) + u_p^*(p_t)g(p_t) > 0$. Mimicking the reasoning at the end Step 3 in Section 1.2.3, one can similarly check that solutions to both problems above still coincide.

Let us derive and analyze optimality conditions for this problem. To handle the constraint

$$\int_0^{p_T} \frac{u_p(\nu)}{f(\nu) + u_p(\nu)g(\nu)} d\nu \leqslant C,$$

we introduce the mapping

$$p_t \mapsto z_p(p_t) = \int_0^{p_t} \frac{u_p(\nu)}{f(\nu) + u_p(\nu)g(\nu)} d\nu.$$

By following the same lines as in the proof of Theorem 1.1 and applying the PMP, one gets the existence of $\lambda \leqslant 0$ such that

$$\lambda \leqslant 0\ , \qquad \lambda(z_p(p_T) - C) = 0. \quad \text{(transversality and slackness condition)} \tag{1.26}$$

and the optimal control $u_p^*$ solves

$$\text{for a.e. } p_t, \quad u_p^*(p_t) \quad \in \quad \arg\max_{v\in\bar{U}} \frac{\lambda v + q^0((1-\alpha)j_1(v)+\alpha)}{f(p_t)+vg(p_t)}. \tag{1.27}$$

In what follows, if $p_T \leqslant \theta$, we will assume without loss of generality that

$$C > C^{p_T}(U), \tag{1.28}$$

the case $C = C^{p_T}(U)$ being straightforward (in that case, one has necessarily $u_p^*(p_t) = U$ on $[0, p_T]$).

Let us show that $q^0 = -1$. To this aim, let us assume by contradiction that $q^0 = 0$. Hence, the optimality condition reads $u_p^*(p_t) \in \arg\max_{v\in\bar{U}} \psi(v)$ where $\psi(v) = \frac{\lambda v}{f(p_t)+vg(p_t)}$, and since the 3-tuple of Lagrange multipliers is nontrivial according to the PMP, we necessarily have $\lambda < 0$ which, by condition (1.26), implies in turn that $z_p(p_T) = C$. If $p_t \in (0,\theta)$ (resp. $p_t \in (\theta, 1)$), $\psi$ is increasing (resp. decreasing). Hence, if $p_T \leqslant \theta$, then $u_p^* = U\mathbb{1}_{[0,p_T]}$. This allows us to write $z_p(p_T) = Ut(p_T)$ leading to a contradiction since $C > Ut(p_T) = z_p(p_T)$ (See Remark 1.5). On the other hand, if $p_T > \theta$ the final state cannot be reached since $u_p^* = U\mathbb{1}_{[0,\theta]} + 0\mathbb{1}_{[\theta,p_T]}$. Given that with this control, $p_{u^*}$ cannot attain $p_T$ (remaining indefinitely at $p_{u^*} = \theta$) we reach again a contradiction. Therefore, it follows that $q^0 = -1$.

**Step 2: analysis of the first-order optimality conditions.**

Before discussing further the optimality conditions of this problem we remark a key fact in this proof. We introduce

$$C_{\mathcal{Q}} := \int_0^{T_{\mathcal{Q}}^*} u_{\mathcal{Q}}^*(t)dt,$$

where $\left(T_{\mathcal{Q}}^*, u_{\mathcal{Q}}^*\right)$ is the solution to Problem $(\mathcal{Q}_{p_T,U}^{1,\alpha})$ for the same value of $\alpha$ considered. Since $\mathcal{U}_{T,C,U} \subset \mathcal{V}_{T,U}$ we have that

$$\inf_{u_p\in\mathcal{V}_{T,U}} \hat{J}_{p,\alpha}(u_p) \leqslant \inf_{u_p\in\mathcal{U}_{T,C,U}} \hat{J}_{p,\alpha}(u_p).$$

This implies that if $C \geqslant C_{\mathcal{Q}}$, then $u^* = u_{\mathcal{Q}}^*$. Moreover, we can also deduce that, in case $C < C_{\mathcal{Q}}$ the constraint $z_p(p_T) \leqslant C$ is always saturated. By contradiction, if $z_p(p_T) < C$, then the slackness condition yields $\lambda = 0$. Therefore $u_p^*(p_t) \in \arg\max_{v\in\bar{U}} -\frac{(1-\alpha)j_1(v)+\alpha}{f(p_t)+vg(p_t)}$, but this is the optimality condition for the unconstrained case and $u_{\mathcal{Q}}^* \notin \mathcal{U}_{T,C,U}$. Thus, the constraint must be saturated and we must have $\lambda < 0$. Consequently, we consider $C < C_{\mathcal{Q}}$ and $\lambda < 0$ from now on.

We begin by discussing the case $\alpha = 1$. From the optimality condition (1.27) we can derive

$$\begin{cases} \frac{1}{\lambda} \geqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = 0\}, \\ \frac{1}{\lambda} = -\frac{f(p_t)}{g(p_t)} \text{ on } \{0 < u_p^* < U\}, \\ \frac{1}{\lambda} \leqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = U\}. \end{cases}$$

Once again these equalities and inequalities must be understood up to a null Lebesgue measure set. From these conditions we see easily that $u_p^*$ is *bang-bang*, since $p_t \mapsto \frac{f(p_t)}{g(p_t)}$ is not constant on any set of positive measure. Also, using the monotonicity of $p_t \mapsto \frac{f(p_t)}{g(p_t)}$ and the fact that $\lambda < 0$ we conclude that $u_p^*$ has, at most, one switch from $U$ to 0. Since the case without constraint

had no switches and we are assuming $C < C_{\mathcal{Q}}$, it follows that $u_p^* = U\mathbb{1}_{[0,p_s]}$, with $p_s$ solving $C^{p_s}(U) = C$. We can easily express this as a function of time since $C^{p_s}(U) = \int_0^{p_s} \frac{U}{f(\nu)+Ug(\nu)} d\nu = U\int_0^{p_s} \frac{d\nu}{f(\nu)+Ug(\nu)} = Ut_s$, thus $u^* = U\mathbb{1}_{[0,t_s]}$, with $t_s = \frac{C}{U}$.

Assuming now $\alpha \in (0,1)$ and following the same lines as in the unconstrained case we introduce

$$v \mapsto F_\lambda(v) := \frac{(1-\alpha)(vj_1'(v) - j_1(v)) - \alpha}{(1-\alpha)j_1'(v) - \lambda}.$$

Then, we can write the optimality conditions for Problem $(\hat{\mathcal{P}}^{1,\alpha}_{p_T,C,U})$ as

$$\begin{cases} F_\lambda(0) \geqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = 0\}, \\ F_\lambda(u_p^*) = -\frac{f(p_t)}{g(p_t)} \text{ on } \{0 < u_p^* < U\}, \\ F_\lambda(U) \leqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = U\}. \end{cases} \tag{1.29}$$

A straightforward computation shows that, like in the unconstrained case, $F_\lambda'(\cdot)$ and $j_1''(\cdot)$ have the same sign. This allows us to draw the same conclusions on the behaviour of $u_p^*$ as in the unconstrained case. We sketch the reasoning hereafter:

— If $j_1''(\cdot) = 0$ then $F_\lambda$ is constant and $u_p^*$ *bang-bang*. Since $F_\lambda(0) = -\frac{\alpha}{(1-\alpha)j_1'(0)-\lambda} \leqslant 0$, then there is at most one switch. Moreover, we know that the constraint $z_p(p_T) \leqslant C$ is saturated and therefore that $u^* = U\mathbb{1}_{[0,t_s]}$ with $t_s = \frac{C}{U}$.

— If $j_1''(\cdot) < 0$, then $F_\lambda$ is decreasing. *Mutatis mutandis*, we can reproduce the calculations done in Theorem 1.1, deducing that the behaviour of $u_p^*$ is identical to the unconstrained case. That is, $u_p^*$ is *bang-bang* with at most one switch from $U$ to 0. Again, using the saturation of the constraint we deduce that $u^* = U\mathbb{1}_{[0,t_s]}$ with $t_s = \frac{C}{U}$.

— If $j_1''(\cdot) > 0$, then $F(\cdot)$ is increasing, and thus the three conditions (1.29) are both necessary and sufficient. This also implies that, once again, $F_\lambda$ defines a bijection, so the optimality conditions (1.29) can be rewritten as

$$\begin{cases} 0 \geqslant F_\lambda^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right) \text{ on } \{u_p^* = 0\}, \\ u_p^* = F_\lambda^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right) \text{ on } \{0 < u_p^* < U\}, \\ U \leqslant F_\lambda^{-1}\left(-\frac{f(p_t)}{g(p_t)}\right) \text{ on } \{u_p^* = U\}. \end{cases}$$

From these conditions we can do a straightforward derivation of the expression of $u^*$.

**Remark 1.6.** Note that the control $u^*$ in the convex case with constraint has a very similar expression to the unconstrained case. Indeed the monotonicity of $p_t \mapsto F_\lambda^{-1}(-f/g(p_t))$ is the same: increasing until $p_t = p^*$ and then decreasing. This translates into $u^*$ being non-decreasing until $t^*$, solving $p_{u^*}(t^*) = p^*$ and non-increasing afterwards. The relative positions of $F_\lambda(0)$ and $F_\lambda(U)$ with respect to $m_*$ and $m^*$ still play the same crucial role in the behaviour of solutions. Nevertheless, the values of $\alpha_0$, $\alpha_1$ and $\alpha_2$ do not make sense anymore, since $F_\lambda$ depends on $\lambda$ which may change for different choices of $\alpha$ and $C$.

## 1.3 Analysis of Family 2 problems

### 1.3.1 Description of solutions

In this section we present and discuss the results obtained for the problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$ of Family 2. As discussed in Section 1.1.2 let us assume $j_2(T,p(T)) = (1-p(T))^2$. Therefore, (1.11) becomes

$$J_\alpha(u) = (1-\alpha)\int_0^T j_1(u(t))dt + \alpha(1-p(T))^2.$$

In this family the time horizon $T$ is fixed and $p(T)$ is free. The existence issues in a broader setting are treated separately in Appendix A.

We introduce the following notations in order to state the main result of this section:

$$U^* := \max_{p\in[0,1]}\left(-\frac{f'(p)}{g'(p)}\right) \tag{1.30}$$

Let us also introduce also $p^{max}$ and $\bar{p}$ defined in the following way:

— If $C \leqslant C^\theta$,

$$p^{max} \quad \text{solves} \quad \int_0^{p^{max}} \frac{d\nu}{f(\nu)+Ug(\nu)} = \min\left\{\frac{C}{U}, T\right\}.$$

— If $C > C^\theta$,

$$p^{max} \quad \text{solves} \quad \int_0^{p^{max}} \frac{d\nu}{f(\nu)+U\mathbb{1}_{(0,\bar{p})}g(\nu)} = T.$$

where $\bar{p}$ is such that

$$\int_0^{\bar{p}} \frac{d\nu}{f(\nu)+Ug(\nu)} = \min\{C/U, T\}. \tag{1.31}$$

We remark that in the first case we have $p^{max} \leqslant \theta$.

Let us also introduce the mapping

$$v \mapsto F_{\lambda,\tau}(v) := \frac{vj_1'(v) - j_1(v) + \tau}{j_1'(v) - \lambda},$$

where $\lambda, \tau \in \mathbb{R}_-$.

Finally let us define

$$\alpha^0 := \frac{Kj_1(U)/U}{2 + Kj_1(U)/U} \quad \text{and} \quad \alpha^{max} = \frac{j_1(U)/\left(f(p^{max})+Ug(p^{max})\right)}{2(1-p^{max}) + j_1(U)/\left(f(p^{max})+Ug(p^{max})\right)}.$$

Note that both parameters satisfy $\alpha^0, \alpha^{max} \in (0,1)$ and, assuming $U \geqslant m^*(p_T)$ and $U > U^*$, they satisfy the inequality $\alpha^0 \leqslant \alpha^{max}$ [4]. Here, $K$ denotes the environmental carrying capacity (see (1.1)). It appears in the definition of $\alpha^0$ and hereafter due to the fact that $g(0) = 1/K$.

4. In order to prove this we recall that $x \mapsto \frac{x}{2+x}$ is an increasing function of x, we have $\alpha^0 \leqslant \alpha^{max}$ if and only if

$$K\frac{j_1(U)}{U} \leqslant \frac{j_1(U)}{(1-p^{max})(f(p^{max})+Ug(p^{max}))}.$$

Reordering this we get $U \geqslant K(1-p^{max})(f(p^{max})+Ug(p^{max}))$. Note that for $p^{max} = 0$ we have the equality, therefore we want to be sure that $p \mapsto (1-p)(f(p)+Ug(p))$ is non-increasing. Computing the derivative we obtain $-K(f(p)+Ug(p)) + K(1-p)(f'(p)+Ug'(p))$. The conditions needed for both terms to be individually smaller than zero are, precisely, $U > m^*(p_T)$ and $U > U^*$.

**Theorem 1.3.** *Let us assume that* (1.2) *is true, and that* $j_1(\cdot)$ *satisfies the assumptions of* ($\mathcal{H}$.1)*. Let us assume that* $U > m^*(p_T)$ *and* $\alpha \in (0,1]$ [5]*. Then, there exists a control* $u^* \in \mathcal{U}_{T,C,U}$ *solving problem* $(\mathcal{P}^{2,\alpha}_{T,C,U})$ *and times* $t^-, t^+ \in [0,T]$ *such that* $u^* = 0$ *in* $(0,t^-) \cup (t^+,T)$ *and in* $(t^-,t^+)$*:*

— *Case where* $j_1$ *is either linear or strictly concave. The optimal control is* $u^* = U\mathbb{1}_{[t^-,t_s]}$*, with* $t_s \leqslant t^+$*. Assuming further that* $U > U^*$ *we have that*
  — *If* $\alpha \leqslant \alpha^0$*,* $u^* = 0$ *for all* $t \in (t^-,t^+)$*.*
  — *If* $\alpha^0 < \alpha < \alpha^{max}$ *then* $u^* = U\mathbb{1}_{[t^-,t_s]}$ *with* $t_s$ *the smallest possible value such that* $p_{u^*}(T) = p^*_T$*,* $p^*_T$ *being the only solution to* $(1-p^*_T)\left(f(p^*_T) + Ug(p^*_T)\right) = \frac{1-\alpha}{2\alpha} j_1(U)$*. This value can be explicitly computed: if* $p^*_T \leqslant \theta$*, then* $t_s = T$ *and if* $p^*_T > \theta$ *then* $t_s$ *solves* $t_s - t^- = \int_0^{p_s} \frac{d\nu}{f(\nu)+Ug(\nu)}$*, with* $p_s$ *the solution of* $\int_0^{p^*_T} \frac{d\nu}{f(\nu)+U\mathbb{1}_{(0,p_s)}g(\nu)} = T$*.*
  — *If* $\alpha \geqslant \alpha^{max}$ *then* $u^* = U\mathbb{1}_{[t^-,t_s]}$ *with* $t_s$ *solving* $t_s - t^- = \int_0^{\bar{p}} \frac{d\nu}{f(\nu)+Ug(\nu)}$*.*

— *Case where* $j_1$ *is convex. Let* $u^*_p$ *be defined by*

$$u^*_p : [0,p_T] \ni p_t \mapsto \max\{\min\{U, F^{-1}_{\lambda,\tau}(-f/g(p_t))\}, 0\}$$

*If* $\alpha \in (0,1)$ *the optimal control* $u^*$ *reads* $u^*(t) = u^*_p(p_t)$ *for all* $t \in [t^-,t^+]$*, where* $p_t$ *denotes the unique solution in* $[0,p_T]$ *to the equation* $t = \int_0^{p_t} \frac{d\nu}{f(\nu)+u^*_p(\nu)g(\nu)}$*.*

*If* $\alpha = 1$ *then* $u^* = U\mathbb{1}_{[t^-,t^+]}$*.*

*Moreover, calling* $T^* \equiv t^+ - t^-$*:*

— *If* $p_{u^*}(T) < \theta$*, then* $t^+ = T$
— *If* $p_{u^*}(T) = \theta$*, control functions* $u^*_\xi$ *such that* $u^*_\xi(\cdot) = u^*(\cdot - \xi)$ *a.e. with* $\xi \in [-t^-, T-t^+]$ *are also solutions.*
— *If* $p_{u^*}(T) > \theta$*, then* $(t^-,t^+) = (0,T)$*, thus* $T^* = T$*.*

**Remark 1.7.** Analogously to Family 1, in the convex case, $\lambda$ and $\tau$ are equal to zero in case the constraints $\int_0^{p(T)} u^*_p(\nu)/(f(\nu) + u^*_p(\nu)g(\nu))d\nu \leqslant C$ and $T^* \leqslant T$, respectively, are not saturated. If the constraints are saturated, $\lambda$ and $\tau$ are defined implicitly by these equalities.

### 1.3.2 A first result: optimization with $T$ free but bounded and $p_T$ fixed

We begin by stating and proving an intermediate result that will be useful for proving Theorem 1.3. In this section we investigate a seemingly unrelated problem, where only the cost term is considered, the final state is fixed, and the final time is free, but bounded. With a slight abuse of notation let us introduce

$$\begin{cases} \inf\limits_{\substack{u \in \mathcal{V}_{T^*,U} \\ T^* \leqslant T}} J(T^*,u) \\ p' = f(p) + ug(p) \text{ in } (0,T^*),\ p(0) = 0\ ,\ p(T^*) = p_T, \end{cases} \tag{$\mathcal{Q}^{2,T}_{p_T,C,U}$}$$

where $J(T^*,u)$ is defined by

$$J(T^*,u) = \int_0^{T^*} j_1(u(t))dt. \tag{1.32}$$

For $\tau \in \mathbb{R}_-$, let us introduce the mapping

$$v \mapsto F_\tau(v) := \frac{vj_1'(v) - j_1(v) + \tau}{j_1'(v)}. \tag{1.33}$$

5. We exclude the case $\alpha = 0$ for simplicity. Note that in that case the answer is trivially $u^* = 0$ a.e. in $[0,T]$.

**Theorem 1.4.** *Let us assume that $p_T \in (0,1)$, that (1.2) is true, and that $j_1(\cdot)$ satisfies the assumptions of $(\mathcal{H}.1)$. Let us assume that $U > m^*(p_T)$ and that*

$$T \geqslant \int_0^{p_T} \frac{d\nu}{f(\nu) + Ug(\nu)}$$

*Then, there exists a pair $(T^*, u^*) \in [0,T] \times \mathcal{U}_{T,C,U}$ solving Problem $(\mathcal{Q}^{2,T}_{p_T,C,U})$. Moreover, let us distinguish between two cases:*

— *Case where $j_1$ is either linear or strictly concave. The optimal time and control read*

$$u^* = U\mathbb{1}_{[0,t_s]} \quad \textit{and} \quad T^* = \int_0^{p_T} \frac{d\nu}{f(\nu) + U\mathbb{1}_{(0,p_s)}g(\nu)}.$$

*Where $p_s$ is the only solution to $t_s = \int_0^{p_s} \frac{d\nu}{f(\nu)+Ug(\nu)}$. Moreover, if $p_T \leqslant \theta$ then $t_s = T^*$ and if $p_T > \theta$ then $t_s$ is such that $T^* = T$.*

— *Case where $j_1$ is convex. Let $u_p^*$ be defined by*

$$u_p^* : [0, p_T] \ni p_t \mapsto \max\{\min\{U, F_\tau^{-1}(-f/g(p_t))\}, 0\}.$$

*The optimal time $T^*$ and control $u^*$ read*

$$T^* = \int_0^{p_T} \frac{d\nu}{f(\nu) + u_p^*(\nu)g(\nu)} \quad \textit{and} \quad \forall t \in [0, T^*], \qquad u^*(t) = u_p^*(p_t)$$

*where $p_t$ denotes the unique solution in $[0, p_T]$ to the equation $t = \int_0^{p_t} \frac{d\nu}{f(\nu)+u_p^*(\nu)g(\nu)}$. Moreover, $\tau \in \mathbb{R}_-$ and if for $\tau = 0$, $T^* \leqslant T$ then $\tau = 0$, otherwise $\tau$ is implicitly determined by the equation $T^* = T$.*

### 1.3.3 Proof of Theorem 1.4

In order to prove Theorem 1.4 we will follow similar steps to the ones in Family 1. The idea behind the proof is to recast Problem $(\mathcal{Q}^{2,T}_{p_T,C,U})$ into a problem of Family 1 with an extra constraint $T^* \leqslant T$. We find the desired results by performing a similar reasoning to the one carried out in the proof of Theorem 1.2. Recall that our conclusions hold true for a larger class of functions $f$ and $g$ (See Remark 1.2).

**Step 1: recasting into a Family 1 control problem with $T^*$ bounded.**

Adapting slightly the reasoning in Lemma 1.1, we see that the result is valid for Problem $(\mathcal{Q}^{2,T}_{p_T,C,U})$. We can therefore repeat the change of variable performed in Sections 1.2.3 and 1.2.4, that is

$$t : p_t \mapsto \int_0^{p_t} \frac{d\nu}{f(\nu) + u(p^{-1}(\nu))g(\nu)} \quad \text{and} \quad u_p(p_t) := u(p^{-1}(p_t)) = u(t).$$

Let us introduce a new problem.

$$\inf_{u \in \hat{\mathcal{V}}_{p_T^*,U}} \hat{J}_p(u_p), \tag{$\hat{\mathcal{Q}}^{2,T}_{p_T,C,U}$}$$

where $\hat{J}_p(u_p) := \int_0^{p_T} \frac{j_1(u_p(\nu))}{f(\nu)+u_p(\nu)g(\nu)} d\nu$ and $\hat{\mathcal{V}}_{p_T^*,U}$ is given by

$$\hat{\mathcal{V}}_{p_T^*,U} := \left\{ u_p \in \hat{\mathcal{V}}_{p_T,U}, \int_0^{p_T} \frac{d\nu}{f(\nu) + u_p(\nu)g(\nu)} \leqslant T \right\}.$$

From this new problem we will be able to recover the solutions of $(\mathcal{Q}^{2,T}_{p_T,C,U})$ by undoing the change of variable.

Similarly to the analysis of the problems of Family 1, we should impose the restriction $f(p(t)) + u^*(t)g(p(t)) > 0$ for $t \in [0,T]$ in the control space. Once again, we will not impose it in order to simplify the derivation of the solutions. Using analogous arguments to those exposed in Section 1.2.3, one can easily check that the solutions we obtain indeed belong to the range of $\mathcal{U}_{T,C,U}$ by the change of variable used.

**Step 2: first-order optimality conditions through the Pontryagin Maximum Principle.**

In addition to the notations used so far, we introduce, abusing of the notation $t(p_t) := \int_0^{p_t} \frac{d\nu}{f(\nu)+u_p(\nu)g(\nu)}$ in order to handle the constraint $T^* \leqslant T$. Applying the PMP we find:

$$\tau \leqslant 0\ , \qquad \tau(t(p_T) - T) = 0, \quad \text{(transversality and slackness condition)}$$

with $\tau$ being a constant. The optimal control $u_p^*$ solves

$$\text{for a.e. } p_t, \quad u_p^*(p_t) \quad \in \quad \arg\max_{v\in\bar{U}} \frac{\tau + q^0 j_1(v)}{f(p_t) + vg(p_t)}. \tag{1.34}$$

We can check that, if $T > \int_0^{p_T} \frac{d\nu}{f(\nu)+Ug(\nu)}$, then $q^0 = -1$. By the PMP the pair $\left(\tau, q^0\right)$ is non-trivial. Assuming $q^0 = 0$, this implies that $\tau < 0$ and $u_p^* \equiv U\mathbb{1}_{[0,p_T]}$. Since $\tau < 0$ by the slackness condition $T^* = T$ and $T^* = \int_0^{p_T} \frac{d\nu}{f(\nu)+Ug(\nu)}$. So, without loss of generality, for the rest of the proof we consider $T > \int_0^{p_T} \frac{d\nu}{f(\nu)+Ug(\nu)}$ and $q^0 = -1$.

**Step 3: analysis of the first-order optimality conditions.**

In the same spirit as in Theorem 1.2, we introduce the switching function

$$\begin{aligned} v \mapsto \psi(v) \quad &:= \quad \frac{\partial \mathcal{H}}{\partial v}(p_t, t, \tau, v) \\ &= \quad \frac{-f(p_t)j_1'(v) - g(p_t)\left(vj_1'(v) - j_1(v) + \tau\right)}{\left(f(p_t) + vg(p_t)\right)^2}. \end{aligned}$$

The maximization condition yields

$$\begin{cases} \psi(0) \leqslant 0 \text{ on } \{u_p^* = 0\}, \\ \psi(u_p^*) = 0 \text{ on } \{0 < u_p^* < U\}, \\ \psi(U) \geqslant 0 \text{ on } \{u_p^* = U\}. \end{cases}$$

We remind that equalities and inequalities in this context must be understood up to a null Lebesgue measure set. Using the mapping $F_\tau(\cdot)$ introduced in (1.33) we can write the optimality conditions as

$$\begin{cases} F_\tau(0) \geqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = 0\}, \\ F_\tau(u_p^*) = -\frac{f(p_t)}{g(p_t)} \text{ on } \{0 < u_p^* < U\}, \\ F_\tau(U) \leqslant -\frac{f(p_t)}{g(p_t)} \text{ on } \{u_p^* = U\}. \end{cases} \tag{1.35}$$

We compute the derivative of $F_\tau$

$$F'_\tau(v) = j_1''(v)\frac{j_1(v)-\tau}{j_1'(v)^2}.$$

The sign of $F'_\tau(\cdot)$ depends exclusively on the sign of $j_1''(\cdot)$, hence we can extract similar conclusions on the behaviour of $u_p^*$ to the ones obtained in Theorem 1.2, namely, $u_p^*$ is *bang-bang* in the linear case and the three optimality conditions are mutually exclusive in the convex case. As for the concave case, we can prove that $u_p^*$ is *bang-bang* too. To do this it suffices to reproduce the computations carried out in Theorem 1.1 but with the switching function of this section. These results lead us to conclude that:

— If $j_1''(\cdot) \leqslant 0$, then $u^* = U\mathbb{1}_{[0,t_s]}$. Using Lemma 1.1 we obtain that if $p_T \leqslant \theta$, then $t_s = T^* = \int_0^{p_T} \frac{d\nu}{f(\nu)+Ug(\nu)}$, since there cannot be any switch. If $p_T > \theta$, since $\int_0^t j_1(U)ds$ is an increasing function of time, by direct comparison we find that the switching time must be as small as possible. Since $t_s = \int_0^{p_s} \frac{d\nu}{f(\nu)+Ug(\nu)}$, a smaller $t_s$ implies a smaller $p_s$. Taking into account that $T^* = \int_0^{p_T} \frac{d\nu}{f(\nu)+U\mathbb{1}_{(0,p_s)}g(\nu)}$ we conclude that minimising $t_s$ is equivalent to maximising $T^*$. Therefore $t_s$ is such that $T^* = T$.

— If $j_1''(\cdot) > 0$, the three optimality conditions are mutually exclusive and therefore necessary and sufficient. Applying $F_\tau^{-1}$ to both sides of the inequalities in (1.35) we obtain the expression in the statement for $u_p^*$.
We conclude arguing by contradiction. Let us call $T_\tau^*$ the $T^*$ obtained for a particular value of $\tau$. If $T_0^* \leqslant T$ then, for bigger values of $T$, the slackness condition implies $\tau = 0$ and therefore $T^* = T_0^*$. The only way we can have $\tau < 0$ is in case $T_0^* > T$, and in that case, using again the slackness condition we need $T_\tau^* = T$. Looking at the definition of $T_\tau^*$ and $u_p^*$, we conclude that $\tau$ must have a value such that $\int_0^{p_T} \frac{d\nu}{f(\nu)+u_p^*(\nu)g(\nu)} = T$.

### 1.3.4 Proof of Theorem 1.3

In order to prove Theorem 1.3 we will characterize an interval in which $p'_{u^*} > 0$. In this interval we will be able to adapt some of the results seen so far, specially those of Theorem 1.4. The solution outside of this interval will be null.

**Step 1: recasting into a Family 1 control problem with $T^*$ bounded.**

**Lemma 1.2.** *Let $u^* \in \mathcal{U}_{T,C,U}$ be a control solving $(\mathcal{P}^{2,\alpha}_{T,C,U})$ and let $\alpha > 0$. Let us introduce $p_{u^*}$ solving*

$$\begin{cases} p'_{u^*} = f(p_{u^*}) + u^* g(p_{u^*}) & \text{in } (0,T), \\ p_{u^*}(0) = 0. \end{cases}$$

*Then, there exists one single interval $(t^-, t^+) \subseteq (0,T)$ in which $p'_{u^*} > 0$. Moreover, outside of this interval, $u^* = 0$ and $p'_{u^*} = 0$, implying that $p_{u^*}(0) = p_{u^*}(t^-) = 0$ and $p_{u^*}(t^+) = p_{u^*}(T)$.*

*Proof.* The proof will be done by contradiction and it will follow the same lines as the one carried in Lemma 1.1. Assuming $p_{u^*}(T) > 0$ (if $p_{u^*}(T) = 0$ the solution is trivially $u^* = 0$), there necessarily exists a non-zero measure set in which $p'_{u^*} > 0$. We call $t^- = \inf\{t \in (0,T) \mid p'_{u^*}(t) > 0\}$ and $t^+ = \sup\{t \in (0,T) \mid p'_{u^*}(t) > 0\}$, therefore $\{t \in (0,T) \mid p'_{u^*}(t) > 0\} \subseteq (t^-, t^+)$. We assume that there exists an interval of non-zero measure $(t_1, t_2) \subset (t^-, t^+)$ such that $p'_{u^*} \leqslant 0$ a.e. on $(t_1, t_2)$.

We split the proof in two parts: first we assume $p_{u^*}(T) \leqslant \theta$, and we define $\tilde{u}$ as

$$\tilde{u}(t) = \begin{cases} 0 & t \in (0, t_2 - t_1) \\ u^*(t - t_2 + t_1) & t \in (t_2 - t_1, t_2), \\ u^*(t) & t \in (t_2, T). \end{cases}$$

We proceed by direct comparison between the cost of both controls, obtaining

$$\begin{aligned} J_\alpha(u^*) - J_\alpha(\tilde{u}) &= (1-\alpha)\left(\int_0^T j_1(u^*(t))dt - \int_0^T j_1(\tilde{u}(t))dt\right) + \alpha((1-p_{u^*}(T))^2 - (1-p_{\tilde{u}}(T))^2) \\ &= (1-\alpha)\int_{t_1}^{t_2} j_1(u^*(t))dt + \alpha((1-p_{u^*}(T))^2 - (1-p_{\tilde{u}}(T))^2). \end{aligned}$$

Since $p'_{\tilde{u}} = 0$ on $(0, t_2 - t_1)$ but $p'_{u^*} \leqslant 0$ in $(t_1, t_2)$ and they are equal on intervals of the same length, it follows that $p_{\tilde{u}}(T) \geqslant p_{u^*}(T)$. Therefore $J_\alpha(u^*) - J_\alpha(\tilde{u}) \geqslant 0$ which leads to a contradiction if the inequality is strict. In order to have the equality we need $p'_{u^*} = 0$ in $(t_1, t_2)$ and since we assumed $p_{u^*}(T) \leqslant \theta$ this can only happen if $p_{u^*}(t_1) = p_{u^*}(t_2) = \theta$ and $u^* = 0$ on $(t_1, t_2)$. But in this case $t_2 = T$, $t_1 = t^+$, so $(t^-, t^+) = \{t \in (0,T) \mid p'_{u^*}(t) > 0\}$ anyway.

Next, we assume $p_{u^*}(T) > \theta$, and we define $\tilde{u}$ as

$$\tilde{u}(t) = \begin{cases} u^*(t) & t \in (0, t_1) \\ u^*(t + t_2 - t_1) & t \in (t_1, T - t_2 + t_1), \\ 0 & t \in (T - t_2 + t_1, T). \end{cases} \tag{1.36}$$

Comparing the cost of both controls we obtain again $J_\alpha(u^*) > J_\alpha(\tilde{u})$, because in this case $p_{\tilde{u}}(T) > p_{u^*}(T)$ always. This yields the desired contradiction.

Since $(t^-, t^+) = \{t \in (0,T) \mid p'_{u^*}(t) > 0\}$ we have that $u^* = 0$ and $p'_{u^*} = 0$ in $(0, t^-)$ and thus $p_{u^*}(t^-) = 0$. On the other hand, we have $p_{u^*}(t^+) \geqslant p_{u^*}(T)$. But we must also have $u^* = 0$ and $p'_{u^*} = 0$ in $(t^+, T)$, otherwise at least one of the two terms in $J_\alpha(u^*)$ would be bigger, thus $p_{u^*}(t^+) = p_{u^*}(T)$. □

This lemma proves that $p_{u^*}(t)$ is a bijection from $(t^-, t^+)$ onto $(p_{u^*}(t^-), p_{u^*}(t^+))$. A straightforward exploration of its consequences already proves the last part of Theorem 1.3. Since we must have $p' = 0$ in $(0, t^-) \cup (t^+, T)$ and $p_{u^*}(t^+) = p_{u^*}(T)$ it follows that:

- If $p_{u^*} < \theta$, then $t^+ = T$, otherwise we would have $p' < 0$ in $(t^+, T)$ and $p_{u^*}(t^+) < p_{u^*}(T)$.
- If $p_{u^*} = \theta$, as long as the length of $(0, t^-) \cup (t^+, T)$ is the same, the length of each interval does not affect the functional $J_\alpha(u)$, hence the conclusion.
- If $p_{u^*}(T) > \theta$, we have $p_{u^*}(t^+) = p_{u^*}(T) > \theta$ so $t^+ = T$, otherwise we would have $p' > 0$ in $(t^+, T)$ and $p_{u^*}(t^+) > p_{u^*}(T)$. We have also that $t^- = 0$,. By contradiction we can construct a function following the same principle as in (1.36) (setting $t_1 = 0$ and $t_2 = t^-$) and prove that $u^*$ is not optimal.

Exploiting this lemma further we can repeat the change of variable of the previous theorems one more time, but only in the subinterval $(t^-, t^+)$.

Let us introduce the following problem:

$$\inf_{\substack{u \in \mathcal{U}^T_{p_T, C, U} \\ p_T \in [0,1)}} \hat{J}_{p,\alpha}(p_T, u_p), \tag{$\hat{\mathcal{P}}^{2,\alpha}_{T,C,U}$}$$

where $\hat{J}_{p,\alpha}(p_T, u_p)$ is defined by

$$\hat{J}_{p,\alpha}(p_T, u_p) = (1-\alpha)\int_0^{p_T} \frac{j_1(u_p(\nu))}{f(\nu)+u_p(\nu)g(\nu)}d\nu + \alpha(1-p_T)^2, \tag{1.37}$$

$\alpha \in (0,1]$ and $\mathcal{U}^T_{p_T,C,U}$ is given by

$$\mathcal{U}^T_{p_T,C,U} := \left\{ u_p \in \hat{\mathcal{U}}_{p_T,C,U}, \int_0^{p_T} \frac{d\nu}{f(\nu)+u_p(\nu)g(\nu)} \leqslant T \right\}.$$

We remark that thanks to the change of variable, actually $T^* = t^+ - t^- = \int_0^{p_T} \frac{d\nu}{f(\nu)+u_p(\nu)g(\nu)}$, therefore $\mathcal{U}^T_{p_T,C,U}$ can also be expressed as $\mathcal{U}^T_{p_T,C,U} := \left\{ u_p \in \hat{\mathcal{U}}_{p_T,C,U}, T^* \leqslant T \right\}$. To recover the solution of $(\mathcal{P}^{2,\alpha}_{T,C,U})$ on the interval $(t^-, t^+)$ from the solution of $(\hat{\mathcal{P}}^{2,\alpha}_{T,C,U})$, we need to undo the change of variable by setting $u(\cdot) = u_p(p(\cdot))$. Next, we need to determine $t^-$ and $t^+$ which will be done in the following steps. Finally, $u^* = 0$ in $(0, t^-)$ and in $(t^+, T)$.

Similarly to the analysis of the problems of Family 1, according to Lemma 1.2, we should impose the restriction $f(p(t)) + u^*(t)g(p(t)) > 0$ for $t \in (t^-, t^+)$ in the control space. Once again, we will not impose it in order to simplify the derivation of the solutions. Using analogous arguments to those exposed before, one can check that the solutions we obtain indeed belong to the range of $\mathcal{U}_{T,C,U}$ by the change of variable introduced in Lemma 1.2.

**Step 2: Finding $p^{max}$ (case $\alpha = 1$).**

Let us define

$$\Phi : [0,1) \ni p_T \mapsto \inf_{u_p \in \mathcal{U}^T_{p_T,C,U}} \int_0^{p_T} \frac{j_1(u_p(\nu))}{f(\nu)+u_p(\nu)g(\nu)}d\nu.$$

Thanks to Theorem 1.4 we know this problem has a solution for all $p_T \in [0,1)$ if $T$ is big enough. And therefore we can rewrite Problem $(\hat{\mathcal{P}}^{2,\alpha}_{T,C,U})$ as a minimisation problem in one variable, namely:

$$\inf_{p_T \in [0,1)} (1-\alpha)\Phi(p_T) + \alpha\left(1-p_T\right)^2.$$

Nevertheless, in Theorem 1.4, no constraint on the total number of mosquitoes used was imposed. Moreover the final time $T$ was supposed big enough for solutions to exist. In order to apply the results of Theorem 1.4 to prove Theorem 1.3 we need to establish first which values of $p_T$ are reachable for a given set of constraints. In other words, depending on $T$, $C$ and $U$, there will be values of $p_T$ such that $\mathcal{U}^T_{p_T,C,U}$ is empty. We note this maximal value $p^{max}$. Once we have characterized the set $[0, p^{max}]$, inside it we can disregard the constraint on $C$ and apply Theorem 1.4 to find the solution.

In order to find the value of $p^{max}$ we study the case $\alpha = 1$ in Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$. We recall it

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

Indeed, when $\alpha$ is set to 1 we are maximising $p_T$ for a given set of constraints $C$ and $T$ regardless of $j_1(\cdot)$. This problem, in the case $T > C/U$, is discussed and solved in [10]. There, it is proven that solutions are *bang-bang* and such that saturate the constraint $\int_0^T u^*(t)dt = C$. Combining this result with Lemma 1.2 and since we are only looking at the subinterval $(t^-, t^+)$ where $p'_{u^*} > 0$, we conclude that solutions have at most one switch from $U$ to 0, and only if $p_{u^*}(T) > \theta$. A straightforward extension of their results yields that in the more general case, where the

$T > C/U$ is not imposed, we have that if $C \leqslant C^\theta$ then $p^{max} \leqslant \theta$ and solves

$$\int_0^{p^{max}} \frac{d\nu}{f(\nu) + Ug(\nu)} = \min\left\{\frac{C}{U}, T\right\}.$$

Instead if $C > C^\theta$, then $p^{max} > \theta$ and solves

$$\int_0^{p^{max}} \frac{d\nu}{f(\nu) + U\mathbb{1}_{(0,\bar{p})}g(\nu)} = T$$

where $\bar{p}$ is such that $\int_0^{\bar{p}} \frac{d\nu}{f(\nu)+Ug(\nu)} = \min\{C/U, T\}$.

**Step 3: Finding $p_T^*$**

Thanks to the previous step we can finally write the expression we want to minimize, that is

$$\inf_{p_T \in [0, p_T^{max}]} (1-\alpha)\Phi(p_T) + \alpha\left(1 - p_T\right)^2.$$

Now, for all $p_T \in [0, p^{max}]$ we know that $\Phi(p_T)$ is well defined and that $u_p^*$ solving Problem $(\hat{\mathcal{Q}}^{2,T}_{p_T,C,U})$ for a given $p_T^*$ solving this minimization problem, will solve Problem $(\hat{\mathcal{P}}^{2,\alpha}_{T,C,U})$ too.

We write the optimality conditions

$$\begin{cases} (1-\alpha)K\frac{j_1(u_p^*(0))}{u_p^*(0)} - 2\alpha \geqslant 0 \quad \text{if} \quad p_T^* = 0 \\ (1-\alpha)\frac{j_1(u_p^*(p_T^*))}{f(p_T^*)+u_p^*(p_T^*)g(p_T^*)} - 2\alpha(1-p_T^*) = 0 \quad \text{if} \quad 0 < p_T^* < p^{max}, \\ (1-\alpha)\frac{j_1(u_p^*(p^{max}))}{f(p^{max})+u_p^*(p^{max})g(p^{max})} - 2\alpha(1-p^{max}) \leqslant 0 \quad \text{if} \quad p_T^* = p^{max}. \end{cases} \tag{1.38}$$

In the convex case, these necessary conditions are not enough to give an explicit answer in a general setting. The first condition not even being well defined since $u_p^*(0)$ can be arbitrarily close to 0. Nevertheless, we focus here in the concave and linear case where these conditions can be further exploited.

If $j_1''(\cdot) \leqslant 0$, using Theorem 1.4 we have $u^* = U\mathbb{1}_{[0,t_s]}$. The switching point happening only if $p_{u^*}(T) > \theta$. In case there is a switch, $u^*(p_T) = 0$ and therefore the only optimality condition that can be satisfied is $-2\alpha(1-p^{max}) \leqslant 0$. Therefore $p_T^* = p^{max}$ and $u_p^* = U\mathbb{1}_{[0,\bar{p}]}$.

In case $u^*(p_T^*) = U$, we can rewrite the optimality conditions (1.38) as

$$\begin{cases} (1-\alpha)K\frac{j_1(U)}{U} - 2\alpha \geqslant 0 \quad \text{if} \quad p_T^* = 0 \\ (1-\alpha)\frac{j_1(U)}{f(p_T^*)+Ug(p_T^*)} - 2\alpha(1-p_T^*) = 0 \quad \text{if} \quad 0 < p_T^* < p^{max}, \\ (1-\alpha)\frac{j_1(U)}{f(p^{max})+Ug(p^{max})} - 2\alpha(1-p^{max}) \leqslant 0 \quad \text{if} \quad p_T^* = p^{max}. \end{cases} \tag{1.39}$$

Assuming $U > U^*$, the three conditions are mutually exclusive. Let us show it by computing the derivative of the condition with respect to $p_T$ and showing that it is strictly increasing

$$-(1-\alpha)\frac{j_1(U)}{(f(p_T)+Ug(p_T))^2}\left(f'(p_T)+Ug'(p_T)\right) + 2\alpha > 0,$$

which is equivalent to

$$f'(p_T) + Ug'(p_T) < \frac{2\alpha}{1-\alpha}\frac{(f(p_T)+Ug(p_T))^2}{j_1(U)}.$$

This inequality needs to be satisfied for all $\alpha$, and the right hand side is non-negative and increasing in $\alpha$, therefore we want to ensure $f'(p_T) + Ug'(p_T) < 0$. This is true for all $p_T$ if and only if $U > \max_{p_T\in[0,1]}\left(-\frac{f'(p_T)}{g'(p_T)}\right) := U^*$ [6]. We can distinguish three cases

— If $\alpha \leqslant \alpha^0$ then $p_T^* = 0$. Therefore $u^* = 0$ for all $t \in [0, T^*]$.

— If $\alpha^0 < \alpha < \alpha^{max}$ then $0 < p_T^* < p^{max}$ and it is the only solution of the equation $(1-p_T^*)(f(p_T^*)+Ug(p_T^*)) = \frac{1-\alpha}{2\alpha}j_1(U)$. If $p_T^* \leqslant \theta$ there will not be any switch. If $p_T^* > \theta$, then since the final state is fixed and $\int_0^t j_1(U)ds$ is an increasing function of time, the switching point will be the smallest possible such that $p_{u^*}(T) = p_T^*$, this is $u_p^* = U\mathbb{1}_{[0,p_s]}$ with $p_s$ solving $T^* = \int_0^{p_T^*}\frac{d\nu}{f(\nu)+U\mathbb{1}_{(0,p_s)}g(\nu)} = T$.

— If $\alpha \geqslant \alpha^{max}$ then $p_T^* = p^{max}$. Therefore $u_p^* = U\mathbb{1}_{[0,\bar{p}]}$. In other words, the switch is only possible if the constraint on the total amount of mosquitoes is saturated.

6. This requirement is not much stronger than the minimum required for the existence of solutions, $U > m^*(p_T)$. For instance, with the parameters considered in Table 1.1 we obtain $m^*(1) \approx 0.0033$ and $U^* \approx 0.077$. On the other hand, the value of $U$ in this table has been fixed to be $U = 10$.

Chapter 2

# Optimal initial time strategies for mosquito population replacement: influence of the carrying capacity on spatial releases

This chapter is the subject of a work in progress in collaboration with L. Almeida, G. Peltier, Y. Privat and N. Vauchelet.

## 2.1 Introduction

In this chapter we explore how an inhomogeneous carrying capacity can influence an instantaneous release of mosquitoes at initial time in the context of the population replacement technique using *Wolbachia*. Previous works having studied population replacement in a similar framework in which space is considered can be found in [46, 134, 98, 11]. In contrast to these works, in this chapter we will not consider diffusion at first. Although mosquitoes do not travel a lot during their lifetimes, diffusion should be considered in any realistic model. Since diffusion adds a lot of complexity to the problem, as a first step towards this ultimate goal, we start by studying a toy model without it. The diffusive case is later explored, only numerically. Despite the lack of realism, this case is nevertheless interesting from a mathematical perspective. This chapter being a work in progress, the case with diffusion will be further developed in the future.

Let us consider the two-species model

$$\begin{cases} \partial_t M = b_M M \left(1 - \dfrac{M+W}{K(x)}\right)\left(1 - s_h \dfrac{W}{M+W}\right) - d_M M, \\ \partial_t W = b_W W \left(1 - \dfrac{M+W}{K(x)}\right) - d_W W, \quad t \in [0,T], \quad x \in \Omega \end{cases} \tag{2.1}$$

where $M = M(t,x)$ represents the density of *Wolbachia*-free mosquitoes and $W = W(t,x)$ the density of *Wolbachia*-infected mosquitoes. The birth rate of both species is denoted $b_i$, $i = M, W$, and the death rate $d_i$, $i = M, W$. The birth rate in mosquitoes is considerably higher

than its death rate, therefore these parameters have the constraint $d_i \leqslant b_i$. Also, due to the way *Wolbachia* affects the biology of the mosquito we can assume that s $b_W \leqslant b_M$ and $d_M \leqslant d_W$. The parameter $s_h$ measures the cytoplasmic incompatibility, $0 \leqslant s_h \leqslant 1$, when $s_h = 1$ the cytoplasmic incompatibility is perfect, when $s_h = 0$ there is no cytoplasmic incompatibility. We assume that, at $t = 0$, there are no *Wolbachia*-infected mosquitoes in the system and that the wild mosquitoes are at equilibrium, that is $W(0, x) = 0$ and $M(0, x) = K(x)\left(1 - \frac{d_M}{b_M}\right)$. In (2.1), $\Omega$ is a given bounded domain of $\mathbb{R}$ or $\mathbb{R}^2$ and $T > 0$ is the time horizon of the problem.

Let $u$ denote a function accounting for the rate at which *Wolbachia*-infected mosquitoes are released in the domain. The addition of this function only modifies the equation on the *Wolbachia*-infected mosquitoes. It does it in the following way

$$\partial_t W = b_W W\left(1 - \frac{M + W}{K(x)}\right) - d_W W + u(t, x), \quad t \in [0, T], \quad x \in \Omega.$$

The goal we pursue is to find an optimal release function, $u$, such that at a given final time $T$ the solution $(M, W)$ to (2.1) is as close as possible of the *Wolbachia* invasion steady state denoted $(0, W^*) = \left(0, K(x)\left(1 - \frac{d_W}{b_W}\right)\right)$. Choosing a least square distance, this leads us to introduce the following cost functional

$$J(u) = \frac{1}{2}\int_\Omega \left(M(T, x)^2 + [(W^* - W(T, x))_+]^2\right) dx. \tag{2.2}$$

We consider some natural constraints on the number of available mosquitoes to realize the experiments and also on the rate at which this mosquitoes can be released. The set of admissible controls is therefore given by

$$\mathcal{U}_{T,C,U} = \left\{ u \in L^\infty([0, T] \times \Omega), \quad 0 \leqslant u \leqslant U \text{ a.e. }, \int_0^T \int_\Omega u(t, x)\, dtdx \leqslant C \right\}. \tag{2.3}$$

With the tools presented so far we can state the optimal control problem we deal with, namely:

$$\inf_{u \in \mathcal{U}_{T,C,U}} J(u), \tag{2.4}$$

where $J$ is defined by (2.2) and $\mathcal{U}_{T,C,U}$ is defined by (2.3).

It has been proved in [134] and [10, Proposition 2.2] that when the fecundity rates are large, that is, if we assume that $b_M = \frac{b_M^0}{\epsilon}$ and $b_W = \frac{b_W^0}{\epsilon}$ and we let $\epsilon \to 0$, then system (2.1) may be reduced to the problem

$$\begin{cases} \partial_t p(t, x) = f(p(t, x)) + \dfrac{u(t, x)}{K(x)} g(p(t, x)), \quad t > 0, \\ p(0, x) = 0, \quad x \in \Omega, \end{cases} \tag{2.5}$$

where

$$f(p) = b_M^0 d_W s_h \frac{p(1 - p)(p - \theta)}{b_M^0(1 - p)(1 - s_h p) + b_W^0 p} \quad \text{and} \quad g(p) = \frac{b_M^0(1 - p)(1 - s_h p)}{b_M^0(1 - p)(1 - s_h p) + b_W^0 p}, \tag{2.6}$$

with

$$\theta = \frac{1}{s_h}\left(1 - \frac{d_M b_W^0}{d_W b_M^0}\right), \tag{2.7}$$

which is strictly comprised between 0 and 1 under the condition $1 - s_h < \frac{d_M b_W^0}{d_W b_M^0} < 1$, which will be assumed from now on. Moreover, the cost functional $J$ reduced to

$$J^0(u) = \int_\Omega K(x)^2 (1 - p(T,x))^2 \, dx, \tag{2.8}$$

as well as an asymptotic version of Problem (2.4) reading

$$\boxed{\inf_{u \in \mathcal{U}_{T,C,U}} \int_\Omega K(x)^2 (1 - p(T,x))^2 \, dx,} \tag{2.9}$$

where $p$ solves (2.5) and $\mathcal{U}_{T,C,U}$ is defined by (2.3). This model reduction allows us to study the problem in simpler terms, knowing that solutions of the simplified problem (2.9) will be asymptotically close to solutions of problem (2.4) in the sense of the Gamma-convergence (see [46, 134] for details).

The case without considering a spatial variable has been studied in detail in [10]. Then the aim of this chapter is to extend the former analysis to the case when the space is considered by adding a global constraint on the whole domain and when the carrying capacity varies on it, which is indeed the case in a natural environment.

## 2.2 The case of a single initial release

### 2.2.1 Simplified optimal control problem

Despite the model reduction performed, problem (2.9) is still a very challenging one. To facilitate the study of this problem we will restrain ourselves to a simplified setting. We assume that the time repartition of the release is given by $u(t,x) = u_0(x)\delta_0(t)$. In other words, we consider that there is one single release, done at the initial time and that the time it takes to do the release is negligible in comparison with the time window considered.

Following the reasoning developed in [46], one can prove that equation (2.5) simplifies into

$$\begin{cases} \partial_t p(t,x) = f(p(t,x)), \quad t \in [0,T], \quad x \in \Omega \\ p(0^+,x) = G^{-1}\left(\frac{u_0(x)}{K(x)}\right), \end{cases} \tag{2.10}$$

where the function $G$ is defined as the primitive vanishing at zero of the inverse of $g$,

$$G(p) = \int_0^p \frac{d\nu}{g(\nu)}.$$

In this simplified setting we are looking for solutions to the optimal control problem

$$\min_{u_0 \in \mathcal{U}_{0,C,U}} \int_\Omega K(x)^2 (1 - p(T,x))^2 \, dx, \tag{$\mathcal{P}_{u_0}$}$$

with the space of admissible controls being

$$\mathcal{U}_{0,C,U} = \left\{ u_0 \in L^\infty(\Omega), \quad 0 \leqslant u_0 \leqslant U \text{ a.e.}, \quad \int_\Omega u_0(x) \, dx \leqslant C \right\}. \tag{2.11}$$

Looking at (2.10) we see there is a one-to-one relation between the release carried at the initial time $u_0(x)$ and the initial data of the equation on the proportion of *Wolbachia*-infected mosquitoes. We can reformulate problem $(\mathcal{P}_{u_0})$ in terms of this initial proportion by defining $p_0(x) := G^{-1}\left(\frac{u_0(x)}{K(x)}\right) = p(0^+, x)$ and considering it the new control variable of the problem. We find that Problem $(\mathcal{P}_{u_0})$ is equivalent to the following optimal control problem

$$\boxed{\min_{p_0 \in \mathcal{P}_{0,C,U}} \int_\Omega K(x)^2 (1 - p(T,x))^2 \, dx} \qquad (\mathcal{P}_{p_0})$$

where $p_0$ is the initial data of the differential equation in (2.10) and the space of admissible controls is

$$\boxed{\mathcal{P}_{0,C,U} = \left\{ p_0 \in L^\infty(\Omega), \quad 0 \leqslant p_0 \leqslant G^{-1}\left(\frac{U}{K(x)}\right) \text{ a.e.}, \quad \int_\Omega K(x) G(p_0(x)) \, dx \leqslant C \right\}.} \qquad (2.12)$$

Since $g$ is decreasing, we have that $G$ is convex. However, unless some restrictive assumptions on $f$, the cost functional is not convex, but clearly continuous.

Before analysing the problem in depth, we can obtain easily the following lemmas that will be useful later for the characterization of the solutions. First, we observe that the constraint of the problem is saturated :

**Lemma 2.1.** *If $u_0^* = K(x)G(p_0^*)$ is an optimal solution then $\int_\Omega u_0^*(x) \, dx = C$, or equivalently $\int_\Omega K(x) G(p_0^*(x)) \, dx = C$.*

*Proof.* This is a trivial consequence of the fact that, on the one hand, $G$ is increasing therefore so is $G^{-1}$, on the other hand, the solutions of (2.10) are ordered, that is if $p_1(0^+, x) \leqslant p_2(0^+, x)$ then $p_1(\cdot, x) \leqslant p_2(\cdot, x)$. □

Using also the monotony of the solutions to (2.10) with respect to their initial data, we have :

**Lemma 2.2.** *If $U|\Omega| \leqslant C$, the optimal solution is given by $u_0^* = U$ or equivalently $p_0^* = p_U := G^{-1}(\frac{U}{K})$.*

Hence, from now on, we will always assume that $U|\Omega| > C$.

**Remark 2.1.** We recall that, despite the results are presented for problem $(\mathcal{P}_{p_0})$, since $G$ is continuous and strictly increasing, we can compute solutions to problem $(\mathcal{P}_{u_0})$ using the simple one-to-one relation

$$u_0^*(x) := K(x) G(p_0^*(x)).$$

### 2.2.2 Optimality conditions

#### First order optimality condition

Let us introduce the Lagrangian

$$\mathcal{L}(p_0) = \frac{1}{2} \int_\Omega K(x)^2 (1 - p(T,x))^2 \, dx + \lambda \left( \int_\Omega K(x) G(p_0) \, dx - C \right),$$

for some $\lambda \in \mathbb{R}^+$. To compute its derivative, we introduce the linearized system

$$\partial_t \delta p = f'(p)\delta p, \qquad \delta p(0^+, x) = h, \tag{2.13}$$

and the adjoint state

$$-\partial_t q = f'(p)q, \qquad q(T,x) = -K(x)^2(1-p(T,x)) < 0. \tag{2.14}$$

In particular, from (2.13) we deduce

$$\frac{\partial p(T,x)}{\partial p_0(x)} = \exp\left(\int_0^T f'(p(s,x))ds\right). \tag{2.15}$$

Then, to verify the first order optimality condition, we compute

$$d\mathcal{L}(p_0)\cdot h = -\int_\Omega K(x)^2(1-p(T,x))\delta p(T,x)\,dx + \lambda\left(\int_\Omega K(x)G'(p_0)h\,dx\right).$$

Using (2.13) and (2.14), we deduce

$$0 = \int_0^T \int_\Omega \partial_t(\delta p q)\,dxdt = \int_\Omega \delta p(T,x)q(T,x)\,dx - \int_\Omega hq(0,x)\,dx.$$

Therefore,

$$d\mathcal{L}(p_0)\cdot h = \int_\Omega h\left(q(0,x) + \lambda K(x)G'(p_0)\right)\,dx = \int_\Omega \frac{K(x)}{g(p_0)}h\left(\frac{1}{K(x)}g(p_0)q(0,x) + \lambda\right)\,dx, \tag{2.16}$$

where we have used the fact that $G' = \frac{1}{g}$. It leads us to introduce the switch function

$$\omega_{x,T}(p_0) = \frac{1}{K(x)}g(p_0(x))q(0,x). \tag{2.17}$$

We may have a more explicit expression of the switch function. Indeed, solving (2.14) we get

$$q(0,x) = -K(x)^2(1-p(T,x))\exp\left(\int_0^T f'(p(s,x))\,ds\right).$$

Injecting into (2.17), we obtain

$$\boxed{\omega_{x,T}(p_0) := -K(x)g(p_0(x))(1-p(T,x))\exp\left(\int_0^T f'(p(s,x))\,ds\right) < 0.} \tag{2.18}$$

Note that function $\omega_{x,T}$ only depends on $x$ through $K(x)$ and the initial condition $p_0(x)$, therefore, when looked as a function of the initial condition, the only dependency of $p_0 \mapsto \omega_{x,T}$ on $x$ is through $K(x)$. It will be useful in the following to work with a different switch function that will allow us to simplify the exposition by rendering the switching function independent of $x$.

This will simplify the characterization of the solutions in Theorems 2.1 and 2.2. We introduce

$$w_T(p_0) := \frac{\omega_{x,T}(p_0)}{K(x)} = -g(p_0(x))(1-p(T,x))\exp\left(\int_0^T f'(p(s,x))\,ds\right) < 0. \tag{2.19}$$

We may also compute some particular values of the switch function :
— In $\{p_0 = 0\}$, i.e. on the set $\{u_0 = 0\}$, we have $p(t,x) = 0$ for all $t \geqslant 0$ and we get $w_0 = -g(0)\exp(Tf'(0))$.
— In $\{p_0 = \theta\}$, $p(t.x) = \theta$ for all $t \geqslant 0$, and $w_\theta = -g(\theta)(1-\theta)\exp(Tf'(\theta))$.
The following result is a classical consequence of the Pontryagin Maximum Principle (PMP):

**Lemma 2.3.** *Let the switch function $w_T$ be as in* (2.19)*. There exists $\lambda^* \geqslant 0$ such that the optimal solution $u_0^*$ verifies :*
— *on $\{u_0^* = U\} = \left\{p_0^* = p_U := G^{-1}\left(\frac{U}{K(x)}\right)\right\}$, we have $w_T \leqslant -\frac{\lambda^*}{K(x)}$,*
— *on $\{u_0^* = 0\} = \{p_0^* = 0\}$, $w_T \geqslant -\frac{\lambda^*}{K(x)}$,*
— *on $\{0 < u_0^* < U\} = \{0 < p_0^* < p_U\}$, $w_T = -\frac{\lambda^*}{K(x)}$.*

**Second order optimality condition**

We compute the second order derivative of the Lagrangian. We have from (2.16)–(2.17),

$$d\mathcal{L}(p_0)\cdot h = \int_\Omega \frac{K(x)^2}{g(p_0)} h\left(w_T + \frac{\lambda}{K(x)}\right) dx.$$

Then,

$$d^2\mathcal{L}(p_0)\cdot h\cdot h = \int_\Omega \frac{K(x)^2 g'(p_0)}{g(p_0)^2} h^2\left(w_T + \frac{\lambda}{K(x)}\right) dx + \int_\Omega \frac{K(x)^2}{g(p_0)} h^2 \frac{\partial w_T}{\partial p_0}\, dx.$$

A first consequence of the computation is that on the set $\{0 < u_0^* < U\} = \{0 < p_0^* < p_U\}$, we have by Lemma 2.3 that

$$d^2\mathcal{L}(p_0)\cdot h\cdot h = \int_\Omega \frac{K(x)^2}{g(p_0)} h^2 \frac{\partial w_T}{\partial p_0}\, dx.$$

At the minimum it must hold that for every $h$, we have $d^2\mathcal{L}(p_0)\cdot h\cdot h \geqslant 0$. Then we have obtained :

**Lemma 2.4.** *On the set $\{0 < u_0^* < U\} = \{0 < p_0^* < p_U\}$, each minimum should verify the condition*

$$\frac{\partial w_T}{\partial p_0} \geqslant 0.$$

### 2.2.3 Study of the switch function

We devote this section to the study of the switch function $w = w_T(p_0)$ defined in (2.19). This function depends on $T$ and the initial condition $p_0(x)$. Nevertheless, in this section, we are only interested in its behaviour as a function of the initial condition. Therefore, in what follows, we fix a $x \in \Omega$ and we consider $T$ as a parameter. To ease the lecture, we simply write $w(p_0)$. We thus

write $w(p_0) = -g(p_0)(1-p(T))\exp\left(\int_0^T f'(p(s))\,ds\right)$. We present a Lemma on the monotonicity of $w$ that will play a crucial role in the characterization of the solutions of problem $(\mathcal{P}_{p_0})$.

Before stating the Lemma, we require some additional preliminaries and notations. Since we assumed $b_2^0 \leqslant b_1^0$ and $d_1 \leqslant d_2$, one can prove (see Appendix B.1) that $f''$ admits a unique zero $\theta_2$ in $(0,1)$. Additionally, for any $p \in [0,1]$, we have $f''(p) > 0$ if and only if $p < \theta_2$. Setting $\bar{\theta} := \max(\theta, \theta_2)$, we now introduce the following function

$$p_0 \mapsto A(p_0) := \frac{g'(p_0)}{g(p_0)} - \frac{1}{1-p(T)} e^{\int_0^T f'(p(s))ds} + \int_0^T f''(p(s)) e^{\int_0^s f'(p(\sigma))d\sigma} ds. \tag{2.20}$$

and the following hypothesis on it

$$\text{Function } p_0 \mapsto A(p_0) \text{ changes sign at most once in } (0, \bar{\theta}). \tag{$\mathcal{H}$.2}$$

We investigate for which parameters $(\mathcal{H}.2)$ is true in Appendix B.1.

**Lemma 2.5.** *Assume $(\mathcal{H}.2)$ holds. There exists $T_0 > 0$ such that, if $T \leqslant T_0$, then $\frac{\partial w}{\partial p_0}(p_0) > 0$ for any $p_0 \in (0,1)$. Meanwhile, if $T > T_0$, there exists one single $p_0^T \in (0, \bar{\theta})$ such that*

$$\frac{\partial w}{\partial p_0}(p_0) < 0, \quad \forall p_0 \in (0, p_0^T) \quad \text{and} \quad \frac{\partial w}{\partial p_0}(p_0) > 0, \quad \forall p_0 \in (p_0^T, 1). \tag{2.21}$$

Let us notice that we have an explicit expression of $T_0$ which is given in (2.23) in the proof below.

*Proof.* We first look at the sign of $\frac{\partial w}{\partial p_0}$ at $p_0 = 0$ to derive the value of $T_0$.

**Sign of $\frac{\partial w}{\partial p_0}$ at $p_0 = 0$.** Recalling (2.15), calculations yield

$$\begin{aligned}\frac{\partial w}{\partial p_0} =& -g'(p_0)(1-p(T))e^{\int_0^T f'(p(s))ds)} + g(p_0)e^{2\int_0^T f'(p(s))ds} \\ & - g(p_0)(1-p(T))e^{\int_0^T f'(p(s))ds} \int_0^T f''(p(s))e^{\int_0^s f'(p(\sigma))d\sigma} ds,\end{aligned} \tag{2.22}$$

As a result, there holds

$$\begin{aligned}\left.\frac{\partial w}{\partial p_0}\right|_{p_0=0} =& -g'(0)e^{Tf'(0)} + g(0)e^{2Tf'(0)} - g(0)e^{Tf'(0)} \int_0^T f''(p(s)))e^{sf'(0)} ds\Big] \\ =& -e^{Tf'(0)}\Big[g'(0) - g(0)e^{Tf'(0)} + g(0)\frac{f''(0)}{f'(0)}\left(e^{Tf'(0)} - 1\right)\Big].\end{aligned}$$

Let us recall that $g(0) > 0 > g'(0)$ and $f'(0) < 0 < f''(0)$. From the above expression we deduce that

$$\begin{aligned}
&\left.\frac{\partial w}{\partial p_0}\right|_{p_0=0} \geqslant 0 \\
\Leftrightarrow\ & g'(0) - g(0)e^{Tf'(0)} + g(0)\frac{f''(0)}{f'(0)}\left(e^{Tf'(0)} - 1\right) \leqslant 0 \\
\Leftrightarrow\ & e^{Tf'(0)}g(0)\left(\frac{f''(0)}{f'(0)} - 1\right) \leqslant g(0)\frac{f''(0)}{f'(0)} - g'(0) \\
\Leftrightarrow\ & e^{Tf'(0)} \geqslant \frac{f''(0)g(0) - f'(0)g'(0)}{g(0)\left(f''(0) - f'(0)\right)} \\
\Leftrightarrow\ & T \leqslant \frac{1}{f'(0)} \ln\left(\frac{f''(0)g(0) - f'(0)g'(0)}{g(0)\left(f''(0) - f'(0)\right)}\right) =: T_0.
\end{aligned} \tag{2.23}$$

One can check that the value of $T_0$ is always well defined and positive. Indeed, the argument of the logarithm is positive since

$$f''(0)g(0) - f'(0)g'(0) = \frac{b_W}{b_M^2}(2d_M b_M s_h + d_W b_M - b_W d_M) > \frac{b_W}{b_M^2} 2d_M b_M s_h > 0.$$

On the other hand, the argument of the logarithm is also smaller than one, since $g(0) = 1$ and $f''(0) - f'(0)g'(0) < f''(0) - f'(0)$. Consequently, if $T > T_0$, then $\frac{\partial w}{\partial p_0} < 0$ in a neighborhood of $p_0 = 0$.

Note that we can rewrite expression (2.22) using $A(p_0)$ as defined in equation (2.20),

$$\begin{aligned}
\frac{\partial w}{\partial p_0} =& - g(p_0)(1 - p(T))e^{\int_0^T f'(p(s))ds)}\left[\frac{g'(p_0)}{g(p_0)}\right. \\
&\left. - \frac{1}{1 - p(T)}e^{\int_0^T f'(p(s))ds} + \int_0^T f''(p(s))e^{\int_0^s f'(p(\sigma))d\sigma} ds\right] \\
=& \ w(p_0)A(p_0),
\end{aligned} \tag{2.24}$$

Recall that $w(p_0) < 0$ and therefore $\frac{\partial w}{\partial p_0}$ changes signs as many times, and in the same points, as $A(p_0)$.

Fix $T > 0$ and set $\bar{\theta} := \max(\theta, \theta_2) \in (0, 1)$. Let us prove $\frac{\partial w}{\partial p_0} > 0$ for all $p_0 \in (\bar{\theta}, 1)$. From (2.24) and (2.19), it is enough to prove that $A = A(p_0)$ defined by (2.20) is negative on $(\bar{\theta}, 1)$. The first two terms of (2.20) are strictly negative for all $p_0 \in (0, 1)$. Therefore it is sufficient to prove that

$$\text{If } p_0 \in (\bar{\theta}, 1), \qquad f''(p(t)) \leqslant 0 \text{ for all } t \in (0, T).$$

Let us recall that $\theta_2$ is the unique zero of $f''$ in $(0, 1)$, and that $f'' < 0$ in $(\theta_2, 1)$ (see Proposition B.1). Let $p_0 > \bar{\theta}$. Then, since $p_0 > \theta$, one can readily check that $t \mapsto p(t)$ is nondecreasing. Therefore $p(t) \geqslant p_0 > \theta_2$, so that $f''(p(t)) \leqslant 0$ for all $t$. Thus $\frac{\partial w}{\partial p_0} > 0$ on $(\bar{\theta}, 1)$.

**Conclusion.** In conclusion, if $T \leqslant T_0$, we proved that $\frac{\partial w}{\partial p_0}\big|_{p_0=0} \geqslant 0$ and so is $\frac{\partial w}{\partial p_0}$ for all $p_0 \in (\bar{\theta}, 1)$. By Hypothesis $(\mathcal{H}.2)$, $\frac{\partial w}{\partial p_0}$ changes sign at most once, by contradiction $\frac{\partial w}{\partial p_0}$ cannot change sign in $(0, \bar{\theta})$, and thus $\frac{\partial w}{\partial p_0} \geqslant 0$ for all $p_0 \in (0, 1)$. On the other hand, if $T > T_0$,

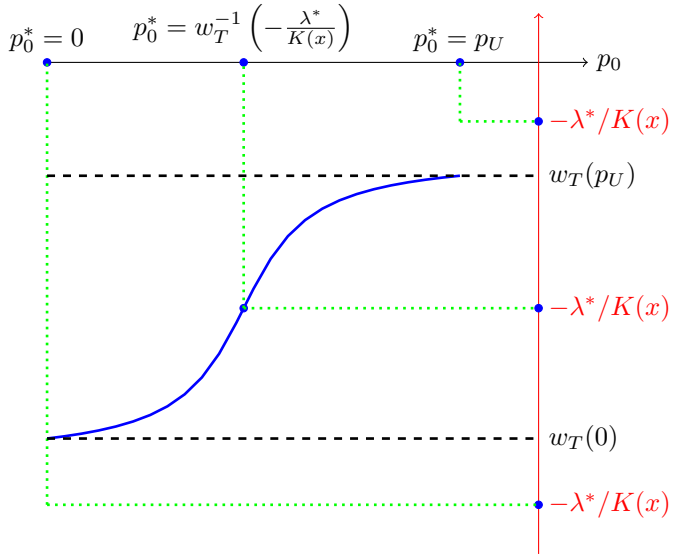


Figure 2.1 – Typical shape of $p_0 \mapsto w_T(p_0)$, in the case $T \leqslant T_0$.

$\frac{\partial w}{\partial p_0}\big|_{p_0=0} < 0$ and $\frac{\partial w}{\partial p_0} > 0$ for all $p_0 > \bar{\theta}$. Therefore $w$ has at least one minimum. Again, by Hypothesis $(\mathcal{H}.2)$, $\frac{\partial w}{\partial p_0}$ changes sign at most once, and thus the minimum, that we note $p_0^T$, must be unique. (2.21) follows straightforwardly.

□

### 2.2.4 The case $T \leqslant T_0$

We place ourselves first in the case $T \leqslant T_0$. Let us introduce the following mappings defined on $\mathbb{R}^+$

$$\Lambda \mapsto \psi_{x,T}(\Lambda) := \begin{cases} 0 & \text{if } -\Lambda \leqslant w_T(0), \\ p_U(x) := G^{-1}\left(\frac{U}{K(x)}\right) & \text{if } -\Lambda \geqslant w_T(p_U(x)), \\ w_T^{-1}(-\Lambda) & \text{if } -\Lambda \in (w_T(0), w_T(p_U(x)))\,. \end{cases} \tag{2.25}$$

and

$$\lambda \mapsto I(\lambda) := \int_\Omega K(x) G\left(\psi_{x,T}\left(\frac{\lambda}{K(x)}\right)\right) dx, \tag{2.26}$$

**Theorem 2.1.** *Assume $T \leqslant T_0$ and $0 < C < U|\Omega|$. Then there exists a unique $p_0^* \in \mathcal{P}_{0,C,U}$, that solves problem $(\mathcal{P}_{p_0})$. It is given by*

$$p_0^*(x) = \psi_{x,T}\left(\frac{\lambda^*}{K(x)}\right) \quad \textit{for any } \lambda^* \textit{such that } \; I(\lambda^*) = C.$$

*Proof.* Fix any $x \in \Omega$ and denote

$$w(p_0) := w_T(p_0(x)), \qquad p_U = p_U(x) := G^{-1}\left(\frac{U}{K(x)}\right) > 0.$$

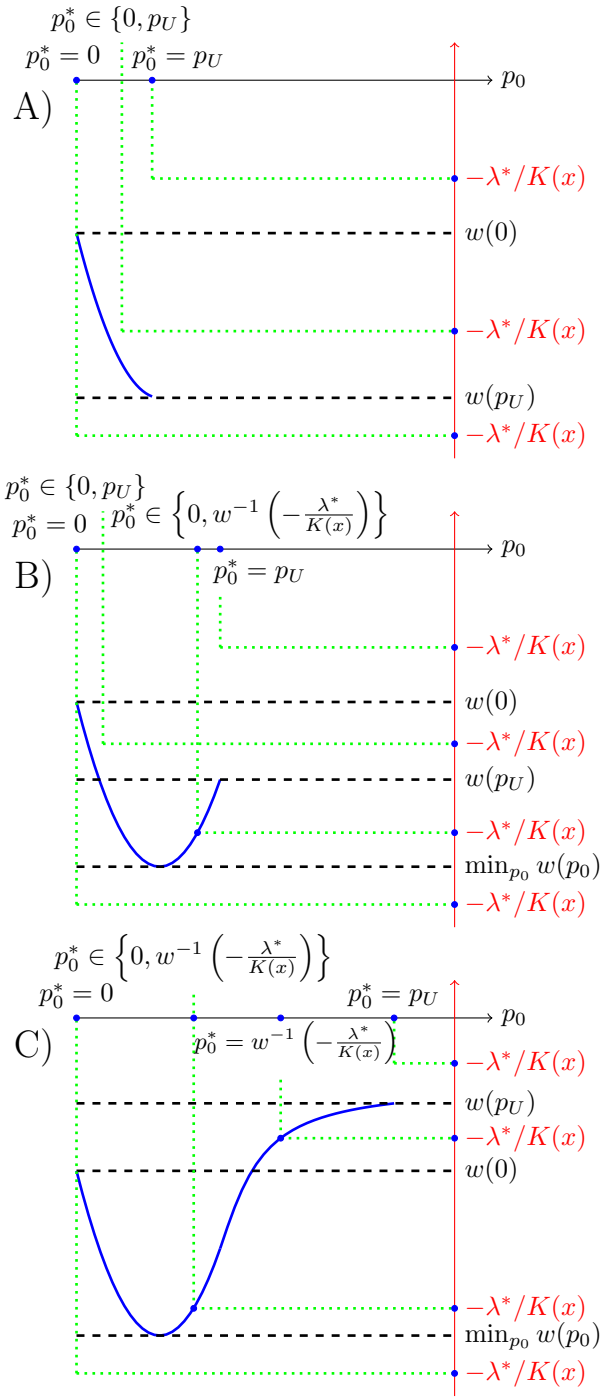


Figure 2.2 – Schematic representation of $w$, as a function of $p_0$ in case $T > T_0$. As $p_U$ increases (from top to bottom) the three diagrams, that we call A, B and C, show the three possible relative positions of $w(0)$, $w(p_U)$ and $\min_{p_0} w$.

Let $\lambda^* \geqslant 0$ be any value given by Lemma 2.3 and assume $p_0^* = p_0^*(x)$ is any optimal control solving problem $(\mathcal{P}_{p_0})$. The optimality conditions given by Lemma 2.3 can be rewritten as:

— If $p_0^* = 0$ then $w(0) \geqslant -\frac{\lambda^*}{K(x)}$.
— If $p_0^* = p_U$ then $w(p_U) \leqslant -\frac{\lambda^*}{K(x)}$.
— If $0 < p_0^* < p_U$ then $w(p_0^*) = -\frac{\lambda^*}{K(x)}$.

Fix now $T \leqslant T_0$. The above allows to compute the value $p_0^* = p_0^*(x)$ as follows. First, we look at the function $p_0 \to w(p_0)$ for $0 \leqslant p_0 \leqslant p_U$. Since $w$ is increasing, we have $w(0) \leqslant w(p_0) \leqslant w(p_U) < 0$ with $w(0) < w(p_U)$. Now, depending on the value $\lambda^*$, we distinguish three cases:

— If $-\frac{\lambda^*}{K(x)} \leqslant w(0)$, then necessarily $p_0^* = 0$.
— If $-\frac{\lambda^*}{K(x)} \geqslant w(p_U)$, then necessarily $p_0^* = p_U$.
— If $-\frac{\lambda^*}{K(x)} \in (w(0), w(p_U))$, then necessarily $p_0^* = w^{-1}\left(-\frac{\lambda^*}{K(x)}\right)$.

In other words, for any given $T \leqslant T_0$ and $x \in \Omega$ we have

$$p_0^*(x) = \psi_{x,T}\left(\frac{\lambda^*}{K(x)}\right) = \begin{cases} 0 & \text{if } -\frac{\lambda^*}{K(x)} \leqslant w_T(0), \\ p_U(x) & \text{if } -\frac{\lambda^*}{K(x)} \geqslant w_T(p_U(x)), \\ w_T^{-1}\left(-\frac{\lambda^*}{K(x)}\right) & \text{if } -\frac{\lambda^*}{K(x)} \in (w_T(0), w_T(p_U(x))). \end{cases} \tag{2.27}$$

As a consequence, if $u_0^*$ is an optimal control, $p_0^*$ must satisfy (2.27), meaning $p_0^*$ is uniquely determined for a given $\lambda^*$. We claim that each value $\lambda^*$, given by Lemma (2.3), leads to the same function $p_0^*$, meaning $p_0^*$ is uniquely determined. Consider $I(\lambda)$ as defined in (2.26). If $p_0^*$ is optimal, then necessarily $I(\lambda^*) = C$, see Lemma 2.1. Note that the function $\psi_{x,T}$ is clearly continuous and nonincreasing, thus so is $I$. Also,

$$I(\lambda) = \int_\Omega K(x)G(0)dx = 0, \qquad \text{if } \lambda \geqslant \lambda_{max} := -w_T(0)\min_x K(x),$$

$$I(\lambda) = \int_\Omega K(x)G(p_U(x))dx = U|\Omega|, \qquad \text{if } \lambda \leqslant \lambda_{min} := -\max_x K(x)w_T(p_U(x)).$$

Since we assumed $0 < C < U|\Omega|$, we deduce that there exist $\lambda_{min} < \lambda_1^* \leqslant \lambda_2^* < \lambda_{max}$ such that

$$I(\lambda) = C \qquad \forall \lambda \in [\lambda_1^*, \lambda_2^*].$$

As a result, there holds $\lambda^* \in [\lambda_1^*, \lambda_2^*]$. While $\lambda^*$ is not uniquely determined, we claim that $\psi_{x,T}$ is constant on $[\lambda_1^*/K(x), \lambda_2^*/K(x)]$ for a.e. $x \in \Omega$. Assume by contradiction that there exists a set $S \subset \Omega$ with positive measure such that $\psi_{x,T}$ is nonconstant on $[\lambda_1^*/K(x), \lambda_2^*/K(x)]$ for all $x \in S$. This implies, since $\psi_{x,T}$ is nonincreasing,

$$\psi_{x,T}\left(\frac{\lambda_1^*}{K(x)}\right) > \psi_{x,T}\left(\frac{\lambda_2^*}{K(x)}\right), \qquad \forall x \in S.$$

On the other hand, there also holds

$$\psi_{x,T}\left(\frac{\lambda_1^*}{K(x)}\right) \geqslant \psi_{x,T}\left(\frac{\lambda_2^*}{K(x)}\right), \qquad \forall x \in \Omega.$$

As a result, since $G$ is increasing, we deduce that

$$\begin{aligned} I(\lambda_1^*) - I(\lambda_2^*) &= \int_{\Omega\setminus S} K(x)\left(G\left(\psi_{x,T}\left(\frac{\lambda_1^*}{K(x)}\right)\right) - G\left(\psi_{x,T}\left(\frac{\lambda_2^*}{K(x)}\right)\right)\right)dx \\ &\quad + \int_S K(x)\left(G\left(\psi_{x,T}\left(\frac{\lambda_1^*}{K(x)}\right)\right) - G\left(\psi_{x,T}\left(\frac{\lambda_2^*}{K(x)}\right)\right)\right)dx \\ &\geqslant \int_S K(x)\left(G\left(\psi_{x,T}\left(\frac{\lambda_1^*}{K(x)}\right)\right) - G\left(\psi_{x,T}\left(\frac{\lambda_2^*}{K(x)}\right)\right)\right)dx \\ &> 0 \end{aligned}$$

where the last inequality follows from the fact that $|S| > 0$ and $K(x) > \min_\Omega K > 0$. This contradicts the fact that $I(\lambda_1^*) = I(\lambda_2^*) = C$. Therefore $\psi_{x,T}$ is constant on $[\lambda_1^*/K(x), \lambda_2^*/K(x)]$ for a.e. $x \in \Omega$. As a result, $p_0^*(x) = \psi_{x,T}\left(\frac{\lambda^*}{K(x)}\right)$ is uniquely determined, for any value $\lambda^* \in [\lambda_1^*, \lambda_2^*]$. □

Notice that Theorem 2.1 implies that releases should be more important where the carrying capacity is high. Since $\lambda^*$ is fixed, the argument of $\psi_{x,T}(\cdot)$, $\lambda^*/K(x)$, is smaller where $K(x)$ is higher. In case $-\frac{\lambda^*}{K(x)} \notin (w_T(0), w_T(p_U(x)))$, we have either $u_0(x) = 0$ or $u_0(x) = U$. On the other hand, in case $-\frac{\lambda^*}{K(x)} \in (w_T(0), w_T(p_U(x)))$, $\psi_{x,T}\left(\frac{\lambda^*}{K(x)}\right) = \omega_T^{-1}\left(-\frac{\lambda^*}{K(x)}\right)$. And since $\omega_T(\cdot)$ is monotonically increasing (see Figure 2.1), a bigger $K(x)$ implies a bigger argument (because of the minus sign), which implies a bigger $p_0^*(x)$. Since $u_0^*(x) = K(x)G(p_0^*(x))$, and $G$ is also monotonically increasing, it follows that $u_0^*(x)$ must be non-decreasing when $K(x)$ increases in general, and strictly increasing with $K(x)$ whenever $u_0^*(x) \notin \{0, U\}$.

### 2.2.5 The case $T > T_0$

We study now the case $T > T_0$, in order to state the results for this case it will be useful to introduce some tools and notations. Let us introduce the following mappings

$$\Lambda \mapsto \psi_{x,T}^0(\Lambda) := \begin{cases} 0 & \text{if } -\Lambda \leqslant w_T(0), \\ p_U(x) & \text{if } -\Lambda > \max\left(w_T(0), w_T(p_U(x))\right), \\ w_T^{-1}(-\Lambda) & \text{if } -\Lambda \in \left(w_T(0), w_T(p_U(x))\right], \end{cases} \tag{2.28}$$

the third case only being defined if $w_T(0) < w_T(p_U(x))$, and

$$\Lambda \mapsto \psi_{x,T}^1(\Lambda) := \begin{cases} 0 & \text{if } -\Lambda < \min\limits_{p_0 \in (0, p_U(x))} w_T(p_0), \\ p_U(x) & \text{if } -\Lambda \geqslant w_T(p_U(x)), \\ w_T^{-1}(-\Lambda) & \text{if } -\Lambda \in \left[\min\limits_{p_0 \in (0, p_U(x))} w_T(p_0), w_T(p_U(x))\right), \end{cases} \tag{2.29}$$

the third case only being defined if $\min\limits_{p_0 \in (0, p_U(x))} w_T(p_0) < w_T(p_U(x))$. It is important to remark that $w^{-1}\left(-\frac{\lambda^*}{K(x)}\right)$ might not be uniquely defined, since the function is not injective on its whole domain. Whenever there is an ambiguity it will be understood that the value of $w^{-1}\left(-\frac{\lambda^*}{K(x)}\right)$ we refer to is the one on the increasing branch of $w(p_0)$ (the one satisfying $\frac{\partial w}{\partial p_0}(p_0) \geqslant 0$), since it is the only one satisfying the second order optimality conditions.

For a given value of $\lambda \geqslant 0$, let us introduce the set:

$$\tilde{\Omega}_\lambda := \left\{ x \in \Omega \mid \psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) \neq \psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right) \right\}. \tag{2.30}$$

By definition, for all $x \in \Omega \setminus \tilde{\Omega}_\lambda$, $\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) = \psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right)$. In order to underline this, for $x \in \Omega \setminus \tilde{\Omega}_\lambda$ we will denote $\psi^\bullet_{x,T}\left(\frac{\lambda}{K(x)}\right) := \psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) = \psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right)$. Note also that in case $\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) \neq \psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right)$, then $\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) = 0$, therefore $\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) = 0$ for all $x \in \tilde{\Omega}_\lambda$.

In the same spirit as in Theorem 2.1, the idea behind Theorem 2.2 is to write the solution in the form $p_0^*(x) = \psi^\bullet_{x,T}\left(\frac{\lambda}{K(x)}\right)$ for certain values of $\lambda$. Therefore, solutions in $\tilde{\Omega}_\lambda$ will be hard to characterize in general. In order to study solutions in this set we introduce a secondary problem, the solution of which, will allow us to determine the solutions of problem $(\mathcal{P}_{p_0})$ in $\tilde{\Omega}_\lambda$. Assuming $|\tilde{\Omega}_\lambda| > 0$, we introduce the quantity

$$\tilde{C}_\lambda := C - \int_{\Omega \setminus \tilde{\Omega}_\lambda} K(x) G\left(\psi^\bullet_{x,T}\left(\frac{\lambda}{K(x)}\right)\right) dx.$$

Assuming $\tilde{C}_\lambda > 0$ we consider the following problem:

**Secondary problem.**

$$\boxed{\min_{\chi_\lambda \in \mathcal{X}} \int_{\tilde{\Omega}_\lambda} K(x)^2(1-p(T,x))^2\chi_\lambda(x) + K(x)^2(1-\chi_\lambda(x))dx \ , \ \int_{\tilde{\Omega}_\lambda} K(x) G\left(\psi^1_{x,T}\left(\frac{\lambda^*}{K(x)}\right)\right)\chi_\lambda(x)dx \leqslant \tilde{C}_\lambda.} \quad (\mathcal{P}_{\tilde{\Omega}_\lambda})$$

Where the new control variable is $\chi_\lambda \in \mathcal{X}$ and

$$\mathcal{X} := \left\{ \chi_\lambda \in L^\infty(\tilde{\Omega}_\lambda) \mid 0 \leqslant \chi_\lambda \leqslant 1 \right\}.$$

Here $p(T,x)$ is assumed to have $\psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right)$ as initial condition.

Finally, let us also define

$$I^0(\lambda) := \int_\Omega K(x) G\left(\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right)\right) dx \quad \text{and} \quad I^1(\lambda) := \int_\Omega K(x) G\left(\psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right)\right) dx. \tag{2.31}$$

and

$$\lambda_0 := \min \lambda \quad \text{such that} \quad I^0(\lambda) = C, \tag{2.32}$$

$$\lambda_1 := \max \lambda \quad \text{such that} \quad I^1(\lambda) = C. \tag{2.33}$$

Note that as long as $0 < C < U|\Omega|$ these two quantities will always be well defined.

**Theorem 2.2.** *Assume $T > T_0$, $0 < C < U|\Omega|$ and $(\mathcal{H}.2)$. Then there exists at least one $p_0^* \in \mathcal{P}_{0,C,U}$ that solves problem $(\mathcal{P}_{p_0})$. It is given by*

$$p_0^*(x) = \psi^\bullet_{x,T}\left(\tfrac{\lambda^*}{K(x)}\right) \text{ for all } x \in \Omega \setminus \tilde{\Omega}_{\lambda^*}, \text{ and } p_0^*(x) = \begin{cases} \psi^1_{x,T}\left(\frac{\lambda^*}{K(x)}\right) & \text{, for } x \in \tilde{\Omega}_{\lambda^*} \text{ s.t. } \chi^*_{\lambda^*}(x) = 1, \\ \psi^0_{x,T}\left(\frac{\lambda^*}{K(x)}\right) & \text{, for } x \in \tilde{\Omega}_{\lambda^*} \text{ s.t. } \chi^*_{\lambda^*}(x) = 0, \end{cases}$$

*where $\psi^0_{x,T}\left(\frac{\lambda^*}{K(x)}\right) = 0$ for all $x \in \tilde{\Omega}_{\lambda^*}$, $\lambda^* \in [\lambda_0, \lambda_1]$ and $\chi^*_{\lambda^*}(x)$ is the solution to problem $(\mathcal{P}_{\tilde{\Omega}_\lambda})$*

*with* $\lambda = \lambda^*$.

*Furthermore, if* $|\tilde{\Omega}_{\lambda_0}| = 0$, *then* $\lambda^* = \lambda_0$ *and* $p_0^*(x) = \psi^{\bullet}_{x,T}\left(\frac{\lambda_0}{K(x)}\right)$ *for all* $x \in \Omega$.

*Proof.* In this proof we use the same notation as in the proof of Theorem 2.1. Let us fix any $x \in \Omega$ and let $\lambda^* \geqslant 0$ be any value given by Lemma 2.3. Let us consider $p_0^* \in \mathcal{P}_{0,C,U}$ be the solution to problem $(\mathcal{P}_{p_0})$.

Using the first and second order optimality conditions (Lemmas (2.3) and (2.4)) we know that there exists a $\lambda^* \geqslant 0$ such that the optimal control $p_0^*$ must satisfy that

— If $p_0^* = 0$ then $w(0) \geqslant -\frac{\lambda^*}{K(x)}$.

— If $p_0^* = p_U$ then $w(p_U) \leqslant -\frac{\lambda^*}{K(x)}$.

— If $0 < p_0^* < p_U$ then $w(p_0^*) = -\frac{\lambda^*}{K(x)}$ and $\frac{\partial w}{\partial p_0}(p_0^*) \geqslant 0$.

We fix $T > T_0$ and exploit these optimality conditions. Under hypothesis $(\mathcal{H}.2)$, by Lemma 2.5, $w(p_0)$ is unimodal, that is, strictly decreasing until a certain $p_0^T \in (0, \bar{\theta})$ and then strictly increasing. Depending on the relative position of $w(0)$,$w(p_U)$ and $\min w(p_0)$ we can have three different behaviours of the optimal control. We detail here as an example the case $w(0) \geqslant w(p_U) > \min w(p_0)$. For cases $w(0) > w(p_U) \geqslant \min w(p_0)$ and $w(p_U) > w(0) > \min w(p_0)$ see Figure 2.2.

Assume $p_U$ is such that $w(0) \geqslant w(p_U) > \min w(p_0)$ (second case in Figure 2.2), then we distinguish four cases:

— If $-\frac{\lambda^*}{K(x)} \geqslant w(0)$, then necessarily $p_0^* = p_U$.

— If $w(0) \geqslant -\frac{\lambda^*}{K(x)} \geqslant w(p_U)$, then necessarily $p_0^* \in \{0, p_U\}$.

— If $w(p_U) \geqslant -\frac{\lambda^*}{K(x)} \geqslant \min w(p_0)$, then necessarily $p_0^* \in \left\{0, w^{-1}\left(-\frac{\lambda^*}{K(x)}\right)\right\}$.

— If $-\frac{\lambda^*}{K(x)} \leqslant \min w(p_0)$, then necessarily $p_0^* = 0$.

Two things remain to be investigated: The values that $\lambda^*$ can take, and, in case $p_0^*$ is not uniquely determined, how to choose between the two options. In order to do this, let us consider mappings $\psi^0_{x,T}$ and $\psi^1_{x,T}$ as defined in (2.28) and (2.29) respectively. Note that these two mappings are always well defined and they give, respectively, the minimum and maximum values $p_0^*$ can take when two values of $p_0$ satisfy the optimality conditions. For instance, if for a given value of $\lambda^*$, $p_0^* \in \{0, p_U\}$, then $\psi^0_{x,T}\left(\frac{\lambda^*}{K(x)}\right) = 0$ and $\psi^1_{x,T}\left(\frac{\lambda^*}{K(x)}\right) = p_U$. Remark also that whenever $\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) \neq \psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right)$, $\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right) = 0$.

Mappings $\psi^0_{x,T}\left(\frac{\lambda}{K(x)}\right), \psi^1_{x,T}\left(\frac{\lambda}{K(x)}\right)$ are non-increasing with respect to $\lambda$. Although in case $T > T_0$, $\psi^0_{x,T}$ and $\psi^1_{x,T}$ are only continuous in case C (see Figure 2.2), it still holds that for all $\lambda \geqslant 0$ we have that $I^0(\lambda) \leqslant I^1(\lambda)$, with $I^0(\lambda), I^1(\lambda)$, as defined in (2.31). Furthermore, if $\lambda^*$ is any value given by Lemma 2.3 we have that

$$I^0(\lambda^*) \leqslant \int_\Omega K(x) G(p_0^*(x)) dx \leqslant I^1(\lambda^*). \tag{2.34}$$

Using Lemma 2.1, (2.34) means that $I^0(\lambda^*) \leqslant C \leqslant I^1(\lambda^*)$. It follows that $\lambda^* \in [\lambda_0, \lambda_1]$.

Fixing now a $\lambda^* \in [\lambda_0, \lambda_1]$, let us consider the set $\tilde{\Omega}_{\lambda^*}$ as defined in (2.30). Note that if $|\tilde{\Omega}_{\lambda^*}| = 0$, we can conclude that $p_0^*(x) = \psi^{\bullet}_{x,T}\left(-\frac{\lambda^*}{K(x)}\right)$ using the same arguments as in the proof of Theorem 2.1. In particular, if $|\tilde{\Omega}_{\lambda_0}| = 0$, since $p_0^*(x) = \psi^{\bullet}_{x,T}\left(\frac{\lambda_0}{K(x)}\right)$, $\psi^{\bullet}_{x,T}(\lambda)$ is non-increasing w.r.t $\lambda$ and $\int_\Omega K(x)^2 \left(1 - p(T,x)\right)^2 dx$ is descreasing w.r.t to the initial data of $p(T,x)$, we can conclude that $\lambda^* = \lambda_0$, proving the last statement of the theorem.

For the rest of the proof we assume that $|\tilde{\Omega}_{\lambda^*}| > 0$. Note also that the optimal control $p_0^*$ must be such that $0 < \tilde{C}_{\lambda^*} \leqslant C$. We consider problem $(\mathcal{P}_{\tilde{\Omega}_\lambda})$ with $\lambda = \lambda^*$. Observing that the criterion to optimize is affine with respect to $\chi_{\lambda^*}$ and that its differential at $\chi^*_{\lambda^*}$ is the linear mapping

$$L^\infty(\Omega) \ni h \mapsto \int_{\tilde{\Omega}_{\lambda^*}} h\ K(x) \left( K(x)p(T,x)(p(T,x)-2) + \tilde{\lambda} G\left(\psi^1_{x,T}\left(\frac{\lambda^*}{K(x)}\right)\right)\right)\ dx,$$

leads to introduce where the switching function $\Phi$ for this problem, namely

$$\Phi(x) := K(x)\ \frac{p(T,x)(2-p(T,x))}{G\left(\psi^1_{x,T}\left(\frac{\lambda^*}{K(x)}\right)\right)}.$$

We infer from the so-called bathtub principle (see e.g. Section 1.14 of [80]) the existence of a unique real number $\tilde{\lambda}^*$ such that

$$\{\tilde{\lambda}^* > \Phi\} \subset \{\chi^*_{\lambda^*} = 0\} \subset \{\tilde{\lambda}^* \geqslant \Phi\}, \qquad \{\tilde{\lambda}^* < \Phi\} \subset \{\chi^*_{\lambda^*} = 1\} \subset \{\tilde{\lambda}^* \leqslant \Phi\}$$

and furthermore, $\{0 < \chi^*_{\lambda^*} < 1\} \subset \{\tilde{\lambda}^* = \Phi\}$. Note that such inclusions must be understood up to a zero Lebesgue measure set.

Let us notate $D := \left\{x \in \tilde{\Omega}_{\lambda^*} \mid 0 < \chi^*_{\lambda^*}(x) < 1\right\}$. In case $|D| = 0$, the optimality conditions become necessary and sufficient. The solution can be written as

$$\chi^*_{\lambda^*}(x) = \begin{cases} 1 & \text{, if } \tilde{\lambda}^* < \Phi, \\ 0 & \text{, if } \tilde{\lambda}^* > \Phi. \end{cases}$$

In case $|D| > 0$, since the problem is linear in $\chi_{\lambda^*}$ we know that there exists a bang-bang solution. That is, a solution that only takes the values $\chi^*_{\lambda^*} = 0$ and $\chi^*_{\lambda^*} = 1$. This means that despite it may exists a solution with $0 < \chi^*_{\lambda^*}(x) < 1$ for $x \in D$, we can always construct a bang-bang alternative that performs just as good. Assuming $\tilde{\lambda}^* = \Phi$ in $D$ ($\Phi$ is constant in $D$ by definition), we introduce

$$\chi^\alpha_{\lambda^*}(x) = \begin{cases} 1, & \text{if } \tilde{\lambda}^* < \Phi \text{ or } x \in D^\alpha, \\ 0, & \text{if } \tilde{\lambda}^* > \Phi \text{ or } x \in D \setminus D^\alpha. \end{cases}$$

where $D^\alpha$ is any subset of $D$ such that $|D^\alpha|/|D| = \alpha$, and $\alpha \in [0,1]$. To compute the value of $\alpha$ we use one more time Lemma 2.1, concluding that, in this case, $\chi^*_{\lambda^*}(x) = \chi^\alpha_{\lambda^*}(x)$ for $\alpha$ such that $\int_{\tilde{\Omega}_{\lambda^*}} K(x) G\left(\psi^1_{x,T}\left(\frac{\lambda^*}{K(x)}\right)\right) \chi^\alpha_{\lambda^*}(x)dx = \tilde{C}_{\lambda^*}$. Note how the solution to this secondary problem, $(\mathcal{P}_{\tilde{\Omega}_\lambda})$, sheds light on the primary problem, $(\mathcal{P}_{p_0})$, by allowing us to write the solution on $\tilde{\Omega}_{\lambda^*}$ as

$$p_0^*(x) = \begin{cases} \psi^1_{x,T}(\lambda^*), & \text{on } \chi^*_{\lambda^*}(x) = 1, \\ \psi^0_{x,T}(\lambda^*), & \text{on } \chi^*_{\lambda^*}(x) = 0, \end{cases}$$

concluding the proof. □

**Corollary 2.1.** Assume $0 < C < U|\Omega|$ and $K(x) = K$ constant in all $\Omega$. Then there exists a $p_0^* \in \mathcal{P}_{0,C,U}$ that solves problem $(\mathcal{P}_{p_0})$.

— If $T \leqslant T_0$, it is given by

$$p_0^*(x) = G^{-1}\left(\frac{C}{K|\Omega|}\right) \text{ for all } x \in \Omega.$$

— If $T > T_0$,
  — If $w(0) < w\left(G^{-1}\left(\frac{C}{K|\Omega|}\right)\right)$, then

$$p_0^*(x) = G^{-1}\left(\frac{C}{K|\Omega|}\right) \text{ for all } x \in \Omega$$

  — If $w(0) \geqslant w\left(G^{-1}\left(\frac{C}{K|\Omega|}\right)\right)$, then there exists at least one $\lambda^* \in [\lambda_0, \lambda_1]$ such that $p_0^*(x)$ can be written as

$$p_0^*(x) = \begin{cases} \psi_{x,T}^1\left(\frac{\lambda^*}{K}\right), & \text{for } x \in D, \\ 0, & \text{for } x \in \Omega \setminus D, \end{cases}$$

  where $D$ can be any subdomain of $\Omega$ with size $|D| = \frac{C}{KG\left(\psi_{x,T}^1\left(\frac{\lambda^*}{K}\right)\right)}$.

*Proof.* The existence of a unique solution written as $p_0^*(x) = \psi_{x,T}\left(\frac{\lambda^*}{K(x)}\right)$ for the case $T \leqslant T_0$ can be easily adapted from the proof of Theorem 2.1. Since the constraint must be saturated, we have that

$$\int_\Omega K(x) G\left(\psi_{x,T}\left(\frac{\lambda^*}{K(x)}\right)\right) dx = K \int_\Omega G\left(\psi_{x,T}\left(\frac{\lambda^*}{K}\right)\right) dx = C,$$

but for $K$ constant, $w$ is constant w.r.t. $x$, and thus, so is $\psi_{x,T}\left(\frac{\lambda^*}{K}\right)$. Therefore,

$$K \int_\Omega G\left(\psi_{x,T}\left(\frac{\lambda^*}{K}\right)\right) dx = KG\left(\psi_{x,T}\left(\frac{\lambda^*}{K}\right)\right)|\Omega| = C.$$

Concluding that

$$p_0^*(x) = \psi_{x,T}\left(\frac{\lambda^*}{K}\right) = G^{-1}\left(\frac{C}{K|\Omega|}\right).$$

The case $T > T_0$ is greatly simplified in this setting. Since $\psi_{x,T}\left(\frac{\lambda^*}{K}\right)$ is constant w.r.t. $x$, either $|\tilde{\Omega}_\lambda| = 0$, or $\tilde{\Omega}_\lambda = \Omega$. Like in the general case, if $|\tilde{\Omega}_{\lambda_0}| = 0$ we have that $p_0^*(x) = \psi_{x,T}^\bullet\left(\frac{\lambda_0}{K}\right) = G^{-1}\left(\frac{C}{K|\Omega|}\right)$, and by the monotonicity of $\int_\Omega (1 - p(T,x))^2\, dx$ w.r.t to the initial condition of $p(T,x)$ we can conclude. On the other hand, in this case, we can put the condition $|\tilde{\Omega}_{\lambda_0}| = 0$ in simpler terms. If $|\tilde{\Omega}_{\lambda_0}| = 0$, then $\psi_{x,T}^0\left(\frac{\lambda_0}{K}\right) = \psi_{x,T}^1\left(\frac{\lambda_0}{K}\right)$. Looking at the two functions, this happens if and only if $w(0) < -\frac{\lambda_0}{K}$ and we have that

$$w(0) < -\frac{\lambda_0}{K} = w(p_0^*(x)) = w\left(\psi_{x,T}^\bullet\left(\frac{\lambda_0}{K}\right)\right) = w\left(G^{-1}\left(\frac{C}{K|\Omega|}\right)\right),$$

therefore

$$|\tilde{\Omega}_{\lambda_0}| = 0 \text{ if and only if } w(0) < w\left(G^{-1}\left(\frac{C}{K|\Omega|}\right)\right).$$

In case $w(0) \geqslant w\left(G^{-1}\left(\frac{C}{K|\Omega|}\right)\right)$, we have that $|\tilde{\Omega}_{\lambda_0}| > 0$ and thus, $|\tilde{\Omega}_{\lambda^*}| > 0$, furthermore, since $K$ is constant, $\tilde{\Omega}_{\lambda^*} = \Omega$.

Fixing a value for $\lambda^*$, $p_0^*(x)$ can only take two values in $\Omega$, $p_0^*(x) = 0$ or $p_0^*(x) = \psi_{x,T}^1(\frac{\lambda^*}{K})$. Therefore, from Lemma 2.1 we can directly deduce the size of the domain where $p_0^*(x) = \psi_{x,T}^1\left(\frac{\lambda^*}{K}\right)$, that we denote $D$,

$$\int_\Omega KG(p_0^*(x))\,dx = \int_D KG\left(\psi_{x,T}^1\left(\frac{\lambda^*}{K}\right)\right)\,dx = |D|KG\left(\psi_{x,T}^1\left(\frac{\lambda^*}{K}\right)\right) = C,$$

thus,

$$|D| = \frac{C}{KG(\psi_{x,T}^1\left(\frac{\lambda^*}{K}\right))}.$$

Therefore the solution can be writen like

$$p_0^*(x) = \psi_{x,T}^1\left(\frac{\lambda^*}{K}\right) \text{ a.e. on } D$$

and $p_0^*(x) = 0$ elsewhere, with $|D| = G^{-1}\left(\frac{C}{K\psi_{x,T}^1\left(\frac{\lambda^*}{K}\right)}\right)$.

□

## 2.3 Numerical Implementation of results

Thanks to Theorems 2.1 and 2.2 we can implement an algorithm for computing solutions to problems $(\mathcal{P}_{u_0})$ and $(\mathcal{P}_{p_0})$. In the case $T \leqslant T_0$, the computations will be a direct application of the results presented in Theorem 2.1, where solutions are unique up to a rearrangement. In the case $T > T_0$, Theorem 2.2 allows us to heavily simplify the problem, by recasting it as a one-dimensional one when solutions cannot be found directly. Namely,

$$\boxed{\min_{\lambda\in[\lambda_0,\lambda_1]} \int_\Omega K(x)^2(1-p(T,x))^2\,dx} \qquad (\mathcal{Q})$$

where we assume that the initial condition for $p(T,x)$ is given by the optimal releasing strategy, $p_0^*(x)$, given by theorem 2.2, assuming that $\lambda = \lambda^*$. The parameters used for the simulations are presented in Table 2.1.

### 2.3.1 1D simulations

The simplest setting in which we can study the problem is considering only one spatial dimension. We present two examples of the solutions obtained exploiting the results proven in this chapter in a 1D setting. We consider the following function representing the carrying

| Category | Parameter | Name | Value |
|---|---|---|---|
| Optimization | $T$ | Final time | $\{1, 25\}$ |
| | $U$ | Maximal instantaneous release rate | 250 |
| | $C$ | Amount of mosquitoes avaliable | $\{30, 200\}$ |
| | $\|\Omega\|$ | Domain size | 1 |
| | $K_0$ | Average carrying capacity | 100 |
| Biology | $b_M^0$ | Normalized wild birth rate | 1 |
| | $b_W^0$ | Normalized infected birth rate | 0.9 |
| | $d_M$ | Wild death rate | 0.27 |
| | $d_W$ | Infected death rate | 0.3 |
| | $s_h$ | Cytoplasmatic incompatibility level | 0.9 |

Table 2.1 – Values of the parameters used in simulations. The values for the biological parameters have been taken from [10].

capacity of the environment

$$K_S(x) = K_0\left(1 + \frac{1}{2}\sin\left(\frac{2\pi x}{|\Omega|} - \frac{\pi}{2}\right)\right), \quad K_P(x) = \frac{3K_0}{2}\mathbb{1}_{[0,|\Omega|/2]} + \frac{K_0}{2}\mathbb{1}_{(|\Omega|/2,|\Omega|]}$$

With the parameters considered, the two functions have the same average carrying capacity, $K_0$. That is, $\int_\Omega K_S(x)\,dx = \int_\Omega K_P(x)\,dx = K_0|\Omega|$, which is also the value we would obtain in case of an homogeneous carrying capacity equal to $K_0$ in all the domain. The domain considered is $\Omega = [0, |\Omega|]$. We chose these two functions in order to have a piecewise constant function and a function non-constant in any positive measure interval for comparison.

For the parameters in Table 2.1, $A(\cdot)$, as defined in (2.20), satisfies hypothesis ($\mathcal{H}.2$). The time when the function stops being increasing and starts being unimodal (decreasing, then increasing) is $T_0 \approx 3.51$, computed using formula (2.23). We choose to show the results for a time smaller than $T_0$ and a time bigger than $T_0$, so both behaviours can be observed. The simulations have been performed using an ad hoc algorithm exploiting the results of Theorems 2.1 and 2.2.

In Figure 2.3 we can see the results for $K(\cdot) = K_S(\cdot)$. This choice models a scenario where mosquitoes are concentrated in the center of the domain studied and its concentration fade out as we move towards the boundaries. In the case $C = 30$ (left column), we observe how the optimal strategy flattens and widens as $T$ increases. To understand this effect, we recall that in case $p_0(x) < \theta$, $p(t, x)$ is decreasing with respect to $t$. In other words, the *Wolbachia*-infected mosquitoes tend to be replaced by wild mosquitoes if they don't surpass a critical threshold. Furthermore, if $p_0(x) > \theta$, $p(t, x)$ is increasing with respect to $t$, and therefore *Wolbachia*-infected mosquitoes take over the population without further intervention. For the parameters considered we have $\theta \approx 0.21$ (The green dash-dotted line in Figure 2.3). According to our interpretation, since for $T$ small, $p(T, x)$ is close to its initial condition, a value of $p_0(x)$ below the threshold does not impact greatly the final result and reaching a bigger initial proportion in places where $K(x)$ is higher is prioritized. On the other hand, when $T$ is big, $p(T, x)$ can be far from its initial condition. Hence, there is an incentive for $p_0^*(x)$ to be above $\theta$, since the proportion of *Wolbachia*-infected mosquitoes in the parts of the domain above $\theta$ will naturally increase with time. This also explains why the end of the release interval is abrupt. If the release is not going to achieve the critical proportion, it is better not to release. This effect can be seen clearly in the bottom-left graph and should be more pronounced the bigger is $T$.

The changes between $T = 1$ and $T = 25$ in the case $C = 200$ are imperceptible. A possible explanation is that in this case $p_0^*(x) > \theta$ for all $x \in \Omega$ already in the first case. Therefore the

proportion of *Wolbachia*-infected mosquitoes is going to increase with time everywhere. This case illustrates how $u_0^*(\cdot)$ is non-decreasing as $K(\cdot)$ increases, and how that is not necessarily the case of $p_0^*(\cdot)$, which decreases when $K(\cdot)$ increases if $p_0^*(\cdot) = p_U(\cdot)$. We recall that we have proven this monotonicity porperty for the case $T \leqslant T_0$ and in case $T > T_0$ but $|\tilde{\Omega}_{\lambda_0}| = 0$, which is the case in the bottom-right graph ($C = 200$, $T = 25$). The only case where $|\tilde{\Omega}_{\lambda_0}| > 0$ in Figure 2.3 is the one with $C = 30$, $T = 25$ (bottom-left graph).

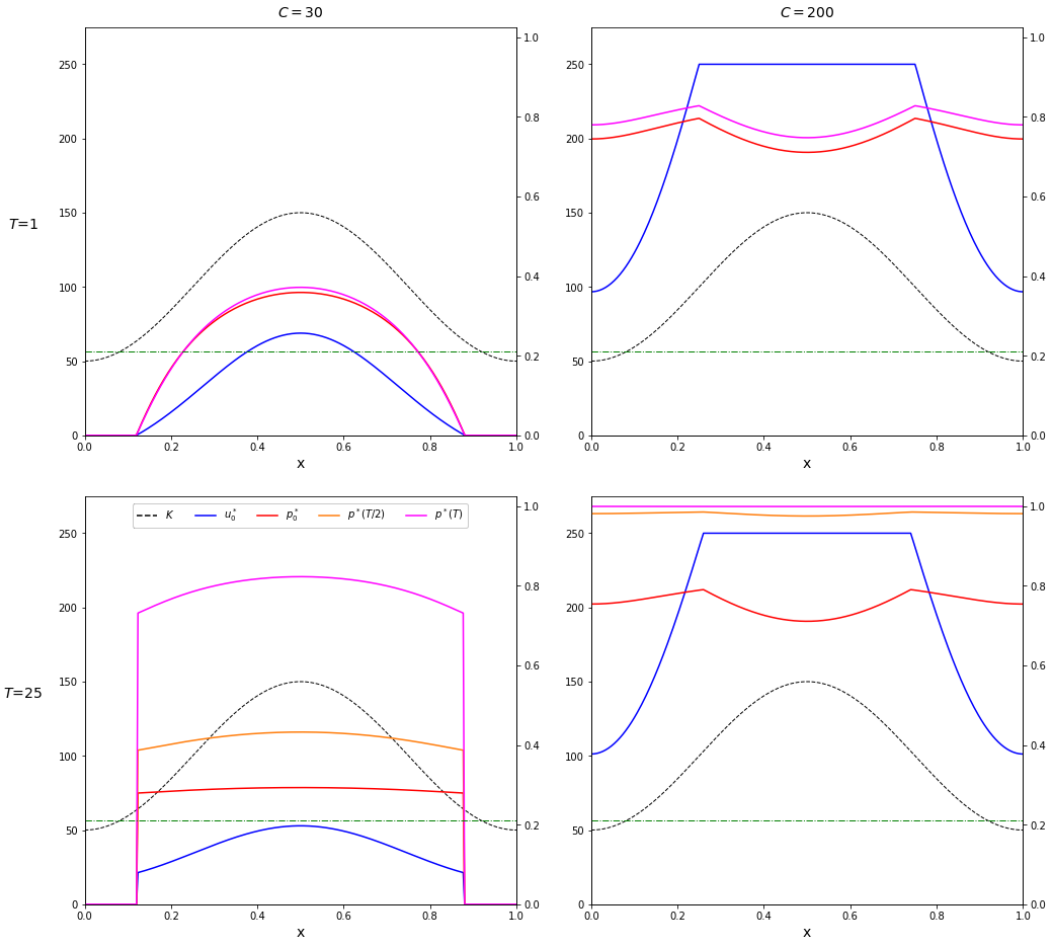


Figure 2.3 – Results for $K(\cdot) = K_S(\cdot)$ for different amount of mosquitoes released, $C$, and different final times, $T$. $K(\cdot)$ and $u_0^*(\cdot)$ must be read in the left axis and $p_0^*(\cdot)$, $p^*(T/2)$ and $p^*(T)$, in the right axis. Here $p^*$ stands for the solution of equation (2.10) with initial data $p_0^*(\cdot)$. In green, the line $p = \theta$.

In Figure 2.4 we show the results for the simulations with $K(\cdot) = K_P(\cdot)$. This figure represents a scenario with two patches of land with two very distinct conditions for mosquitoes, as it can be the case, for example, of an urban area close to a wetland. In the case $C = 30$ we can observe again the difference between the short-term and long-term strategies. With $T = 1$ reaching a higher proportion on the left patch is prioritized, leaving the second patch untreated. Meanwhile, when the time horizon is increased, it also increases the incentive to release in a wider area above the critical proportion $p_0(x) = \theta$. Therefore the optimal releasing strategy consists in releasing

a slightly smaller amount on the left patch in order to release in a certain domain in the right one.

In this case, on the bottom-left graph, we are in the case where $|\tilde{\Omega}_{\lambda_0}| > 0$, and thus the secondary problem must be solved for the values of $\lambda$ in $[\lambda_0, \lambda_1]$ (see $(\mathcal{Q})$). Since $K(\cdot)$ is simple, the amount of mosquitoes released and the size of each subdomain of the right patch can be determined almost explicitely. For a fixed value of $\lambda \in [\lambda_0, \lambda_1]$, the amount of mosquitoes released in the left patch is

$$\int_0^{\frac{|\Omega|}{2}} K(x)G\left(p_0^*(x)\right)\,dx = \int_0^{\frac{|\Omega|}{2}} \frac{3K_0}{2} G\left(\psi^1_{x,T}\left(\frac{2\lambda}{3K_0}\right)\right)\,dx = \frac{3|\Omega|K_0}{4} G\left(\psi^1_{x,T}\left(\frac{2\lambda}{3K_0}\right)\right),$$

analogously in the right patch $p_0^*(x) = \psi^1_{x,T}\left(\frac{2\lambda}{K_0}\right)$ wherever it is not 0. Therefore the size of the subdomain $D$, where mosquitoes are released in the right patch is such that

$$C = \frac{3|\Omega|K_0}{4} G\left(\psi^1_{x,T}\left(\frac{2\lambda}{3K_0}\right)\right) + \frac{|D|K_0}{2} G\left(\psi^1_{x,T}\left(\frac{2\lambda}{K_0}\right)\right).$$

This equality can be satisfied for different values of $\lambda$ and $|D|$. To find the optimal value $\lambda$ and thus the optimal value of $|D|$, we solve the one-dimensional optimization problem $(\mathcal{Q})$, which in this case reads

$$\begin{aligned}
&\min_{\lambda\in[\lambda_0,\lambda_1]} \frac{3|\Omega|K_0^2}{16}((1-p^l(T))^2) + \frac{|D|K_0^2}{4}((1-p^r(T))^2) \\
&= \min_{\lambda\in[\lambda_0,\lambda_1]} \frac{3|\Omega|}{4}((1-p^l(T))^2) + |D|((1-p^r(T))^2 \\
&= \min_{\lambda\in[\lambda_0,\lambda_1]} \frac{3|\Omega|}{4}((1-p^l(T))^2) + \frac{1}{G(p_0^r)}\left(\frac{2C}{K_0} - \frac{3|\Omega|}{2}G(p_0^l)\right)((1-p^r(T))^2
\end{aligned}$$

where $p^l(T)$ and $p^r(T)$ solve equation $p'(t) = f(p(t))$ with initial condition $p_0^l = \left(\psi^1_{x,T}\left(\frac{2\lambda}{3K_0}\right)\right)$ and $p_0^r = \left(\psi^1_{x,T}\left(\frac{2\lambda}{K_0}\right)\right)$ respectively. This solution, nonetheless, is what we have been calling unique 'up to a rearrangement'. As long as the size of the domain where mosquitoes are released is preserved, the solution can be moved on the right half of the domain and still being optimal. In Figure 2.5 we show another choice for the solution.

Once again, in the case $C = 200$ (right column) the solution does not change significantly when $T$ is increased. We can see how the monotonicity of $u_0^*(\cdot)$ with respect to $K(\cdot)$ is respected, but not for $p_0^*(\cdot)$. In this case, releasing a smaller amount of mosquitoes in the right patch induces a higher initial proportion due to the smaller carrying capacity there.

### 2.3.2 The case with diffusion

So far, we have not considered diffusion in the system. Considering that mosquitoes do not disperse simplifies the analysis of the problem, but this comes at the expense of losing realism in the modeling. In this section we present some simulations in which diffusion is taken into account to see how the solutions presented above are modified. This is a perspective work, which, at the time of writing this thesis, is under development. The simulations have been carried out using GEKKO (see [20]).

When diffusion is considered, equation (2.10) has to be modified. When the carrying capacity is homogeneous this can be done by just adding a Laplacian of the proportion of *Wolbachia-*

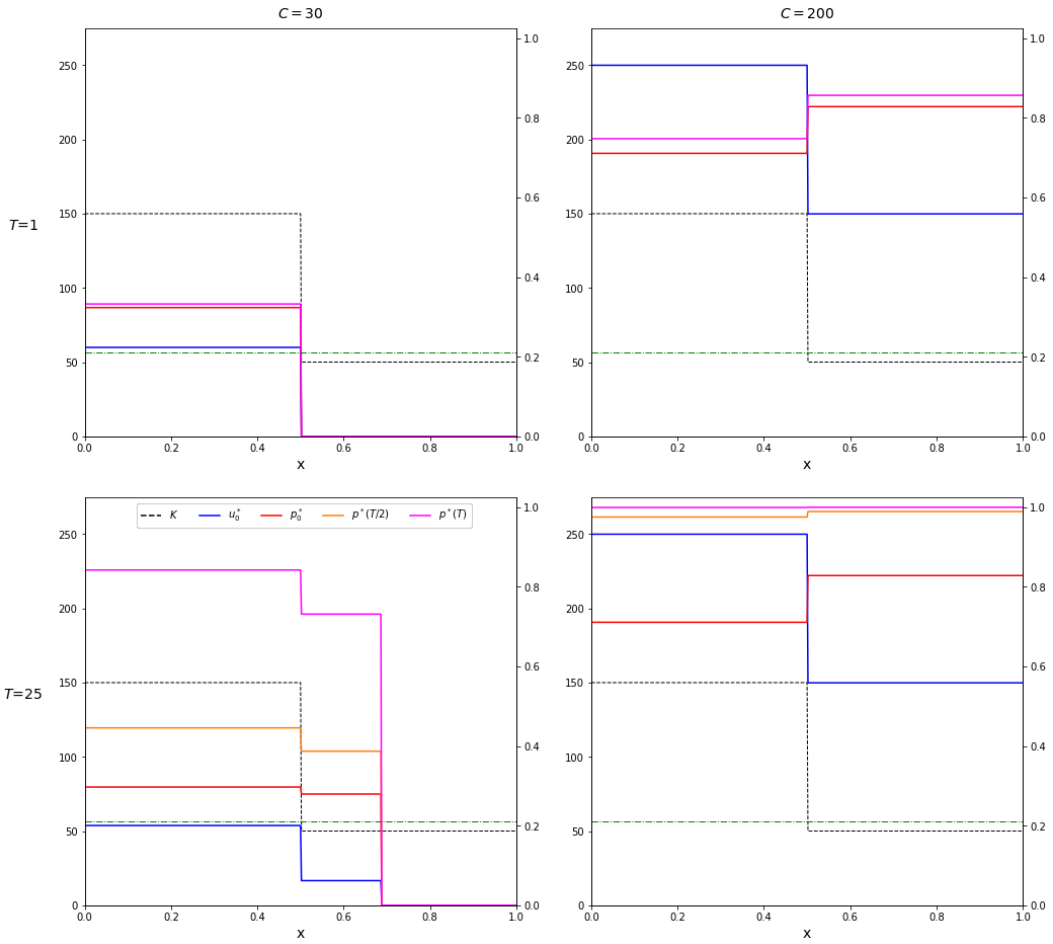


Figure 2.4 – Results for the piecewise constant carrying capacity, $K(\cdot) = K_P(\cdot)$, for different values of $C$ and $T$. They are presented in an identical way to Figure 2.3. The green dash-dotted line represents $p = \theta$.

infected mosquitoes, obtaining

$$\partial_t p - D\Delta p = f(p), \quad (t, x) \in [0, T] \times \Omega.$$

The proper deduction of this equation from a two population system with the same diffusion rate like the one introduced in (7) can be found in [134] and [46]. The obtention of this limit is slightly more complicated in the case we are interested in, which is that of an inhomogeneous carrying capacity. For clarity, in order to understand the apparition of the new terms, we go over the computations here. A detailed deduction nonetheless can be found in [98]. We start by

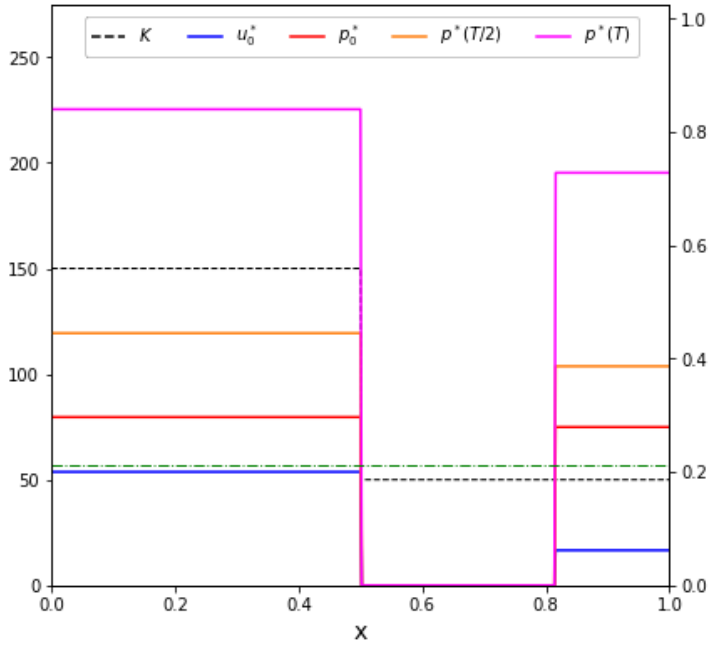


Figure 2.5 – Alternative arrangement of the solution for the case $K(\cdot) = K_P(\cdot)$ with $C = 30$ and $T = 25$ (bottom left graph of Figure 2.4).

considering the full controlled system, but taking diffusion into account

$$\begin{cases} \partial_t M - D\Delta M = b_M M\left(1 - \dfrac{M+W}{K(x)}\right)\left(1 - s_h \dfrac{W}{M+MW}\right) - d_M M, \\ \partial_t W - D\Delta W = b_W W\left(1 - \dfrac{M+W}{K(x)}\right) - d_W W + u, \quad t \in [0,T], \quad x \in \Omega, \\ M(0,x) = M^0(x), \quad W(0,x) = 0, \quad x \in \Omega, \\ \partial_\nu M(t,x) = \partial_\nu W(t,x) = 0, \quad x \in \partial\Omega, \end{cases} \tag{2.35}$$

Assuming a high fecundity, $b_M = \frac{b_M^0}{\varepsilon}$ and $b_W = \frac{b_W^0}{\varepsilon}$ with $\varepsilon \ll 1$, and introducing the total population $N = M + W$ and the proportion of the species $W$, $p = \frac{W}{M+W}$, from system (2.35) we compute

$$\partial_t N - D\Delta N = N\left(\frac{1}{\varepsilon}\left(1 - \frac{N}{K}\right)\left(b_W^0 p + b_M^0(1-p)(1-s_h p)\right) - d_W p - d_M(1-p)\right) + u, \tag{2.36}$$

$$\partial_t p - D\Delta p - 2D\frac{\nabla p \cdot \nabla N}{N} = p(1-p)\left(\frac{1}{\varepsilon}\left(1 - \frac{N}{K}\right)\left(b_W^0 - b_M^0(1-s_h p)\right) + d_M - d_W\right) - \frac{1-p}{N}u. \tag{2.37}$$

For $\varepsilon$ small enough, we can expand $N = N^\varepsilon(t,x)$ as

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

From here, we deduce the relation

$$n^\varepsilon(t,x) = \frac{d_W p(t,x) + d_M(1-p(t,x)) - D\Delta K(x)/K(x) - u/K(x)}{b_W^0 p(t,x) + b_M^0(1-p(t,x))(1-s_h p(t,x))}.$$

Injecting this expression into the right hand side of (2.37), we obtain that $p$ solves the following scalar reaction-diffusion equation :

$$\begin{cases} \partial_t p - D\Delta p - 2D\dfrac{\nabla p \cdot \nabla K}{K} = f(p) + \dfrac{u}{K} g(p) - D\dfrac{\Delta K}{K}\psi(p), \quad t>0,\ x\in\Omega, \\ \partial_\nu p = 0, \qquad t>0,\ x\in\partial\Omega, \\ p(0,x) = 0, \qquad x\in\Omega, \end{cases} \tag{2.38}$$

where $f$ and $g$ are the same as in (2.6) and

$$\psi(p) = p(1-p)\frac{b_W^0 - b_M^0(1-s_h p)}{b_M^0(1-p)(1-s_h p) + b_W^0 p}. \tag{2.39}$$

We are interested in observing how diffusion modifies the results presented so far. We place ourselves in the case with a bigger time horizon, $T = 25$, corresponding with the lower rows of Figures 2.3 and 2.4. We show the results for two different diffusion rate values: a smaller one, $D = 0.001$, and a bigger one, $D = 0.02$. In Figure 2.6, we set $K(\cdot) = K_S(\cdot)$. In the left column, diffusion seems to concentrate the initial distribution of mosquitoes, making it slightly narrower and taller, although with a little decrease happening in the center of the release for a small diffusion value (upper left graph). Solutions in this case, nonetheless, seem quite robust to the addition of diffusion for the parameters considered. In the case of a piece-wise constant carrying capacity [1] $K(\cdot) = K_P(\cdot)$ (Figure 2.7) the addition of diffusion immediately breaks the monotonicity of $u_0^*(\cdot)$ with respect to $K(\cdot)$. This means that, contrary to the case without diffusion, releases do not need to be stronger where there are more wild mosquitoes, and that optimal releasing policies may be more complex. We also observe how mosquitoes are released in a way such that a big density difference is created in the area close to the boundary between patches. As we can see, specially in the bottom left graph, by setting an initial density difference in this boundary, an invasive wave propagates from the patch with a higher carrying capacity to the other one. It is also noteworthy that in this case a new stationary state appears strictly between $p = 0 \cdot \mathbb{1}_{[0,|\Omega|]}$ and $p = \mathbb{1}_{[0,|\Omega|}$.

### 2.3.3 2D simulations

The method developed in this chapter can be applied any dimension. Problems $(\mathcal{P}_{u_0})$ and $(\mathcal{P}_{p_0})$ can be solved using Theorems 2.1 and 2.2 or, at least, reduced to the one-dimensional optimization problem $(\mathcal{Q})$, independently of the number of spatial dimensions considered. For a real application, nonetheless, the most interesting case is 2D.

Despite it does not present any novelties conceptually speaking, to illustrate the potential of the results, we show also two more simulations done in a 2D setting. We considered the following

1. Note that $K_P$ as defined is not differentiable and thus $\nabla K_P$ and $\Delta K_P$ are not defined. Nevertheless, we can always consider a differentialble function $\tilde{K}_P$ such that $\tilde{K}_P(x) = 3K_0/2$ for $x < |\Omega|/2 - \epsilon$, $\tilde{K}_P(x) = K_0/2$ for $x > |\Omega|/2 + \epsilon$ and such that $\epsilon$ is smaller than the space step considered in the discretization done by the numerical algorithm implemented to compute the solutions. The carrying capacity in these simulations should be interpreted as the latter case.

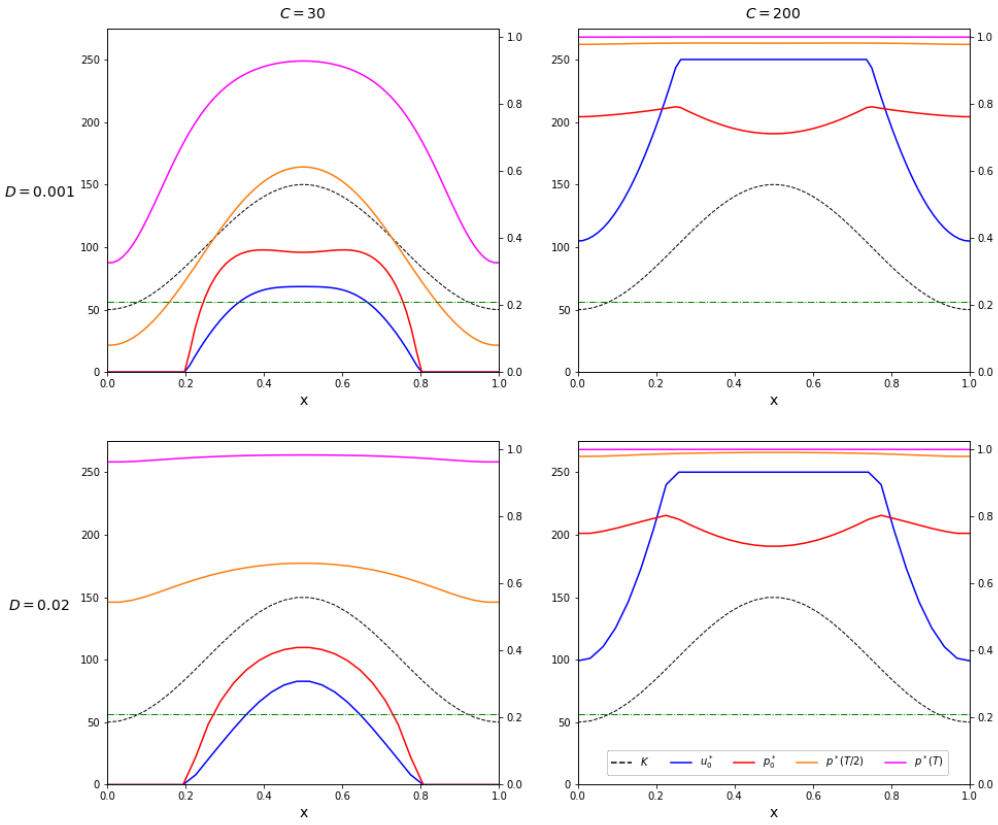


Figure 2.6 – Results for $K(\cdot) = K_S(\cdot)$ for the diffusive system. For different diffusion rates, $D \in \{0.001, 0.02\}$, total amount of mosquitoes $C \in \{30, 200\}$ and final time $T = 25$.

carrying capacity

$$K_{2D}(x, y) = K_0 \left(1 + \frac{1}{6} \sin\left(\frac{2\pi x}{L_x} - \frac{\pi}{2}\right) + \frac{1}{3} \sin\left(\frac{2\pi y}{L_y} - \frac{\pi}{2}\right)\right).$$

As in the case with $K_S$, $K_{2D}$ models a scenario with a higher concentration of mosquitoes towards the center of the domain and a smaller one towards the boundaries. Nevertheless, note that $K_{2D}$ is not radially symmetric.

For the simulations we took $\Omega = [0, L_x] \times [0, L_y]$, with $L_x = L_y = 1$. Once again, for the parameters chosen, $\int_\Omega K_{2D}(x, y)\, dx\, dy = K_0|\Omega|$. The results of the simulations can be seen in Figure 2.8. We portray only the case $T = 25$ for two values of $C$. Results match the intuition one can have from the related 1D case $K(\cdot) = K_S(\cdot)$. When a small amount of mosquitoes is considered, $C = 30$ the solution is flat and wide to surpass the critical proportion $p_0 = \theta$ in

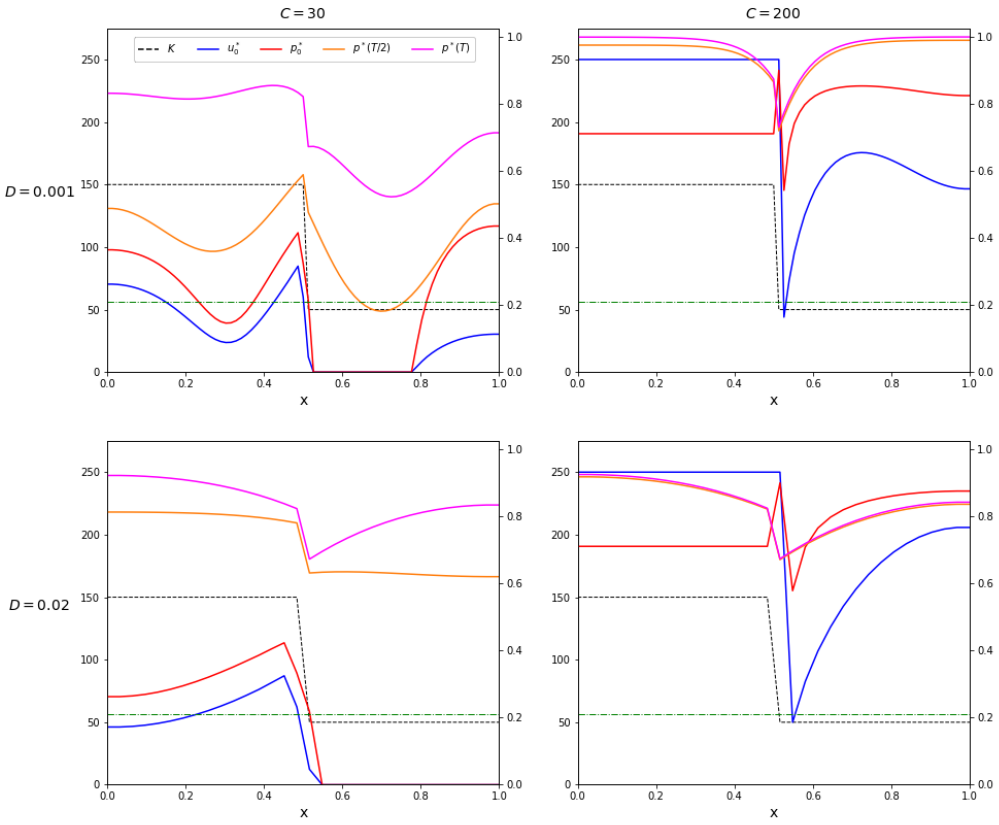


Figure 2.7 – Results for a piecewise carrying capacity $K(\cdot) = K_P(\cdot)$ for the system with diffusion. Diffusion rates $D \in \{0.001, 0.02\}$ and total amount of mosquitoes $C \in \{30, 200\}$.

a bigger area, since the proportion of *Wolbachia*-infected mosquitoes will naturally increase in those places. Also, $u_0^*(x) = 0$ outside of this area for the reasons already exposed. On the other hand when a bigger amount of mosquitoes is considered, $C = 200$, the solution is bigger than $p_0 = \theta$ everywhere and varies more rapidly, being higher where the carrying capacity is higher, but flattening out when $u_0^* = U$ is reached.

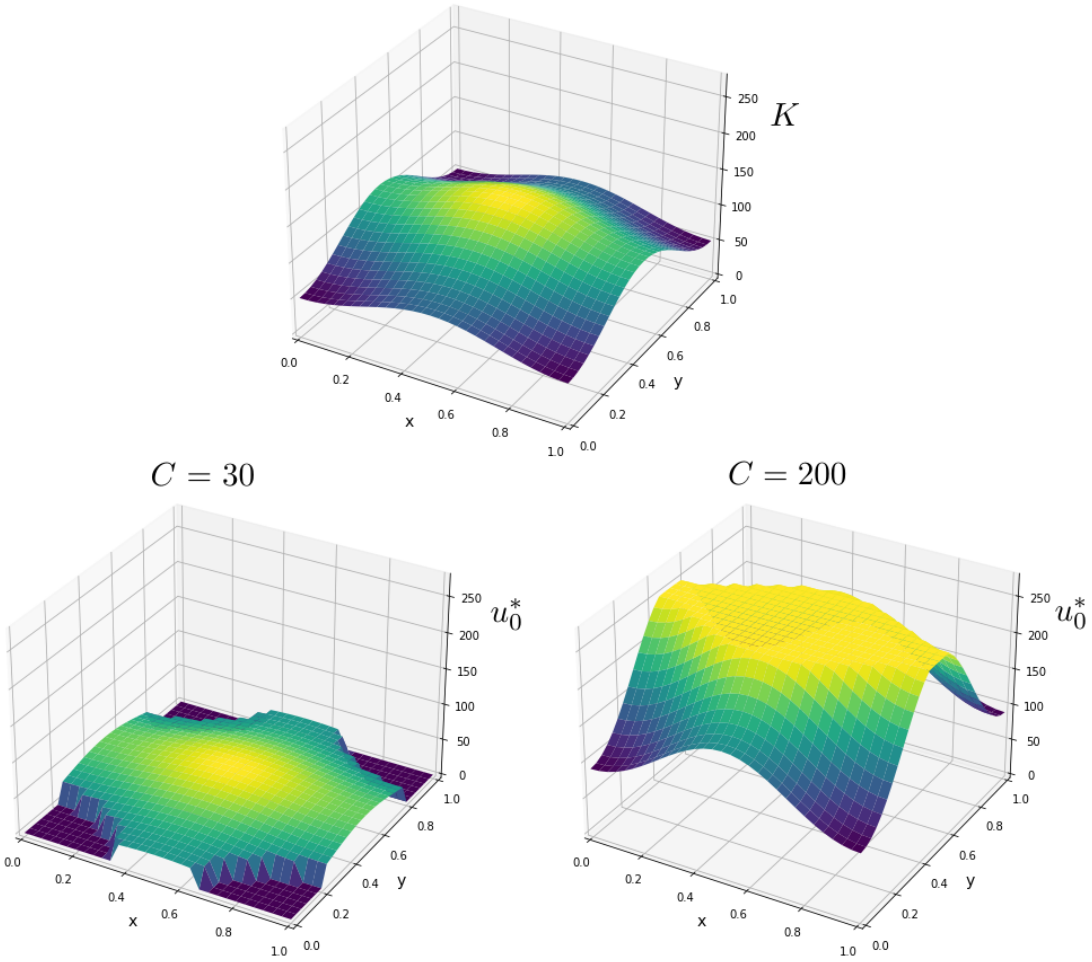


Figure 2.8 – Results in a 2D setting, $K = K_{2D}$, $T = 25$ and $C \in \{30, 200\}$.

Chapter 3

# Vector-borne disease outbreak control via instant vector releases

This chapter is the subject of L. Almeida, J. Bellver Arnau, Y. Privat and C. Rebelo. "Vector-borne disease outbreak control via instant vector releases", submitted for publication [5].

## 3.1 Introduction

Vector-borne diseases have a large impact on human health around the world, representing 17% of all infectious diseases. These diseases can be due to parasites, bacteria or viruses and be transmitted by different types of vectors like, for instance, ticks, fleas or mosquitoes. A significant part of the models presented in this chapter are applicable in a general setting. In particular, the part concerning the Sterile Insect Technique (SIT) is applicable to any vector borne disease where male vectors do not transmit the disease and where the vector has sexual reproduction which will be significantly perturbed by the release of sterile males.

Many of these diseases, such as dengue, Zika, chikungunya, yellow fever or the West Nile fever are caused by arboviruses. The vector responsible for the transmission of many arboviruses are the mosquitoes of the genus *Aedes*, specially the species *Aedes Aegipty* and *Aedes Albopictus*. Dengue is the most prevalent of these diseases, with more than 3.9 billion people in over 129 countries at risk of contracting it, and an estimated 40,000 death toll every year according to the World Health Organization [154]. Since, at present, there is no effective vaccine or antiviral drug, the only treatment option is to relieve the symptoms. As for preventing the spread of the disease, current methods consist of directly targeting the vector.

In the fight against arboviruses, and in particular dengue, two of the main control techniques targeting the mosquitoes are the SIT and the use of *Wolbachia*. Both methods rely on introducing mosquitoes into the wild population with certain modifications, which allow to control the infections. The SIT consists on the release of large amounts of sterile male mosquitoes in order to reduce the mosquito population by mating with the females in the place of the fertile ones. This technique has been both studied mathematically [27] and tested in the field [22, 62], not only with mosquitoes but also with other pests. The *Wolbachia* technique has mostly been used for *Aedes* mosquitoes (and this is the context in which we chose to present it in this chapter) but there are also many promising signs indicating that it should be possible to use it for other

types of mosquitoes or even other vectors [108]. The release of Wolbachia-infected mosquitoes on the other hand, does not seek to eradicate the mosquito population, but rather to replace it with a new one, less capable of transmitting several diseases. Thus, both males and females need to be released in order to establish a new population. More details on the functioning of these techniques and its biological insights can be found in the Introduction of this thesis, sections II.2 for the SIT and II.1 for population replacement technique using *Wolbachia*.

Our main goal in this chapter is to study and compare the effect of these techniques in interaction with the disease dynamics, in order to determine optimal strategies to mitigate the effects of vector-borne disease outbreaks using mosquito releases. These techniques are not usually applied in an epidemiological context. In case of an outbreak other alternatives with more immediate effects exist, like the use of pesticides. Also, the population replacement technique using *Wolbachia* requires the release of female mosquitoes, which, though being much poorer vectors than its wild counterparts, raises ethical questions when used in the case a virus is actively circulating in a population. This work should be seen as a first step towards understanding better the effects of modified vector releasing in epidemiological contexts, opening the debate around broadening the scope of application of these techniques. Since the releases occur in a much shorter time scale than the duration of the outbreak, they will be considered instantaneous. Therefore, impulsive controls are a natural setting to model field releases. This will be properly detailed in section 3.3. As stated before, our models are valid in a much wider setting but, for the sake of clarity, for the remaining of the chapter we will describe them in the setting of arboviruses and of *Aedes* mosquitoes as vectors. Although with several differences, previous works model and study the arboviruses transmission between *Wolbachia*-infected mosquitoes, wild-type mosquitoes and humans [102, 69]. A previous study of optimal control related issues, considering only bang-bang controls, can be found in [158].

In order to model the virus dynamics between mosquitoes and humans we consider a SEIR (Susceptible-Exposed-Infectious-Recovered) model for the humans and a SEI model for the mosquitoes (their short lifespan leads us to neglect the recovered compartment for the mosquitoes). As for the population dynamics we assume the humans to have the same birth and death rate and consider a logistic growth with a death term for the mosquitoes. The human and mosquito populations are subscripted $H$ and $M$ respectively.

$$\begin{aligned}
S'_H &= b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H \\
E'_H &= \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H \\
I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H \\
S'_M &= b_M M \left(1 - \frac{M}{K}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M \\
E'_M &= \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M \\
I'_M &= \gamma_M E_M - d_M I_M
\end{aligned} \tag{3.1}$$

The (positive) parameters used in system (3.1) are:

— $b_H$, $b_M$, the birth rates for humans and mosquitoes.

— $d_M$, the death rate for mosquitoes. For humans the death rate is assumed to be equal to the birth rate.

— $\beta_M$ is the rate of mosquito bites giving rise to a transmission between infected mosquitoes and humans, or infected humans and mosquitoes.

— $\gamma_H$ and $\gamma_M$ are the progression rates from latent to infectious compartments in humans and mosquitoes, respectively.

— $\sigma_H$ is the recovery rate from the disease.

— $H$ is the total amount of humans, $H = S_H + E_H + I_H + R_H$.
— $M$ is the total amount of mosquitoes, $M = S_M + E_M + I_M$.

The equation for the recovered human reads $R'_H = \sigma_H I_H - b_H R_H$. Since $H$ is constant we can remove $R_H$ from the system of differential equations and compute it as $R_H = H - S_H - E_H - I_H$. System (3.1) can be used for modeling, a priori, any vector-borne disease without other means of transmission and for which reinfection cannot occur.

In order to study these disease controlling techniques we need to modify this basic system in a way that takes into account the particularities of each one of them.

**Remark 3.1.** It is important to remark that throughout the chapter whenever we refer to 'mosquitoes' we are referring exclusively to the *female* mosquitoes, unless the contrary is specified. Male mosquitoes do not bite humans and therefore are unable of transmitting diseases. Thus, the variables referring to the mosquitoes such as $S_M$, $I_M$ or $I_M$, refer to female mosquitoes. An exception being when the SIT is treated (see section II.2). In the SIT only male mosquitoes are released, thus, $M_S$ will refer to *male* mosquitoes. In order to be able to do this simplification, we assume that male and female population have the same dynamics. We assume that the probability at birth of female and male is the same (50%) and that they both have the same life expectancy ($d_{♂} = d_{♀} = d_M$).

### 3.1.1 The sterile insect technique

To model the effects of the addition of sterile mosquitoes into the system we have to add an equation for them and a term accounting for the interaction between them and the mosquito population. Following the same approach as in [7] we introduce the following system

$$\begin{aligned}
S'_H &= b_H H - \frac{\beta_M}{H} I_M S_H - b_H S_H \\
E'_H &= \frac{\beta_M}{H} I_M S_H - \gamma_H E_H - b_H E_H \\
I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H \\
S'_M &= b_M M \left(1 - \frac{M}{K}\right) \frac{M}{M + s_c M_S} - \frac{\beta_M}{H} S_M I_H - d_M S_M \\
E'_M &= \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M \\
I'_M &= \gamma_M E_M - d_M I_M \\
M'_S &= u - d_S M_S
\end{aligned} \tag{SIT}$$

Since sterile mosquitoes don't reproduce we only consider a death term and the function $u$, representing the rate at which sterile mosquitoes are introduced in the population and interpreted as a control term for this system. We also add a birth term in the susceptible mosquitoes compartment, proportional to the probability that a female mosquito encounters a fertile male to mate (assuming that there are the same amount of male and female mosquitoes in the wild population). The positive parameter $s_c$ accounts for the competitiveness of the sterile mosquitoes since female mosquitoes may be less inclined to mate with them. This parameter presents a huge variation in the literature, from works estimating it to be low ($s_c = 0.14$ in [107]) to works where no difference in competitiveness was found [130]. According to [107], it would be relevant to assume the parameter $s_c$ depending on the ratio of sterile to fertile mosquitoes which would imply $s_c = s_c(M_S/M)$. Nevertheless, for simplicity, we will assume it to be constant. Note that there is no need to consider the dynamics of dengue in the sterile mosquito population, since the released mosquitoes are only male and therefore they do not feed on human blood. Thus, they are unable to transmit the disease.

### 3.1.2 The *Wolbachia* method

In this case we add a second mosquito population. This new population is composed by mosquitoes carrying Wolbachia, and the related quantities will be subscripted by $W$. It has been shown that *Wolbachia* decreases the fecundity and increases the mortality rates of mosquitoes [147], therefore $b_W < b_M$ and $d_W > d_M$. Also, *Wolbachia* reduces the vector capacity of the mosquitoes. We thus introduce $0 < \beta_{WH} < \beta_{HW} < \beta_M$ to make the distinction between the rate of mosquito bites giving rise to a transmission from human to Wolbachia-carrying mosquitoes, $\beta_{HW}$, and the rate of mosquito bites giving rise to a transmission from Wolbachia-carrying mosquitoes to humans, $\beta_{WH}$. The first one is smaller than $\beta_M$ since *Wolbachia* affects the capability of mosquitoes to feed due to a deformation in the trunk [143]. The second one should be smaller than the first one since *Wolbachia* also affects the way the disease develops inside the body of the mosquitoes and reduces the viral load in their saliva [92, 23]. We also introduce the term $1 - s_h \frac{W}{M+W}$ to take into account the cytoplasmic incompatibility. $s_h$ represents the level of cytoplasmic incompatibility achieved by the strain of *Wolbachia*. We have $0 \leqslant s_h \leqslant 1$, with $s_h = 0$ meaning that there is not any incompatibility and $s_h = 1$ meaning that the incompatibility is perfect. Finally we introduce $\gamma_W$ since *Wolbachia* also delays the amount of time it takes for dengue virus to reach the saliva of the mosquitoes, lengthening like this the effective incubation period of the disease in the mosquitoes carrying it [157].

$$
\begin{aligned}
S'_H &= bH - \frac{\beta_M}{H} I_M S_H - \frac{\beta_{WH}}{H} I_W S_H - b_H S_H \\
E'_H &= \frac{\beta_M}{H} I_M S_H + \frac{\beta_{WH}}{H} I_W S_H - \gamma_H E_H - b_H E_H \\
I'_H &= \gamma_H E_H - \sigma_H I_H - b_H I_H \\
S'_M &= b_M M \left(1 - \frac{M+W}{K}\right)\left(1 - s_h \frac{W}{M+W}\right) - \frac{\beta_M}{H} S_M I_H - d_M S_M \\
E'_M &= \frac{\beta_M}{H} S_M I_H - \gamma_M E_M - d_M E_M \\
I'_M &= \gamma_M E_M - d_M I_M \\
S'_W &= b_W W \left(1 - \frac{M+W}{K}\right) - \frac{\beta_{HW}}{H} S_W I_H - d_W S_W + u \\
E'_W &= \frac{\beta_{HW}}{H} S_W I_H - \gamma_W E_W - d_W E_W \\
I'_W &= \gamma_W E_W - d_W I_W
\end{aligned}
\tag{WB}
$$

Before moving on to the control problem we perform two simplifications on the system. We consider the following variables: $M := S_M + E_M + I_M$ and $W := S_W + E_W + I_W$. These variables account for the mosquito population regardless of the dengue dynamics. These variables present the following dynamics

$$
\begin{aligned}
M' &= b_M M \left(1 - s_h \frac{W}{M+W}\right)\left(1 - \frac{M+W}{K}\right) - d_M M \\
W' &= b_W W \left(1 - \frac{M+W}{K}\right) - d_W W + u
\end{aligned}
\tag{3.2}
$$

These equations describing the population dynamics of the mosquitoes in our model are those of the model in [10]. One can observe looking at the values in table 3.1 that $b_M \gg d_M$ and $b_W \gg d_W$. That is, that the birth rate of the mosquitoes is much higher than the death rate in both populations. In [10, Prop. 1], it is proven that in the high birth rate limit, i.e. considering $b_M = b_M^0/\varepsilon$, $b_W = b_W^0/\varepsilon$ and taking the limit $\varepsilon \to 0$, the proportion of mosquitoes

$p = W/(M+W)$ converges uniformly to the solution of a simple equation on the proportion of *Wolbachia*-infected mosquitoes. The asymptotic system (3.2) hence reads:

$$p' = f(p) + ug(p).$$

where

$$f(p) = p(1-p)\frac{d_M b_W^0 - d_W b_M^0(1-s_h p)}{b_M^0(1-p)(1-s_h p) + b_W^0 p} \quad \text{and} \quad g(p) = \frac{1}{K}\frac{b_M^0(1-p)(1-s_h p)}{b_M^0(1-p)(1-s_h p) + b_W^0 p}.$$

Another consequence is that $M+W$ converges to $K$ and so, in the limit, $W = (M+W)\frac{W}{M+W} = Kp$, and therefore $M = K(1-p)$.

This limit leaves the equations for the humans and for the infected mosquitoes unchanged. In order to modify the equations for the latent mosquitoes we can straightforwardly set $M+W = K$. Finally, using that $S_M = M - E_M - I_M$ and $S_W = W - E_W - I_W$ we can eliminate the two equations for the susceptible mosquitoes of the system. The equations for the exposed mosquitoes become:

$$\begin{aligned} E_M' &= \frac{\beta_M}{H}(K(1-p) - E_M - I_M)I_H - \gamma_M E_M - d_M E_M \\ E_W' &= \frac{\beta_{HW}}{H}(Kp - E_W - I_W)I_H - \gamma_W E_W - d_W E_W \end{aligned} \tag{3.3}$$

Incorporating these changes into system $(WB)$ we obtain the system we are going to study

$$\begin{aligned} S_H' &= bH - \frac{\beta_M}{H} I_M S_H - \frac{\beta_{WH}}{H} I_W S_H - b_H S_H \\ E_H' &= \frac{\beta_M}{H} I_M S_H + \frac{\beta_{WH}}{H} I_W S_H - \gamma_H E_H - b_H E_H \\ I_H' &= \gamma_H E_H - \sigma_H I_H - b_H I_H \\ E_M' &= \frac{\beta_M}{H}(K(1-p) - E_M - I_M)I_H - \gamma_M E_M - d_M E_M \\ I_M' &= \gamma_M E_M - d_M I_M \\ E_W' &= \frac{\beta_{HW}}{H}(Kp - E_W - I_W)I_H - \gamma_W E_W - d_W E_W \\ I_W' &= \gamma_W E_W - d_W I_W \\ p' &= f(p) + ug(p) \end{aligned} \tag{$WB'$}$$

## 3.2 Study of the uncontrolled system

In this section we study the uncontrolled systems (setting $u = 0$ for all $t \in [0, T]$) and compute the equilibria and the per stage reproduction number given by the next generation technique, $R_0$, of dengue in each case. This $R_0$ is a useful tool in the study of epidemiological systems with two stages, in this case host-vector and vector-host. It stands for the number of secondary infections generated per stage in a population where all individuals are susceptible to the disease ($S_H = H$ and $S_M =$ total population of vectors), which is the setting in which we will perform the numerical simulations. This number is the square root of the basic reproduction number [84, Page 110].

### 3.2.1 Sterile insect technique

Since we consider $u = 0$ and $M_S(0) = 0$, $M_S(t) = 0$ for all $t \in [0, T]$, turning system $(SIT)$ into (3.1). So computing the equilibria and $R_0$ of this system boils down to computing those of

system (3.1). In order to compute the $R_0$ of the system (that we denote $R_0^M$) we proceed as in [44]. For details of these computations, we refer to Appendix C.1. We find a $R_0^M$ value of

$$R_0^M = \beta_M \sqrt{\frac{K^* \gamma_M \gamma_H}{H d_M (b_H + \sigma_H)(\gamma_M + d_M)(\gamma_H + b_H)}},$$

where $K^* = K(1 - d_M/b_M)$. Since $M = S_M + E_M + I_M$, for any equilibrium of the system $(S_M^*, E_M^*, I_M^*)$, we have that $M^* = S_M^* + E_M^* + I_M^*$ must also be an equilibrium of the equation

$$M' = b_M M \left(1 - \frac{M}{K}\right) - d_M M. \tag{3.4}$$

This equation presents two equilibria, $M^* = 0$ and $M^* = K(1 - d_M/b_M)$. We can use this to simplify the study of the equilibria of system (3.1). The system to solve becomes

$$\begin{aligned}
0 &= b_H H - \frac{\beta_M}{H} I_M^* S_H^* - b_H S_H^* \\
0 &= \frac{\beta_M}{H} I_M^* S_H^* - \gamma_H E_H^* - b_H E_H^* \\
0 &= \gamma_H E_H^* - \sigma_H I_H^* - b_H I_H^* \\
0 &= d_M M^* - \frac{\beta_M}{H} S_M^* I_H^* - d_M S_M^* \\
0 &= \frac{\beta_M}{H} S_M^* I_H^* - \gamma_M E_M^* - d_M E_M^* \\
0 &= \gamma_M E_M^* - d_M I_M^*
\end{aligned} \tag{3.5}$$

Solving this simpler system we obtain three different equilibria:

— The extinction equilibrium

$$(S_H^*, E_H^*, I_H^*, R_H^*, S_M^*, E_M^*, I_M^*) = (H, 0, 0, 0, 0, 0, 0)$$

— The disease-free equilibrium

$$(S_H^*, E_H^*, I_H^*, R_H^*, S_M^*, E_M^*, I_M^*) = (H, 0, 0, 0, K^*, 0, 0)$$

— The endemic equilibrium

$$(S_H^*, E_H^*, I_H^*, R_H^*, S_M^*, E_M^*, I_M^*) = \left(H - a_H I_H^*, \tfrac{\sigma_H + b_H}{\gamma_H} I_H^*, I_H^*, \tfrac{\sigma_H}{b_H} I_H^*, K^* - a_M I_M^*, \tfrac{d_M}{\gamma_M} I_M^*, I_M^*\right)$$

where $a_H = \frac{(\gamma_H + b_H)(\sigma_H + b_H)}{b_H \gamma_H}$, $a_M = \frac{\gamma_M + d_M}{\gamma_M}$,

$$I_H^* = \frac{K^* \beta_M}{H b_H a_M + K^* \beta_M} \left(1 - \frac{1}{(R_0^M)^2}\right) \frac{H}{a_H} \quad \text{and} \quad I_M^* = \frac{\beta_M}{a_H d_M + \beta_M} \left(1 - \frac{1}{(R_0^M)^2}\right) \frac{K^*}{a_M}.$$

It is enlightening to write the endemic equilibrium in terms of $R_0^M$, since it clearly shows that if $R_0^M < 1$ the endemic equilibrium does not exist.

For the parameters considered in table 3.1 we find $R_0^M \approx 1.67$, which gives a basic reproduction number of $\left(R_0^M\right)^2 \approx 2.80$.

### 3.2.2 *Wolbachia* method

Since the equation $p' = f(p)$ is independent of the rest we can solve it separatedly. The function $f(p)$ has only three zeros, $p^* = 0$, $p^* = 1$ and $p^* = \theta$, satisfying $0 < \theta < 1$. The last zero only exists assuming further that $1 - s_h < \frac{d_M b_W^0}{d_W b_M^0} < 1$, which is satisfied in our case. The value of $\theta$ can be computed from the parameters of the problem, obtaining $\theta = \frac{1}{s_h}\left(1 - \frac{d_M b_W^0}{d_W b_M^0}\right)$. This implies that, independently of the epidemiological part of the model, there exists a *Wolbachia*-free equilibrium, a full invasion equilibrium and a coexistence equilibrium in the mosquito population.

We compute now the solutions to

$$\begin{aligned}
0 &= b_H H - \frac{\beta_M}{H} I_M^* S_H^* - \frac{\beta_{WH}}{H} I_W^* S_H^* - b_H S_H^* \\
0 &= \frac{\beta_M}{H} I_M^* S_H^* + \frac{\beta_{WH}}{H} I_W^* S_H^* - \gamma_H E_H^* - b_H E_H^* \\
0 &= \gamma_H E_H^* - \sigma_H I_H^* - b_H I_H^* \\
0 &= \frac{\beta_M}{H}(K(1-p^*) - E_M^* - I_M^*) I_H^* - \gamma_M E_M^* - d_M E_M^* \\
0 &= \gamma_M E_M^* - d_M I_M^* \\
0 &= \frac{\beta_{HW}}{H}(Kp^* - E_W^* - I_W^*) I_H^* - \gamma_W E_W^* - d_W E_W^* \\
0 &= \gamma_W E_W^* - d_W I_W^*
\end{aligned} \tag{3.6}$$

as a function of $p^*$.

Let us define $a_W := \frac{\gamma_W + d_W}{\gamma_W}$,

$$R_0^W := \sqrt{\frac{\beta_{HW}\beta_{WH} K \gamma_W \gamma_H}{H d_W (b_H + \sigma_H)(\gamma_W + d_W)(\gamma_H + b_H)}},$$

and $R_0^M$ as defined before but using $K$ instead of $K^*$. Note that in the high birth rate limit, $K^* = K(1 - \frac{d_M}{b_M})$ tends to $K$. These $R_0^M$ and $R_0^W$ are the per stage reproduction numbers associated with the disease-free equilibria, for $p^* = 0$ (Wolbachia-free) and $p^* = 1$ (full invasion) respectively. They are also computed following the procedure detailed in Appendix C.1. Let us also define $R_{p^*}^2 := \left(R_0^W\right)^2 p^* + \left(R_0^M\right)^2 (1 - p^*)$ (an analogous closed formula was considered in [34]). We find that system (3.6) has the trivial solution $(S_H^*, E_H^*, I_H^*, E_M^*, I_M^*, E_W^*, I_W^*) = (H, 0, 0, 0, 0, 0, 0)$, which gives three different equilibria for system $(WB')$: $(H, 0, 0, 0, 0, 0, 0, 0)$,$(H, 0, 0, 0, 0, 0, 0, \theta)$ and $(H, 0, 0, 0, 0, 0, 0, 1)$. In case $R_{p^*} > 1$, system (3.6) presents another real solution

$$\left(H - a_H I_H^*, \tfrac{\sigma_H + b_H}{\gamma_H} I_H^*, Hr, \tfrac{d_M}{\gamma_M} I_M^*, \tfrac{K}{a_M} \tfrac{\beta_M r}{H b_H a_W + \beta_M r}(1 - p^*), \tfrac{d_W}{\gamma_W} I_W^*, \tfrac{K}{a_W} \tfrac{\beta_{HW} r}{H b_H a_W + \beta_{HW} r} p^*\right),$$

where $r$ is the positive root of the second order polynomial

$$\begin{aligned}
P(Z) &= Z^2 \left(\beta_M \beta_{HW} + a_H \left(\beta_M d_W \left(R_0^M\right)^2 (1 - p^*) + \beta_{HW} d_M \left(R_0^W\right)^2 p^*\right)\right) \\
&\quad + Z\left(R_{p^*}^2 a_H d_M d_W - \left(R_{p^*}^2 - 1\right)(\beta_M d_W + \beta_{HW} d_M)\right) - \left(R_{p^*}^2 - 1\right) d_M d_W.
\end{aligned}$$

That means that system $(WB')$ can have up to six equilibria, due to the fact that there are three different values of $p^*$ and that $R_{p^*}$ can be bigger than one for some values of $p^*$ but not for others.

The per stage reproduction number $R_0^M$ is slightly higher than the per stage reproduction number for the sterile insect model due to the change of $K^*$ by $K$. For the values in Table 3.1

we find $R_0^M \approx 1.68$ and $R_0^W \approx 1.03$, which give basic reproduction numbers of $\left(R_0^M\right)^2 \approx 2.83$ and $\left(R_0^W\right)^2 \approx 1.08$ respectively. That means that even in a fully invaded population, outbreaks could still appear, but would have a smaller impact. Nevertheless these values should be taken with a grain of salt, since most of the parameters considered present a lot of variability in the literature.

We present here a result on the persistence of the disease in the system. Its proof can be found in Section C.2 of the Appendix.

**Theorem 3.1.** *If there exists $p^*$ such that $R_{p^*} > 1$ then the system $(WB')$ is uniformly persistent in the space of the initial conditions such that $p(t) \to p^*$, that is there exists $\eta > 0$ such that for each initial condition with $p(0)$ such that $p(t) \to p^*$ we have that*

$$\lim_{t\to+\infty}(E_H + I_H + E_N + I_N + E_W + I_W)(t) > \eta.$$

*If $R_{p^*} < 1$ for each initial condition with $p(0)$ such that $p(t) \to p^*$ we have that $\lim_{t\to+\infty}(E_H + I_H + E_N + I_N + E_W + I_W)(t) = 0$.*

## 3.3 Control Problem and Impulsive Dynamics

We place ourselves in the case of a dengue outbreak in a fully susceptible population. The goal of the releases will be to minimize the amount of cases during the duration of the outbreak. Therefore, considering a time window of size $T$, we want to find $u$ minimizing $\int_0^T I_H(t)\,dt$. Other works have studied related problems in the case of *Wolbachia* [158], or problems involving only the mosquito population [4, 6, 3, 7] considering controls in $L^\infty(0,T)$.

Field releases are done with a certain periodicity and in a short amount of time with respect to the time window considered, this leads us to consider the control denoted $u(\cdot)$ as a linear combination of pulses, namely

$$u(t) = \sum_{i=1}^{n} c_i \delta(t - t_i).$$

where $\delta(t)$ is the Dirac measure at $t = 0$ and $0 \leqslant t_1 \leqslant \cdots \leqslant t_n$ are the release times. It is natural to impose some constraints on the control function. Usually it is assumed that the rate at which mosquitoes are released is bounded ($u \in L^\infty(0,T)$) but also that the total amount of mosquitoes used is bounded ($\int_0^T u(t)dt \leqslant C$). Our approach is different. We also assume that we have a limited amount of mosquitoes at our disposal, $C$, but we assume that all of them are used. Since our control function is a linear combination of pulses, this translates into imposing the constraint $\sum_{i=1}^n c_i = C$. Therefore, for both systems $(SIT)$ and $(WB')$, the optimization problem we will study is

$$\begin{aligned}&\textit{Minimize } J(u) \textit{ over the set of time jumps } (t_i)_{1\leqslant i\leqslant n} \in [0,T]^n \textit{ and the nonnegative coeffi-}\\ &\textit{cients } (c_i)_{1\leqslant i\leqslant n} \textit{ such that } \sum_{i=1}^{n} c_i = C,\end{aligned} \tag{$\mathcal{P}$}$$

where the number of jumps, $n$, and the time horizon, $T$, are fixed and the cost functional $J$ stands for the total number of infected humans, given by

$$J(u) := \int_0^T I_H(t)dt. \tag{3.7}$$

Since we are going to deal with several jumps it is convenient to introduce some notation first. We consider $n$ jumps performed at times $t_i$, for $i = 1, \dots, n$. If needed for the sake of notational simplicity, we will denote $t_0 = 0$ and $t_{n+1} = T$. Since functions may present discontinuities we introduce the notations

$$F(t_i^-) := \lim_{t \to t_i^-} F(t), \qquad F(t_i^+) := \lim_{t \to t_i^+} F(t),$$

where $F(t)$ represents any function. We also introduce the characteristic function of a set $\mathcal{S}$, equal to 1 when its variable belongs to $\mathcal{S}$ and 0 elsewhere. In what follows, we will denote it $\mathbb{1}_{\mathcal{S}}$.

The equations for $M_S$ and $p$ in systems $(SIT)$ and $(WB')$ must be adapted to the impulsive formulation of the problem. By considering $u$ defined by $u(t) = \sum_{i=1}^{n} c_i \delta(t - t_i)$ in systems $(WB')$ and $(SIT)$ we can pass from a infinite dimensional optimization problem to a discrete one. Here we detail how, by doing this passage, these systems where the control appears become differential equations with jump discontinuities. In order to do so we consider $u$ given by $u(t) = \sum_{i=1}^{n} \frac{c_i}{\varepsilon} \mathbb{1}_{[t_i, t_i+\varepsilon]}$ and we take the limit $\varepsilon \to 0$. The following proof is adapted from [103]. We detail the deduction of equation (3.11). However, equation (3.8) can be easily obtained following the same reasoning.

**Proposition 3.1.** *Let us consider $p_\varepsilon$, solving the following equation*

$$\begin{cases} p'_\varepsilon(t) = f(p_\varepsilon(t)) + \frac{c_i}{\varepsilon} \mathbb{1}_{[t_i, t_i+\varepsilon]} g(p_\varepsilon(t)), \quad t \in [t_{i-1}, t_{i+1}] \\ p_\varepsilon(t_{i-1}) = p_{i-1}. \end{cases}$$

*Let $G$ be the antiderivative vanishing at zero of $1/g(p)$, that is $G(p) := \int_0^p \frac{dq}{g(q)}$. Then when $\varepsilon$ tends to 0, $p_\varepsilon(\cdot)$ converges pointwise to $p(\cdot)$ given by*

$$p(t) = \begin{cases} p^-(t), & t \in [t_{i-1}, t_i] \\ p^+(t), & t \in (t_i, t_{i+1}] \end{cases}$$

*where $p^-$ and $p^+$ solve*

$$\begin{cases} \frac{dp^-}{dt}(t) = f(p^-(t)) \\ p^-(t_{i-1}) = p_{i-1}, \end{cases} \quad \text{and} \quad \begin{cases} \frac{dp^+}{dt}(t) = f(p^+(t)) \\ p^+(t_i) = G^{-1}(G(p^-(t_i)) + c_i), \end{cases}$$

*respectively.*

*Proof.* Outside the interval $[t_i, t_i + \varepsilon]$ the behaviour of $p(t)$ is clear. We study the behaviour of $p_\varepsilon(t)$ in $[t_i, t_i + \varepsilon]$, in order to establish the jump of $p(t)$ at $t_i$.

$$p_\varepsilon(t) = p^-(t_i) + \int_{t_i}^{t} f(p_\varepsilon(s)) + \frac{c_i}{\varepsilon} g(p_\varepsilon(s)) ds,$$

then for every $t \in [t_i, t_i + \varepsilon]$, one has

$$\begin{aligned} |p_\varepsilon(t)| &\leqslant |p^-(t_i)| + \int_{t_i}^{t} |f(0)| + \frac{c_i}{\varepsilon} |g(0)| \, ds + \int_{t_i}^{t} \left( L_f + \frac{c_i}{\varepsilon} L_g \right) |p_\varepsilon(s)| \, ds \\ &\leqslant 1 + \frac{c_i}{K} + \int_{t_i}^{t} \left( L_f + \frac{c_i}{\varepsilon} L_g \right) |p_\varepsilon(s)| \, ds \end{aligned}$$

where $L_f$ and $L_g$ are the Lipschitz constants of $f(\cdot)$ and $g(\cdot)$ respectively. These constants exist

since both functions are $C^1$ in $[0,1]$. Using Grönwall's inequality we obtain that

$$|p_\varepsilon(t)| \leqslant \left(1+\frac{c_i}{K}\right)\exp\left(\varepsilon L_f + c_i L_g\right),$$

which is bounded. Let us consider now $z_\varepsilon$, the solution to

$$\begin{cases} z'_\varepsilon(t) = \frac{c_i}{\varepsilon} g(z_\varepsilon(t)) \\ z_\varepsilon(t_i) = p(t_i^-), \end{cases}$$

We prove now that, in the limit, both $z_\varepsilon$ and $p_\varepsilon$ present the same jump at $t_i$. In order to do this we compute for $t \in [t_i, t_i+\varepsilon]$,

$$\begin{aligned} |z_\varepsilon(t) - p_\varepsilon(t)| &\leqslant \int_{t_i}^t |f(p_\varepsilon(s))|\,ds + \int_{t_i}^t \frac{c_i}{\varepsilon}\,|g(z_\varepsilon(s)) - g(p_\varepsilon(s))|\,ds \\ &\leqslant \varepsilon M_f + \int_{t_i}^t \frac{c_i}{\varepsilon} L_g\,|z_\varepsilon(s) - p_\varepsilon(s)|\,ds \end{aligned}$$

where $M_f = \max_{p\in[0,1]} f(p)$. Using again Grönwall's Lemma we obtain

$$|z_\varepsilon(t) - p_\varepsilon(t)| \leqslant \varepsilon M_f \exp\left(c_i L_g\right) \to 0 \text{ as } \varepsilon \to 0.$$

This proves that $\sup_{t\in[t_i,t_i+\varepsilon]} |z_\varepsilon(t) - p_\varepsilon(t)| \to 0$ when $\varepsilon \to 0$, and therefore $z_\varepsilon$ and $p_\varepsilon$ present the same jump at $t_i$ in the limit. To conclude, we solve $z_\varepsilon(t)$ in $[t_i, t_i+\varepsilon]$,

$$\int_{t_i}^{t_i+\varepsilon} \frac{z'(s)}{g(z_\varepsilon(s))} ds = \int_{t_i}^{t_i+\varepsilon} \frac{c_i}{\varepsilon} ds = c_i,$$

which leads to $G(z_\varepsilon(t_i+\varepsilon)) - G(z_\varepsilon(t_i)) = c_i$ and thus $z_\varepsilon(t_i+\varepsilon) = G^{-1}(G(z_\varepsilon(t_i)) + c_i)$. Taking the limit $\varepsilon \to 0$ we conclude that $p^+(t_i) = G^{-1}(G(p^-(t_i)) + c_i)$.

□

Proposition 3.1 can be used to deduce the differential equations with jump discontinuities that follow $M_S$ and $p$ in systems $(SIT)$ and $(WB')$ repectively.

### 3.3.1 Sterile insect technique

In order to find the equation satisfied by $M_S$ we take

$$u(t) = \sum_{i=1}^n \frac{c_i}{\varepsilon} \mathbb{1}_{[t_i, t_i+\varepsilon]},$$

so the equation satisfied by $M'_S$ becomes

$$M'_S(t) = \sum_{i=1}^n \frac{c_i}{\varepsilon} \mathbb{1}_{[t_i, t_i+\varepsilon]} - d_S M_S(t).$$

Taking the limit $\varepsilon \to 0$ we obtain that the equation converges to

$$\begin{cases} M'_S(t) &= -d_S M_S(t), \quad t \in [t_i, t_{i+1}], \quad i = 0, \dots, n \\ M_S(t_i^+) &= M_S(t_i^-) + c_i, \quad i = 1, \dots, n \end{cases} \tag{3.8}$$

We can solve this equation explicitly. Since the initial condition is $M_S(0) = 0$ the solution reads

$$M_S(t) = \sum_{j=1}^{i} c_j e^{-d_S(t-t_j)}, \quad t \in [t_i, t_{i+1}], \quad i = 1, \dots, n \tag{3.9}$$

### 3.3.2 *Wolbachia* method

Looking at the equation on $p$ in system $(WB')$ and substituting the control function by

$$u(t) = \sum_{i=1}^{n} \frac{c_i}{\varepsilon} \mathbb{1}_{[t_i, t_i+\varepsilon]},$$

we obtain

$$p'(t) = f(p(t)) + g(p(t)) \sum_{i=1}^{n} \frac{c_i}{\varepsilon} \mathbb{1}_{[t_i, t_i+\varepsilon]}. \tag{3.10}$$

Let $G$ be the antiderivative vanishing at zero of $1/g(p)$, that is $G(p) := \int_0^p \frac{dq}{g(q)}$, when we take the limit $\varepsilon \to 0$ in equation (3.10) we obtain:

$$\begin{cases} p'(t) &= f(p(t)), \quad t \in [t_i, t_{i+1}], \quad i = 0, \dots, n \\ p(t_i^+) &= G^{-1}(G(p(t_i^-)) + c_i), \quad i = 1, \dots, n \end{cases} \tag{3.11}$$

## 3.4 Optimality conditions

We devote this section to the computation of the gradients of the functional $J$ in problem $(\mathcal{P})$ for systems $(SIT)$ and $(WB')$. These gradients will be used in the numerical simulations of section 3.5. We discuss it first in a general setting to later apply to our problems.

Let $\mathbf{X} : \mathbb{R}^+ \to \mathbb{R}^N$ be the solution to

$$\begin{cases} \mathbf{X}'(t) = A(\mathbf{X}(t)) + B(\mathbf{X}(t))y(t), \quad t \in [0, T] \\ \mathbf{X}(0) = \mathbf{X_0}, \end{cases} \tag{3.12}$$

with $A, B : \mathbb{R}^+ \to \mathbb{R}^N$ continuous and $y : \mathbb{R}^+ \to \mathbb{R}$ the solution to the differential equation with jump discontinuities

$$\begin{cases} y'(t) = a(y(t)), & t \in [0, T] \setminus \{t_i\}_{i=1,\dots,n} \\ y(t_i^+) = b(y(t_i^-), c_i), & i = 1, \dots, n \end{cases}$$

with $a, b : \mathbb{R}^+ \to \mathbb{R}$. Now, consider $y_\varepsilon(t)$, the solution to

$$\begin{cases} y_\varepsilon'(t) = a(y_\varepsilon(t)), & t \in [0, T] \setminus \{t_i\}_{i=1,\dots,n} \\ y_\varepsilon(t_i^+) = b(y_\varepsilon(t_i^-), c_i), & i \neq k \\ y_\varepsilon(\tilde{t}_k^+) = b(y_\varepsilon(\tilde{t}_k^-), c_k), & \end{cases}$$

where $\tilde{t}_k = t_k + \varepsilon$. Finally, lets consider also $\mathbf{X}_\varepsilon$ the solution to

$$\begin{cases} \mathbf{X}_\varepsilon'(t) = A(\mathbf{X}_\varepsilon(t)) + B(\mathbf{X}_\varepsilon(t))y_\varepsilon(t), \quad t \in [0, T] \\ \mathbf{X}_\varepsilon(0) = \mathbf{X_0}, \end{cases}$$

We consider $\mathbf{X}$ to be a function of time, nevertheless, the value of the parameters $t_i$ and $c_i$,

$i = 1, \ldots, n$ affects the value of $\mathbf{X}(t)$ for any $t > t_1$. In general, and for the rest of the section, we define the variation of any given function of time, $F_\chi$, depending on a parameter, $\chi$, as

$$\delta_\chi F_\chi(t) := \lim_{\varepsilon \to 0} \frac{F_{\chi+\varepsilon}(t) - F_\chi(t)}{\varepsilon}.$$

As an example, in the case of the variation of $\mathbf{X}$ with respect to a given $t_k$ we have

$$\delta_{t_k} \mathbf{X}(t) := \lim_{\varepsilon \to 0} \frac{\mathbf{X}_\varepsilon(t) - \mathbf{X}(t)}{\varepsilon}.$$

From equation (3.12) we have that

$$\mathbf{X}(t) = \mathbf{X}_0 + \int_0^t A(\mathbf{X}(s))ds + \int_0^t B(\mathbf{X}(s))y(s)ds.$$

For a given $k \in \{1, \ldots, n\}$, in case $t < t_k$, one has $\delta_{t_k}\mathbf{X}(t) = 0$, since the time of the jump has no effect until it occurs. In case $t > t_k$

$$\begin{aligned}
\delta_{t_k}\mathbf{X}(t) &= \delta_{t_k} \int_0^t A(\mathbf{X}(s))ds + \delta_{t_k} \left( \int_0^{t_k} B(\mathbf{X}(s))y(s)ds + \int_{t_k}^t B(\mathbf{X}(s))y(s)ds \right) \\
&= \int_0^t \delta_{t_k} A(\mathbf{X}(s))ds + B(\mathbf{X}(t_k))y(t_k^-) - B(\mathbf{X}(t_k))y(t_k^+) + \int_0^t \delta_{t_k} \left( B(\mathbf{X}(s))y(s) \right) ds \\
&= \int_0^t \left( \mathbf{D}A(\mathbf{X}(s)) + \mathbf{D}B(\mathbf{X}(s))y(s) \right) \delta_{t_k}\mathbf{X}(s)ds + B(\mathbf{X}(t_k))(y(t_k^-) - y(t_k^+)) \\
&\quad + \int_0^t B(\mathbf{X}(s))\delta_{t_k} y(s)ds.
\end{aligned}$$

We can express this as an ordinary differential equation with a jump discontinuity:

$$\begin{cases}
\left(\delta_{t_k}\mathbf{X}\right)'(t) = \left(\mathbf{D}A(\mathbf{X}(t)) + \mathbf{D}B(\mathbf{X}(t))y(t)\right) \delta_{t_k}\mathbf{X}(t) + B(\mathbf{X}(t))\delta_{t_k} y(t), & t \in [0,T] \setminus \{t_k\} \\
\delta_{t_k}\mathbf{X}(0) = 0, \\
\delta_{t_k}\mathbf{X}(t_k^+) = \delta_{t_k}\mathbf{X}(t_k^-) + B(\mathbf{X}(t_k))(y(t_k^-) - y(t_k^+)).
\end{cases}$$

But since $\delta_{t_k}\mathbf{X}(t) = 0$ for $t < t_k$, we can simplify this system to:

$$\begin{cases}
\left(\delta_{t_k}\mathbf{X}\right)'(t) = \left(\mathbf{D}A(\mathbf{X}(t)) + \mathbf{D}B(\mathbf{X}(t))y(t)\right) \delta_{t_k}\mathbf{X}(t) + B(\mathbf{X}(t))\delta_{t_k} y(t), & t \in [t_k,T] \\
\delta_{t_k}\mathbf{X}(t_k^+) = B(\mathbf{X}(t_k))(y(t_k^-) - y(t_k^+))
\end{cases} \tag{3.13}$$

where $\delta_{t_k} y(t) := \lim_{\varepsilon \to 0}(y_\varepsilon(t) - y(t))/\varepsilon$.

Following the same lines we consider now $y_\varepsilon(t)$ as the solution to

$$\begin{cases}
y_\varepsilon'(t) = a(y_\varepsilon(t)), & t \in [0,T] \setminus \{t_i\}_{i=1,\ldots,n} \\
y_\varepsilon(t_i^+) = b(y_\varepsilon(t_i^-), c_i), & i \neq k, \\
y_\varepsilon(t_k^+) = b(y_\varepsilon(t_k^-), c_k + \varepsilon).
\end{cases}$$

In this case, for $t > t_k$ we have

$$\begin{aligned}\delta_{c_k}\mathbf{X}(t) &= \int_0^t \delta_{c_k}A(\mathbf{X}(s)) + \delta_{c_k}B(\mathbf{X}(s))y(s) + B(\mathbf{X}(s))\delta_{c_k}y(s)\,ds \\ &= \int_0^t \left(\mathbf{D}A(\mathbf{X}(s)) + \mathbf{D}B(\mathbf{X}(s))y(s)\right)\delta_{c_k}\mathbf{X}(s) + B(\mathbf{X}(s))\delta_{c_k}y(s)\,ds.\end{aligned}$$

Since $\delta_{c_k}\mathbf{X}(t) = 0$ for $t < t_k$, we can express this as the following ordinary differential equation:

$$\begin{cases} \left(\delta_{c_k}\mathbf{X}\right)'(t) = \left(\mathbf{D}A(\mathbf{X}(t)) + \mathbf{D}B(\mathbf{X}(t))y(t)\right)\delta_{c_k}\mathbf{X}(t) + B(\mathbf{X}(t))\delta_{c_k}y(t), \quad t \in [t_k, T] \\ \delta_{c_k}\mathbf{X}(t_k^+) = 0. \end{cases} \tag{3.14}$$

with, again, $\delta_{c_k}y(t) := \lim_{\varepsilon\to 0}(y_\varepsilon(t) - y(t))/\varepsilon$.

In problem $(\mathcal{P})$, the functional we want to minimize is $J(u) = \int_0^T I_H(t)dt$. Since $I_H(t)$ is continuous we have that

$$\delta_{t_k}J(u) = \int_0^T \delta_{t_k}I_H(t)dt,$$

we also have that $\delta_{c_k}J(u) = \int_0^T \delta_{c_k}I_H(t)dt$. Hereafter we use expressions (3.13) and (3.14) in order to compute $\delta_{t_k}J$ and $\delta_{c_k}J$ for systems $(SIT)$ and $(WB')$.

### 3.4.1 Sterile Insect Technique

We consider system $(SIT)$. The variable satisfying a differential equation with a jump discontinuity is $M_S(t)$. Therefore, considering $\mathbf{X}(t) = (S_H(t), E_H(t), I_H(t), S_M(t), E_M(t), I_M(t))$ and $y(t) = M_S(t)$ we find that $\delta_{t_k}J = \int_{t_k}^T \left(\delta_{t_k}\mathbf{X}(t)\right)_3 dt$ and $\delta_{c_k}J = \int_{t_k}^T \left(\delta_{c_k}\mathbf{X}(t)\right)_3 dt$ where $\delta_{t_k}\mathbf{X}(t)$ and $\delta_{c_k}\mathbf{X}(t)$ are defined by equations (3.13) and (3.14) respectively and the subscript stands for the third component of the vector. There are nonetheless two more terms to compute, $\delta_{t_k}M_S(t)$ and $\delta_{c_k}M_S(t)$. In the case of the Sterile Insect Technique we have a closed expression for $M_S(t)$, see equation (3.9), therefore the computation of the variation of $J$ with respect to $t_k$ and $c_k$ is straightforward. We have

$$\delta_{t_k}M_S(t) = \begin{cases} 0, & t \in [0, t_k] \\ d_S c_k e^{-d_S(t-t_k)} & t \in (t_k, T], \end{cases} \tag{3.15}$$

and

$$\delta_{c_k}M_S(t) = \begin{cases} 0, & t \in [0, t_k] \\ e^{-d_S(t-t_k)} & t \in (t_k, T]. \end{cases} \tag{3.16}$$

### 3.4.2 *Wolbachia* method

In the case of the use of *Wolbachia* (system $(WB')$) the variable satisfying a differential equation with a jump discontinuity is the proportion of *Wolbachia* infected mosquitoes, $p(t)$. We consider now $\mathbf{X}(t) = (S_H(t), E_H(t), I_H(t), E_M(t), I_M(t), E_W(t), I_W(t))$ and $y(t) = p(t)$. Once more, $\delta_{t_k}J = \int_{t_k}^T \left(\delta_{t_k}\mathbf{X}(t)\right)_3 dt$ and $\delta_{c_k}J = \int_{t_k}^T \left(\delta_{c_k}\mathbf{X}(t)\right)_3 dt$. Since the expressions of $\delta_{t_k}p(t)$ and $\delta_{c_k}p(t)$ are significantly harder to find than in the sterile insect case we compute them in the following propositions.

**Proposition 3.2.** *Let $p$ solve*

$$\begin{cases} p'(t) = f(p(t)) + \sum_{i=1}^{n} c_i \delta(t - t_i) g(p(t)), & t \in [0, T] \\ p(0) = p_0. \end{cases}$$

*with $p(t_i^+) \neq \theta$ for all $i = 1, \dots, n$. Let $c_i$ be fixed for all $i = 1, \dots, n$ and let $p_\varepsilon(t)$ solve*

$$\begin{cases} p'_\varepsilon(t) = f(p_\varepsilon(t)) + \sum_{\substack{i=1 \\ i \neq k}}^{n} c_i \delta(t - t_i) g(p(t)) + c_k \delta(t - (t_k + \varepsilon)) g(p_\varepsilon(t)), \\ p_\varepsilon(0) = p_0. \end{cases}$$

*Then, the variation of $p(t)$ with respect to $t_k$, $\delta_{t_k} p(t) := \lim_{\varepsilon \to 0} \frac{p_\varepsilon(T) - p(T)}{\varepsilon}$, is*

$$\delta_{t_k} p(t) = \begin{cases} 0, & t \in [0, t_k] \\ \frac{f(p(t_k^-)) g(p(t_k^+)) - f(p(t_k^+)) g(p(t_k^-))}{g(p(t_k^-))} \frac{f(p(t))}{f(p(t_i^+))} \prod_{j=k+1}^{i} \frac{g(p(t_j^+))}{g(p(t_j^-))} \frac{f(p(t_j^-))}{f(p(t_{j-1}^+))}, & t \in (t_i, t_{i+1}], k \leqslant i \leqslant n. \end{cases} \tag{3.17}$$

*Proof.* We begin considering $t \in [t_i, t_{i+1}]$. In each one of these intervals we have that $p'(t) = f(p(t))$. Since $f$ is bistable, $f(p) < 0$ in $(0, \theta)$ and $f(p) > 0$ in $(\theta, 1)$. Therefore, since we assumed $p(t_i^+) \neq \theta$ for all $i = 1, \dots, n$, $p(t)$ is injective in $[t_i, t_{i+1}]$, and we can write

$$\int_{p(t_i^+)}^{p(t)} \frac{dq}{f(q)} = t - t_i.$$

We define $F$ to be the antiderivative of $1/f$ vanishing at $p(t_i^+)$, that is $F(p) := \int_{p(t_i^+)}^{p} \frac{dq}{f(q)}$, thus we obtain the relationship

$$F(p(t)) - F(p(t_i^+)) = t - t_i. \tag{3.18}$$

We remark that $p(t) = p_\varepsilon(t)$ for all $t \in [0, t_k]$. Therefore in that interval $\delta_{t_k} p(t) = 0$. Hence, we can restrict ourselves to the case $k \leqslant i \leqslant n$. Differentiating implicitly this equation, we get

$$\frac{1}{f(p(t))} \delta_{t_k} p(t) - \frac{1}{f(p(t_i^+))} \delta_{t_k} p(t_i^+) = 0$$

and thus

$$\delta_{t_k} p(t) = \frac{f(p(t))}{f(p(t_i^+))} \delta_{t_k} p(t_i^+).$$

To compute $\delta_{t_k} p(t_i^+)$ we use that $p(t_i^+) = G^{-1}(G(p(t_i^-)) + c_i)$, therefore

$$\delta_{t_k} p(t_i^+) = (G^{-1})'(G(p(t_i^-)) + c_i) G'(p(t_i^-)) \delta_{t_k} p(t_i^-) = \frac{g(p(t_i^+))}{g(p(t_i^-))} \delta_{t_k} p(t_i^-)$$

where we used the inverse function theorem to write $(G^{-1})' = 1/(G' \circ G^{-1})$. Analogously to equation (3.18) we find that $F(p(t_i^-)) - F(p(t_{i-1}^+)) = t - t_{i-1}$, so $\delta_{t_k} p(t_i^-) = \frac{f(p(t_i^-))}{f(p(t_{i-1}^+))} \delta_{t_k} p(t_{i-1}^+)$. We can repeat this process iteratively until we get to $F(p(t_{k+1}^-)) - F(p(t_k^+)) = t - t_k$, then

$$\frac{1}{f(p(t_{k+1}^-))} \delta_{t_k} p(t_{k+1}^-) = -1 + \frac{1}{f(p(t_k^+))} \delta_{t_k} p(t_k^+) = -1 + \frac{1}{f(p(t_k^+))} \frac{g(p(t_k^+))}{g(p(t_k^-))} \delta_{t_k} p(t_k^-)$$

and $\delta_{t_k} p(t_k^-) = \delta_{t_k} \int_{t_{k-1}}^{t_k} (f(p(t)))dt = f(p(t_k^-))$ from which we can deduce the final expression. □

Note that in the expression of $\delta_{t_k} p(t)$ we are using the convention that if the productory subscript is bigger than the superscript, then its equal to 1.

**Proposition 3.3.** *Let $p$ solve*

$$\begin{cases} p'(t) = f(p(t)) + \sum_{i=1}^{n} c_i \delta(t - t_i) g(p(t)), \quad t \in [0, T] \\ p(0) = p_0. \end{cases}$$

*with $p(t_i^+) \neq \theta$ for all $i = 1, \ldots, n$. Let $t_i$ be fixed for all $i = 1, \ldots, n$ and let $p_\varepsilon(t)$ solve*

$$\begin{cases} p'_\varepsilon(t) = f(p_\varepsilon(t)) + \sum\limits_{\substack{i=1 \\ i \neq k}}^{n} c_i \delta(t - t_i) g(p_\varepsilon(t)) + (c_k + \varepsilon)\delta(t - t_k) g(p_\varepsilon(t)), \\ p_\varepsilon(0) = p_0. \end{cases}$$

*Then, the variation of $p(t)$ with respect to $c_k$, $\delta_{c_k} p(t) := \lim_{\varepsilon \to 0} \frac{p_\varepsilon(t) - p(t)}{\varepsilon}$, is*

$$\delta_{c_k} p(t) = \begin{cases} 0, \quad t \in [0, t_k] \\ g(p(t_k^+)) \frac{f(p(t))}{f(p(t_i^+))} \prod\limits_{j=k+1}^{i} \frac{g(p(t_j^+))}{g(p(t_j^-))} \frac{f(p(t_j^-))}{f(p(t_{j-1}^+))}, \quad t \in (t_i, t_{i+1}], k \leqslant i \leqslant n. \end{cases} \tag{3.19}$$

*Proof.* Following a very similar process to the one carried out in the proof of Proposition 3.2, we obtain $\delta_{c_k} p(t) = \frac{f(p(t))}{f(p(t_i^+))} \delta_{c_k} p(t_i^+)$. In problem $(\mathcal{P})$, the $c_i$ must satisfy the constraint $\sum_{i=1}^{n} c_i = C$, but we are not dealing with this constraint for the moment, therefore $\delta_{c_k} c_i = \delta_{ki}$, where $\delta_{ki}$ is the Kronecker's delta.

We compute $\delta_{c_k} p(t_i^+)$, obtaining

$$\begin{aligned} \delta_{c_k} p(t_i^+) &= (G^{-1})'(G(p(t_i^-)) + c_i) \left( G'(p(t_i^-)) \delta_{c_k} p(t_i^-) + \delta_{ki} \right) \\ &= \frac{g(p(t_i^+))}{g(p(t_i^-))} \delta_{c_k} p(t_i^-) + \delta_{ki} g(p(t_i^+)). \end{aligned}$$

Following the same lines of the proof of Proposition 3.2, from equation (3.18) applied in the interval $[t_{i-1}, t_i]$, differentiating implicitly we obtain $\delta_{c_k} p(t_i^-) = \frac{f(p(t_i^-))}{f(p(t_{i-1}^+))} \delta_{c_k} p(t_{i-1}^+)$. Finally, iterating the process until the interval $[t_k, t_{k+1}]$ and rearranging the terms we obtain the result. □

## 3.5 Results

We present in this section the optimal solutions of problem $(\mathcal{P})$, obtained through numerical simulations. We optimize simultaneously the time profile of the releases and the amount of mosquitoes released in each one. We allow two releases to occur at the same time. This implies that at that time a release with the total amount of mosquitoes of the two releases combined is done, reducing the number of effective releases by one. The simulations have been performed using *Python*. For the numerical optimization, the time variables are updated by using a standard step variable gradient descent method. Regarding the weights $(c_i)_{1 \leqslant i \leqslant n}$, due to the constraint $\sum_{i=1}^{n} c_i = C$, we used an augmented Lagrangian algorithm. An explanation of the method used

can be found in section 3.6. The details about the computation of the gradients of the functional are detailed in section 3.4. The models considered in this work capture the essence of the interaction of the modified vectors with the disease and its effect on the transmission. Nevertheless, in order to be precise, more complex models should be considered. These simulations do not intend to give quantitative results, but rather qualitative ones.

To model the start of an outbreak we place ourselves in the context of a fully susceptible population where there are present a small amount of infected humans and mosquitoes. Since in our model the total amount of humans is constant and since we consider at $t = 0$ the mosquito compartment at equilibrium, we need to subtract this initial amount of infectious from the respective susceptible compartments. Thus, the initial conditions for our simulations will be

$$(S_H(0), E_H(0), I_H(0), S_M(0), E_M(0), I_M(0)) = (H - I_H^0, 0, I_H^0, K^* - I_M^0, 0, I_M^0),$$

with $I_H^0 \ll H$ and $I_M^0 \ll K^*$ (in particular for the simulations we chose $I_H^0 = I_M^0 = 20$). All the other variables in the two systems are set to 0 at the start, namely

$$M_S(0) = 0 \quad \text{and} \quad (E_W(0), I_W(0), p(0)) = (0, 0, 0).$$

Since $R_0^M$ is greater than 1, this will lead to an outbreak of the disease and a spike in the number of cases. We perform several simulations for different values of $C$. Throughout the simulations we will fix the parameters of the systems to the values in Table 3.1, which correspond to the particular case of dengue.

Table 3.1 – Parameter values for dengue

| Category | Parameter | Name | Value | Source |
|---|---|---|---|---|
| Biology | $b_M$ | Wild mosquitoes birth rate | 4.4 day$^{-1}$ | [10, 132] [1] |
| | $b_W$ | *Wolbachia* infected birth rate | 3.96 day$^{-1}$ | [10, 132] |
| | $d_M$ | Wild mosquitoes death rate | 0.04 day$^{-1}$ | [10, 132] |
| | $d_W$ | *Wolbachia* infected death rate | 0.044 day$^{-1}$ | [10, 132] |
| | $d_S$ | Sterile mosquitoes death rate | 0.12 day$^{-1}$ | [6] |
| | $s_h$ | Cytoplasmic incompatibility level | 0.9 | [10] |
| | $s_c$ | Competitiveness level | 0.9 | |
| | $K$ | Carrying capacity | 65234 [2] | |
| | $b_H$ | Human birth/death rate | 0.013 year$^{-1}$ | |
| | $\sigma_H$ | Human recover time | 0.2 day$^{-1}$ | [102] |
| | $H$ | Human population size | 65000 | [70] |
| | $\beta_M$ | Transmission rate H↔M | 0.1647 day$^{-1}$ | [102] |
| | $\beta_{HW}$ | Transmission rate H→W | 0.157 day$^{-1}$ | [102] |
| | $\beta_{WH}$ | Transmission rate H←W | 0.0785 day$^{-1}$ | [102] |
| | $\gamma_M$ | Non infected incubation period | 0.186 day$^{-1}$ | [157] |
| | $\gamma_W$ | *Wolbachia* infected incubation period | 0.146 day$^{-1}$ | [157] |
| | $\gamma_H$ | Human incubation period | 0.17 day$^{-1}$ | [36] |
| Optimization | $T$ | Final time | 450 days | |
| | $C$ | Amount of mosquitoes released | $10^4$ - $6 \cdot 10^7$ | |

1. In the model studied in [132] the term accounting for the birth of mosquitoes is not straightforwardly equivalent to the one in our model. Its value has been adapted in order to account for this difference.

2. $K$ to $H$ ratios present a huge variability in the literature. Indeed, the ratio may depend on numerous factors and may not be constant in time. Lacking on solid evidence to pick a value, we choose $K$ such that the size of the mosquito population at equilibrium is equal to the human population size.

### 3.5.1 Sterile Insect Technique

The optimal solution for problem $(\mathcal{P})$ in the SIT setting consists of a combination of consecutive pulses with a similar spacing. The fact that several spaced jumps are more efficient in reducing the number of susceptible mosquitoes, eventually leading to a reduction in the number of infections, is a result of the fact that the amount of sterile mosquitoes decreases exponentially between releases. Therefore, by spacing the releases a population of sterile mosquitoes can be sustained longer than doing one single release with all the mosquitoes together. We also observe that results do not only depend on the amount of mosquitoes released, but also in the number of releases considered. Comparing Figures 3.1 and 3.2 we can see how, by increasing the number of releases from 10 to 20, the final amount of infections is considerably reduced, specially with a comparatively high amount of mosquitoes. Nevertheless, this trend does not continue indefinitely. Increasing the number of releases way above 20 does not reduced significantly the number of infections anymore, even though there is no clear cut in the number of releases for which the reduction is significant and may depend on the $C$ considered. The times and costs of the instant releases at Figures 3.1 and 3.2 are given in Tables 3.2 and 3.3 respectively.

Table 3.2 – Results of the simulations performed for the SIT with 10 releases

| $C$ | Time of releases | Amount of mosquitoes released | $\int_0^T I_H(t)dt$ |
|---|---|---|---|
| $3 \cdot 10^7$ | $t_1 = 172.0$, $t_2 = 178.4$<br>$t_3 = 185.6$, $t_4 = 193.0$<br>$t_5 = 200.7$, $t_6 = 208.7$<br>$t_7 = 217.3$, $t_8 = 226.6$<br>$t_9 = 237.0$, $t_{10} = 249.1$ | $c_1 = 2277164.9$, $c_2 = 3118801.0$<br>$c_3 = 3457741.0$, $c_4 = 3525953.9$<br>$c_5 = 3458904.6$, $c_6 = 3328601.2$<br>$c_7 = 3157284.8$, $c_8 = 2932013.1$<br>$c_9 = 2615241.0$, $c_{10} = 2128294.3$ | 250375.4 |
| $6 \cdot 10^7$ | $t_1 = 78.8$, $t_2 = 90.3$<br>$t_3 = 102.9$, $t_4 = 116.3$<br>$t_5 = 130.6$, $t_6 = 146.3$<br>$t_7 = 163.5$, $t_8 = 182.9$<br>$t_9 = 205.0$, $t_{10} = 230.8$ | $c_1 = 6568442.3$, $c_2 = 8417318.4$<br>$c_3 = 8619401.9$, $c_4 = 8082975.5$<br>$c_5 = 7239149.0$, $c_6 = 6225676.6$<br>$c_7 = 5173640.8$, $c_8 = 4146284.4$<br>$c_9 = 3194370.6$, $c_{10} = 2332740.8$ | 72862.0 |

As we can observe in Figures 3.1 and 3.2, with a comparatively low amount of mosquitoes, $C = 3 \cdot 10^7$, the releases are concentrated around the peak of the infections, with the largest releases occurring right during the peak. Their effect is of only mitigating the outbreak, that is, the curve of infections remains fairly similar but peaking a bit earlier and lower. For this amount of mosquitoes we do not observe a great reduction in the number of cases by using 20 releases instead of 10. Namely, for 10 releases we obtain $J_{10} = 250375.4$ and for 20, $J_{20} = 244012.2$. We can compute the reduction in the number of cases by comparing, numerically, $J(u)$ for the uncontrolled system with $J(u)$ for the controlled one. The value of $J(u) = \int_0^T I_H(t)dt$ in the case of the uncontrolled system yields $J_0 = 293644.1$. This means that with $C = 3 \cdot 10^7$ we obtain approximately a 14.7% reduction in the total amount of cases for 10 releases and a 16.9% reduction for 20.

A possible interpretation for this solution is that, with the amount of mosquitoes considered, the population of susceptible mosquitoes cannot be consistently kept low for a long period. Therefore, the best use of the sterile males is to release them to reduce as much as possible the amount of susceptible mosquitoes when the transmission is at its prime.

On the other hand, with a comparatively big amount of mosquitoes, $C = 6 \cdot 10^7$, the releases shift to the beginning and present an asymmetrical, skewed shape. We see this happening with 10 releases, attenuating considerably further the outbreak, but even more in the case with 20 releases. In this case, the first release occurs at $t_1 = 0.0$ and it results in an almost complete

Table 3.3 – Results of the simulations performed for the SIT with 20 releases

| $C$ | Time of releases | Amount of mosquitoes released | $\int_0^T I_H(t)dt$ |
|---|---|---|---|
| $3 \cdot 10^7$ | $t_1 = 167.7$, $t_2 = 171.5$<br>$t_3 = 175.7$, $t_4 = 179.9$<br>$t_5 = 184.0$, $t_6 = 188.1$<br>$t_7 = 192.1$, $t_8 = 196.1$<br>$t_9 = 200.2$, $t_{10} = 204.4$<br>$t_{11} = 208.7$, $t_{12} = 213.2$<br>$t_{13} = 217.8$, $t_{14} = 222.7$<br>$t_{15} = 227.8$, $t_{16} = 233.3$<br>$t_{17} = 239.1$, $t_{18} = 245.5$<br>$t_{19} = 252.4$, $t_{20} = 259.9$ | $c_1 = 1084557.5$, $c_2 = 1529725.4$<br>$c_3 = 1720612.9$, $c_4 = 1786314.4$<br>$c_5 = 1793907.7$, $c_6 = 1781311.8$<br>$c_7 = 1750939.8$, $c_8 = 1708089.2$<br>$c_9 = 1674451.1$, $c_{10} = 1653637.3$<br>$c_{11} = 1641097.9$, $c_{12} = 1597815.1$<br>$c_{13} = 1544202.8$, $c_{14} = 1491664.7$<br>$c_{15} = 1438846.7$, $c_{16} = 1380652.5$<br>$c_{17} = 1308476.4$, $c_{18} = 1199302.0$<br>$c_{19} = 1056512.9$, $c_{20} = 857882.1$ | 244012.2 |
| $6 \cdot 10^7$ | $t_1 = 0.0$, $t_2 = 3.7$<br>$t_3 = 8.2$, $t_4 = 13.0$<br>$t_5 = 18.1$, $t_6 = 23.4$<br>$t_7 = 29.2$, $t_8 = 35.5$<br>$t_9 = 42.4$, $t_{10} = 50.2$<br>$t_{11} = 59.0$, $t_{12} = 69.1$<br>$t_{13} = 80.8$, $t_{14} = 94.2$<br>$t_{15} = 109.9$, $t_{16} = 128.1$<br>$t_{17} = 149.5$, $t_{18} = 174.9$<br>$t_{19} = 205.7$, $t_{20} = 243.9$ | $c_1 = 4230525.4$, $c_2 = 4214863.5$<br>$c_3 = 4175080.6$, $c_4 = 4104782.5$<br>$c_5 = 4025147.5$, $c_6 = 3942640.9$<br>$c_7 = 3855009.1$, $c_8 = 3759644.0$<br>$c_9 = 3651466.3$, $c_{10} = 3522392.6$<br>$c_{11} = 3362768.5$, $c_{12} = 3162408.6$<br>$c_{13} = 2913468.2$, $c_{14} = 2614816.3$<br>$c_{15} = 2275534.3$, $c_{16} = 1912277.7$<br>$c_{17} = 1548925.6$, $c_{18} = 1209010.4$<br>$c_{19} = 911714.1$, $c_{20} = 607524.1$ | 2124.4 |

eradication of the outbreak. The largest releases occur soon after the first one. Releases get more sparse and smaller as time advances, specially for 20 releases, where some of them are clearly detached from the rest and occur after the peak of the outbreak. The fact that mosquitoes keep being released once the outbreak is suppresed is related to the fact that our model does not incorporate an Allee effect. This means that even when the wild mosquito population is very low, it can grow again to its initial values if the releases of sterile mosquitoes stop. Therefore, releases of small amounts of mosquitoes are needed so the outbreak does not start again inside the time horizon considered. The difference observed as a result of the different number of jumps in this case is more abrupt. We obtain a value of $J_{10} = 72862.0$ for 10 releases, which means a 75.2% less infections in the time window considered, and a value of $J_{20} = 2124.4$ for 20 releases, that is, a 99.3% reduction.

With this amount of mosquitoes, specially when they are spread over 20 releases, the population can be kept low for a long time. Our interpretation of these results is that, due to this capability of long term population reduction, the optimal solution consists in releasing as soon as possible, preventing the outbreak from gaining traction in the first place. Then, smaller releases keep being done to prevent the population from increasing again. Hence, being able to divide the mosquitoes in more releases becomes more important in this case. We see clearly how the number of releases can affect the outcome, even for the same $C$, in the lower rows of figures 3.1 and 3.2. With 10 releases, although initially the outbreak is greatly reduced, the population cannot be kept low consistently in all the time window considered and the cases rise again substantially towards the end.

Another approach we can take, arguably more in line with applications on the field, is to optimize only the times of the releases while keeping the amount of mosquitoes constant. This corresponds to having the mosquitoes conditioned in recipients all containing approximately the

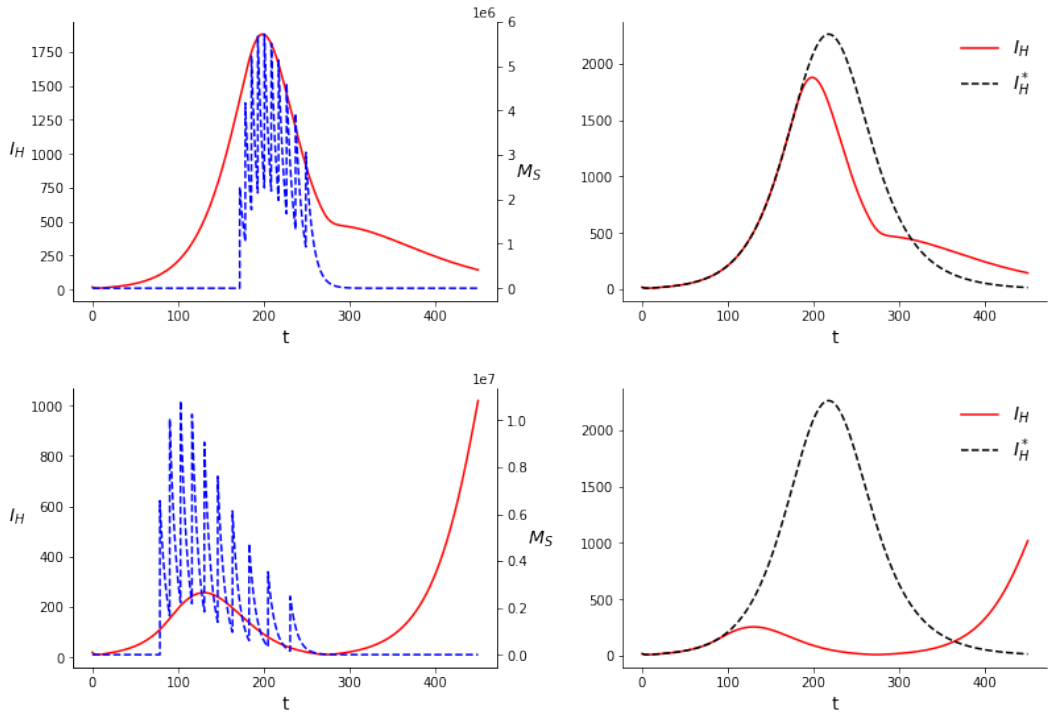


Figure 3.1 – Results of the simulations for the SIT with $C = 3 \cdot 10^7$ (upper row) and $C = 6 \cdot 10^7$ (lower row) considering 10 releases. The dashed blue line corresponds to the amount of sterile mosquitoes released. $I_H^*$, on the right column, corresponds to the uncontrolled case.

same number of individuals. Of course, the result in the reduction of the infections will be worse than the counterpart we have just presented. Nevertheless it raises a reasonable question: to which extent it is preferable the use of a more sophisticated technique over a less efficient but simpler one? The results are presented tables 3.4 and 3.5.

Table 3.4 – Results of the simulations performed for the SIT with 10 releases and all $c_i = C/10$.

| $C$ | Time of releases | $\int_0^T I_H(t)dt$ |
|---|---|---|
| $3 \cdot 10^7$ | $t_1 = 173.2$, $t_2 = 180.6$, $t_3 = 187.4$, $t_4 = 194.1$, $t_5 = 201.1$<br>$t_6 = 208.3$, $t_7 = 216.3$, $t_8 = 225.1$, $t_9 = 235.4$, $t_{10} = 248.0$ | 250880.3 |
| $6 \cdot 10^7$ | $t_1 = 98.4$, $t_2 = 109.2$, $t_3 = 119.5$, $t_4 = 130.1$, $t_5 = 141.5$<br>$t_6 = 154.3$, $t_7 = 169.0$, $t_8 = 186.5$, $t_9 = 208.3$, $t_{10} = 236.4$ | 99223.3 |

In figures 3.3 and 3.4 we can see that optimal strategies in time do not differ a lot with those of figures 3.1 and 3.2 respectively. Still, releases are done around the peak of the outbreak in the case of a relatively low amount of mosquitoes. As we increase the amount of mosquitoes and the number of releases they shift to the left, resulting in a further reduction of the infections.

As for the effectiveness of this approach, we show a comparison of the results of the optimization of the times alone and that of the times and the costs in tables 3.6 and 3.7. As we can see there does not seem to be a significant advantage in optimizing both times and costs except in one case, the case with $C = 6 \cdot 10^7$ and 10 releases.

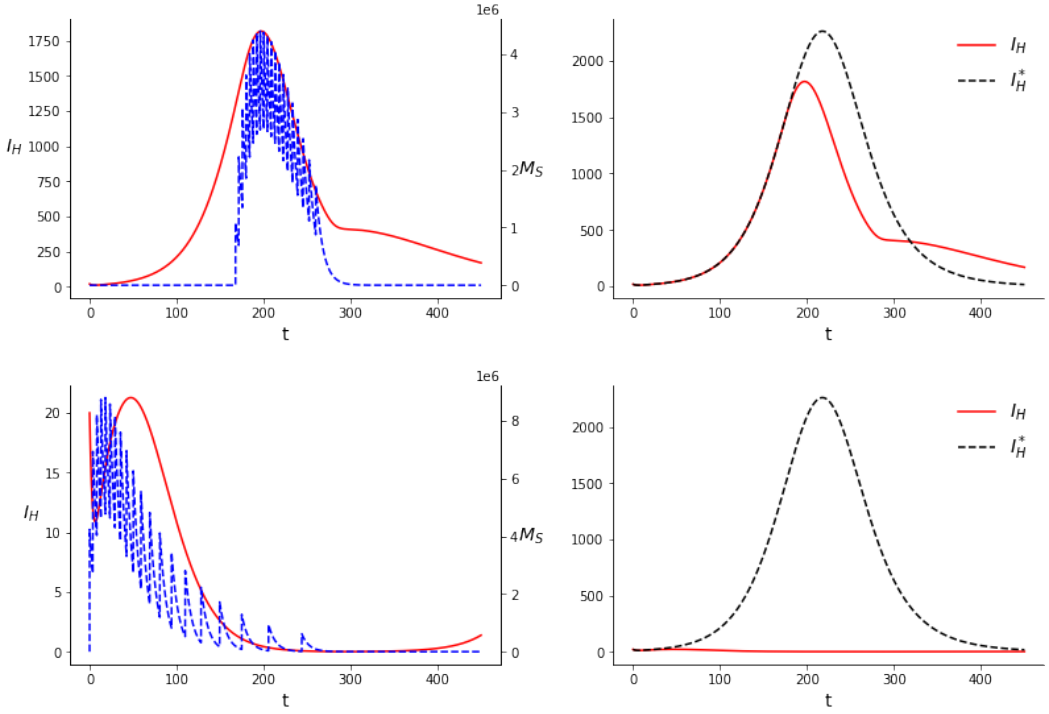


Figure 3.2 – Results of the simulations for the SIT with $C = 3 \cdot 10^7$ (upper row) and $C = 6 \cdot 10^7$ (lower row) considering 20 releases.

Table 3.5 – Results of the simulations performed for the SIT with 20 releases and all $c_i = C/20$.

| $C$ | Time of releases | $\int_0^T I_H(t)dt$ |
|---|---|---|
| $3 \cdot 10^7$ | $t_1 = 168.3$, $t_2 = 172.8$, $t_3 = 176.8$, $t_4 = 180.6$, $t_5 = 184.2$<br>$t_6 = 187.8$, $t_7 = 191.4$, $t_8 = 195.0$, $t_9 = 198.7$, $t_{10} = 202.5$<br>$t_{11} = 206.5$, $t_{12} = 210.6$, $t_{13} = 214.9$, $t_{14} = 219.5$, $t_{15} = 224.4$<br>$t_{16} = 229.8$, $t_{17} = 235.7$, $t_{18} = 242.3$, $t_{19} = 250.0$, $t_{20} = 259.5$ | 244623.4 |
| $6 \cdot 10^7$ | $t_1 = 0.0$, $t_2 = 3.8$, $t_3 = 8.0$, $t_4 = 12.4$, $t_5 = 17.0$<br>$t_6 = 21.7$, $t_7 = 26.8$, $t_8 = 32.1$, $t_9 = 38.0$, $t_{10} = 44.4$<br>$t_{11} = 51.6$, $t_{12} = 59.6$, $t_{13} = 68.9$, $t_{14} = 79.7$, $t_{15} = 92.6$<br>$t_{16} = 108.1$, $t_{17} = 127.4$, $t_{18} = 151.7$, $t_{19} = 183.3$, $t_{20} = 225.5$ | 2556.1 |

The fact that the optimal strategy can change significantly when the number of releases is increased suggests that solutions for this setting are very sensitive to changes on the problem characteristics. Comparing figures 3.1 with 3.3, and 3.2 with 3.4, we see that optimizing the amount of mosquitoes at each release makes the first releases move to the left but also increases their time span, a similar effect to the addition of new releases. Elaborating further in our biological interpretation of the results, this suggests that for ten releases and $C = 6 \cdot 10^7$ we can keep the population low during a certain amount of time, but not enough to prevent the outbreak. A slight improvement of the technique in this setting (either an increase in the number of releases or an optimization of the number of mosquitoes released at each impulse) can make

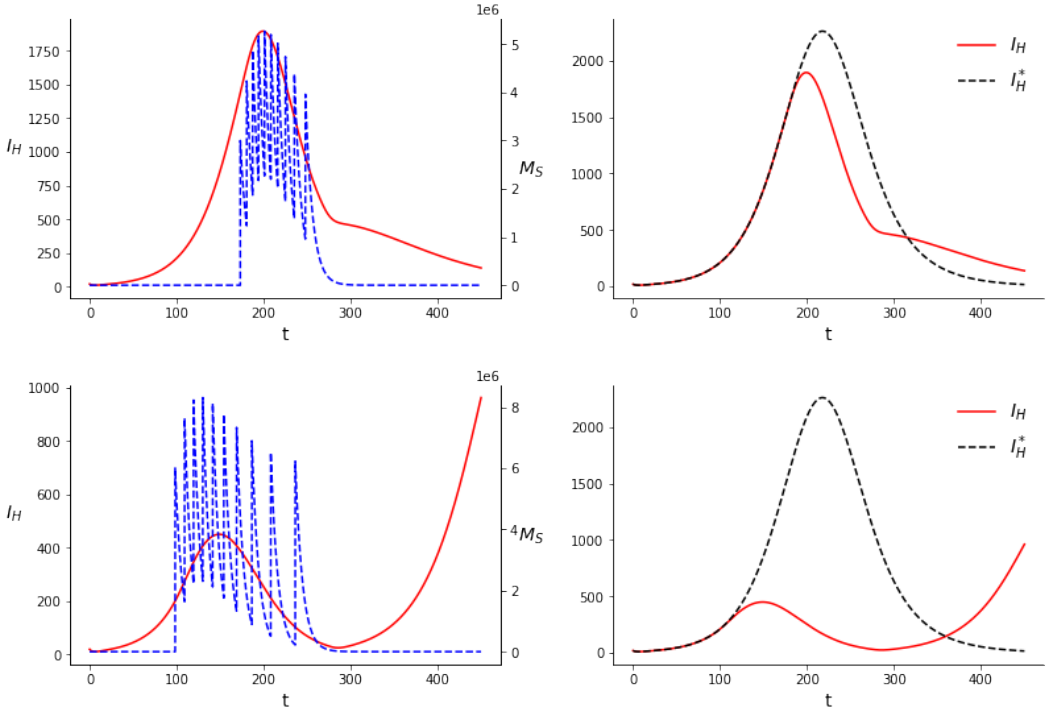


Figure 3.3 – Results of the simulations for the SIT with $C = 3 \cdot 10^7$ (upper row) and $C = 6 \cdot 10^7$ (lower row) considering 10 releases and an equal distribution of the mosquitoes between the releases.

a difference in the ability to control the outbreak by keeping the wild mosquito population at a low level over a longer period of time, thus improving the results. On the other hand, when we are far from significantly reducing the outbreak or when we can almost prevent it, the advantage of also optimizing the amount of mosquitoes at each release becomes smaller.

Table 3.6 – Comparison of the reductions in the infections obtained on the simulations performed for the SIT with 10 releases.

| $C$ | Times | Times and costs |
|---|---|---|
| $3 \cdot 10^7$ | 14.6% | 14.7% |
| $6 \cdot 10^7$ | 66.2% | 75.1% |

Table 3.7 – Comparison of the reductions in the infections obtained on the simulations performed for the SIT with 20 releases.

| $C$ | Times | Times and costs |
|---|---|---|
| $3 \cdot 10^7$ | 16.7% | 16.9% |
| $6 \cdot 10^7$ | 99.1% | 99.3% |

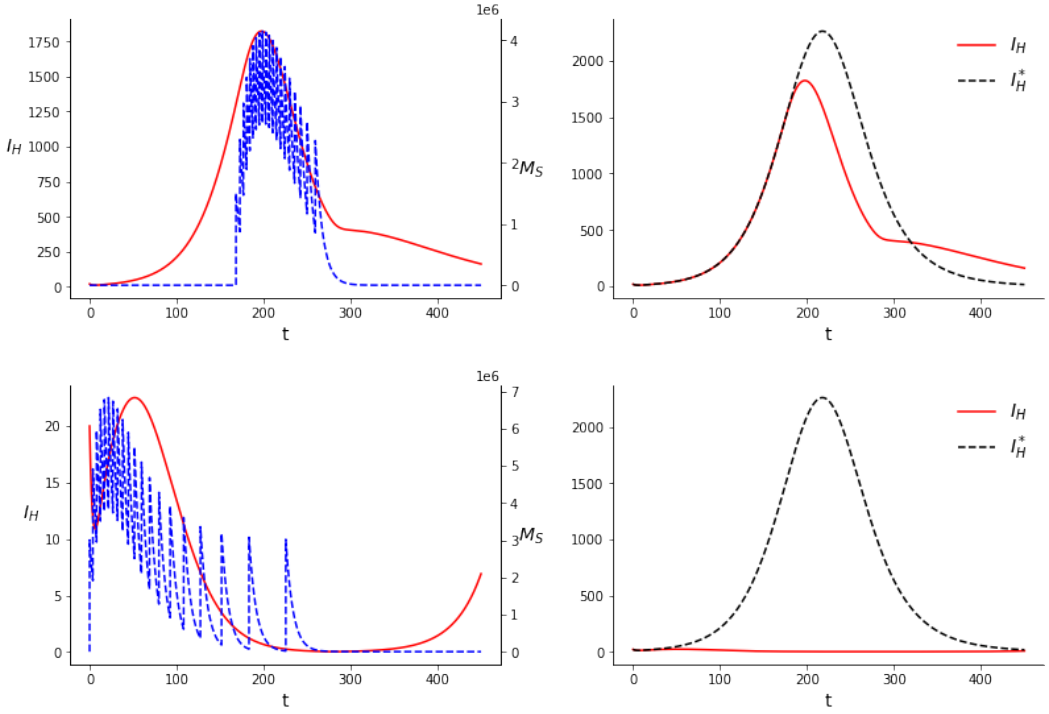


Figure 3.4 – Results of the simulations for the SIT with $C = 3 \cdot 10^7$ (upper row) and $C = 6 \cdot 10^7$ (lower row) considering 20 releases and an equal distribution of the mosquitoes between the releases.

### 3.5.2 *Wolbachia* method

Regarding the *Wolbachia* method in all cases all the pulses cluster in one single pulse. In other words, the optimal solution is performing a single release with all the available mosquitoes. This makes useless to optimize the amount of mosquitoes released in each jump and turns the problem into a one-dimensional optimization one: $\min_{t_1 \in [0,T]} J(u)$, with $J(u) = \int_0^T I_H(t)dt$ and $u(t) = C\delta(t - t_1)$.

As found in other works studying the use of *Wolbachia* to produce a mosquito population replacement [4, 10], solutions present two clearly distinct behaviours. Since the equation $p' = f(p)$ is bi-stable, if the proportion of *Wolbachia* infected mosquitoes exceeds a certain threshold, $p = \theta$, then the system moves to a full invasion state without further intervention. The parameter determining the two regimes is the total amount of mosquitoes, $C$. If there are more mosquitoes than the amount needed to lead the system to $p = \theta$ we will observe one kind of behaviour, different from the case where there are less. From the initial conditions we have $p(0) = 0$. We can compute the amount of mosquitoes needed to reach $p = \theta$ in a single jump. If we reach $p = \theta$ in the first jump, $\theta = p(t_1^+) = G^{-1}\left(G(p(t_1^-) + C)\right) = G^{-1}(C)$, thus $C = G(\theta)$. For the parameters considered here, $G(\theta) \approx 14850$.

In figure 3.5 we plot the optimal solutions to problem $(\mathcal{P})$ for system $(WB')$ with the parameters of table 3.1. In case $C < G(\theta)$ the jump occurs before the outbreak reaches its peak. The larger is $C$, the smaller is $t_1$. In Figure 3.5, for $C = 10000$, $t_1 = 147.5$. Instead, in case $C > G(\theta)$ the jump is at $t_1 = 0$. The system from this point tends to $p = 1$ without the need of releasing

mosquitoes anymore. The value of $J(u) = \int_0^T I_H(t)dt$ in the case of the uncontrolled system yields $J_0 = 294501.4$. With $C = 10000$ the profile of the outbreak is not altered very much, but it peaks at a lower value. The value of $J(u)$ in this case is $J_{10000} = 288362.7$, roughly a 2.1% reduction in the total amount of cases. With $C = 20000$ the change is the infected humans curve is much more appreciable. The curve peaks at a much lower level but decays slower. In this case the value of $\int_0^T I_H(t)dt$ is $J_{20000} = 128899.1$, which is a 56.2% reduction in the number of cases.

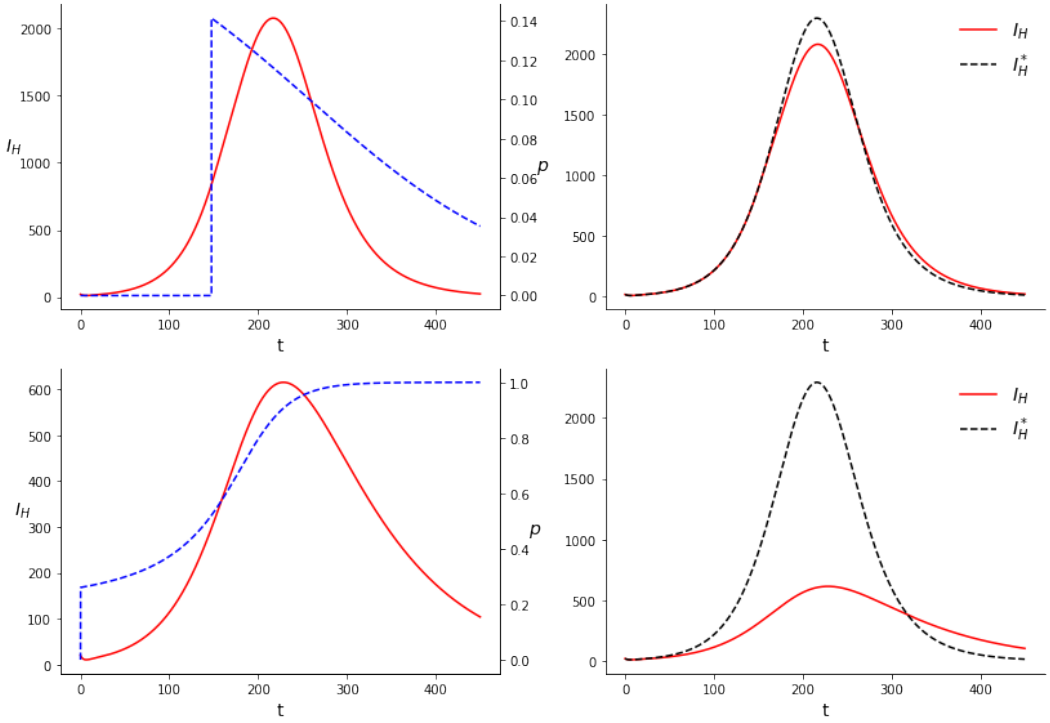


Figure 3.5 – Results of the simulations for the *Wolbachia* method with $C = 10000$ (upper row) and $C = 20000$ (lower row). The proportion of *Wolbachia* infected mosquitoes corresponds to the dashed blue line on the left column. $I_H^*$, on the right column, corresponds to the uncontrolled case.

The biological interpretation of these results is in line with the one for the sterile mosquitoes. When it is not possible to trigger a population replacement, the optimal strategy is to release the mosquitoes before the peak of the epidemic. Since the number of Wolbachia-infected mosquitoes declines with time, this policy minimizes the presence of the wild mosquitoes (with a greater vector capacity) during the phase of largest transmission. On the other hand, if it is possible to trigger the population replacement, the sooner we act in the system, the better. Since the proportion of Wolbachia-infected mosquitoes is going to increase naturally there are no incentives in waiting to make the release.

We remark that the amount of mosquitoes needed for this technique to be effective is much lower than for the SIT. This makes sense, since the *Wolbachia* population is self-sustainable while the sterile mosquitoes must be constantly released. Nonetheless, the exact values of mosquitoes released, or the ratio of mosquitoes needed in one technique with respect to the other cannot be drawn directly from our study due to the limitations of the model and the uncertainty on the

parameters.

## 3.6 Numerics: an augmented Lagrangian algorithm

In this section, we explain and detail further the numerical method used for obtaining the results. We implemented a gradient descent to optimize the times of the releases, $t_i$. At each step, the coefficients $(c_i)_{1\leqslant i\leqslant n}$ being given, the control function was updated according to

$$u_{k+1} = \Pi_{\mathcal{T}}\left(u_k - \varepsilon_t \nabla_t J(u_k)\right), \text{ where } \quad \nabla_t J(u) = (\delta_{t_1} J(u), \ldots, \delta_{t_n} J(u))$$

and where $\Pi_{\mathcal{T}}$ denotes the projection onto the set of controls

$$\left\{ \sum_{i=1}^{n} c_i \delta(t - t_i),\ 0 \leqslant t_1 \leqslant \cdots \leqslant t_n \right\}.$$

Here, $J(u) = \int_0^T I_H(t)dt$. The values of $\delta_{t_i} J(u)$ for $i = 1, \ldots, n$ have been computed in Proposition 3.2 (see Section 3.4).

Starting from a random initial condition we optimize the time of the releases, $t_i$, until a certain level of functional flatness is attained. Then we optimize the $c_i$, that is, the amount of mosquitoes released at each $t_i$.

The costs, $c_i$, have been optimized using an augmented Lagrangian algorithm, which comes to consider the following functional

$$L(u, \lambda) = \int_0^T I_H(t)dt + \lambda \left( \sum_{i=1}^{n} c_i - C \right) + \frac{\rho}{2} \left( \sum_{i=1}^{n} c_i - C \right)^2.$$

The second term is added in order to take into account the constraint $\sum_{i=1}^{n} c_i = C$. The real number $\lambda$ is the Lagrange multiplier associated this constraint, which has to be find numerically at the same time than $u$. The augmented Lagrangian method transforms the constrained minimization problem into an unconstrained one, similarly to the Uzawa algorithm. The new functional has to be minimized with respect to $u$, and maximized with respect to $\lambda$. The solution to the problem is hence searched as a saddle point of $L$. The addition of the third term can be seen as a convexification of the dual problem. The addition of the squared term to the Lagrangian accelerates the convergence whenever $\rho$ is chosen carefully.

In order to find the saddle point of $L$ we take one step at a time, minimizing with respect to $u$ and maximizing then it with respect to $\lambda$, following the scheme:

$$\begin{array}{rcl} u_{k+1} & = & u_k - \varepsilon_c \left( \nabla_c J(u_k) + \lambda_k + \rho \left( \sum_{i=1}^{n} c_i - C \right) \right), \\ \lambda_{k+1} & = & \max\left( \lambda_k + \rho \left( \sum_{i=1}^{n} c_i - C \right), 0 \right). \end{array}$$

Where $\nabla_c J(u)$ is the gradient of the functional $J(u)$ with respect to the costs, analogous to $\nabla_t J(u)$. The components of $\nabla_c J(u)$ have been computed in Proposition 3.3 (see Apendix 3.4). Additional explanations regarding *augmented Lagrangian type algorithms* can be found in [72].

In order to picture better the algorithm implemented we provide in figure 3.6 an example of history of two key quantities along the iterations of the algorithm, namely $J(u) = \int_0^T I_H(t)dt$ and $\sum_i c_i - C$ during a simulation. We take as an example the simulation for the sterile insect technique with 20 releases and $C = 3 \cdot 10^7$. The value of $J$ falls sharply at the begginning as the times of the releases, $(t_i)_{1\leqslant i\leqslant n}$, move from their initial random positions. The small oscillations

observed later correspond to the first time we optimize the weights, $(c_i)_{1\leqslant i\leqslant n}$. Since we are looking for a saddle point of $L$ there are iterations where the value of $J$ actually increases. Then it starts a slow convergence to the final state where the values of $(t_i)_{1\leqslant i\leqslant n}$ and $(c_i)_{1\leqslant i\leqslant n}$ are refined. The simulation stops when a certain level of functional flatness is attained. In Figure 3.6, on the right, the x-axis presents slightly less iterations since we only show the iterations on the weights. At first this quantity oscillates until the value of $L$ stabilizes. Since we alternate the optimization of the times and the weights, whenever the times are adjusted, new oscillations appear as the weights, $(c_i)_{1\leqslant i\leqslant n}$, adjust to the new $(t_i)_{1\leqslant i\leqslant n}$ values. As expected, in the long run $\sum_i c_i - C$ stabilizes around 0, so the constraint $\sum_i c_i = C$ is respected.

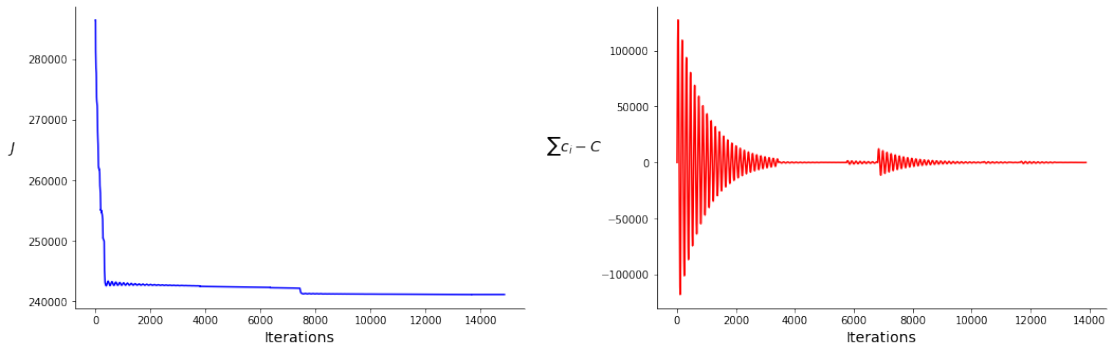


Figure 3.6 – Evolution of the functional $J(u)$ and $\sum c_i - C$ during the sterile insect simulation for 20 releases and $C = 3 \cdot 10^7$.

Appendix A

# Existence of solutions for Chapter 1 problems

This appendix is devoted to studying existence issues for problems $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ and $(\mathcal{P}^{2,\alpha}_{T,C,U})$. Note that the existence property for Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ is a bit more intricate to show since the horizon of time $T$ is let free.

Nevertheless, we will have to distinguish between the case where $j_1$ is convex or concave: the first case is standard whereas the second one needs a particular approach.

The existence of solutions for problems $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ and $(\mathcal{P}^{2,\alpha}_{T,C,U})$ will be studied with less restrictive hypothesis on the regularity of $j_1(\cdot)$ and $j_2(\cdot)$. We introduce:

$$\left\{\begin{array}{l} j_1(\cdot) \text{ is a non-negative increasing function such that } j_1(0)=0, \\ \text{either strictly concave, linear or strictly convex on } (0,T). \\ \\ j_2(\cdot) \text{ is a non-negative function, strictly increasing w.r.t. its first variable} \\ \text{and strictly decreasing w.r.t. its second variable. Moreover, for all } p\in[0,1], \\ \lim\limits_{T\to+\infty} j_2(T,p)=+\infty. \end{array}\right. \tag{$\mathcal{H}'$}$$

## A.1 Existence for Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$ in the case where $j_1$ is convex

The proof is standard and rests upon the direct method in the calculus of variations.

**Proposition A.1.** *Let us assume that $j_1(\cdot)$ and $j_2(\cdot)$ satisfy $(\mathcal{H}')$. Let $T>0$, $U>0$, $C>0$ and let us assume that $j_1$ is convex in $\mathbb{R}$ and that for every $T$, $p_T\mapsto j_2(T,p_T)$ is lower semi-continuous in $[0,1]$. Then, Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$ has a solution.*

*Proof.* Since $\mathcal{U}_{T,C,U}$ is non-empty, let us consider a minimizing sequence $(u_n)_{n\in\mathbb{N}}\in\mathcal{U}^{\mathbb{N}}_{T,C,U}$ for Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$. We have $0\leqslant u_n\leqslant U$ a.e. in $(0,T)$ for all $n\in\mathbb{N}$ and, according to the Banach-Alaouglu theorem, we conclude that $\mathcal{U}_{T,C,U}$ is compact for the weak-star topology of $L^\infty(0,T)$. Therefore, up to a subsequence, $u_n$ converges to $u^*$ for the weak-star topology of

$L^\infty(0,T)$, and by a property of the weak star convergence, one gets that $0 \leqslant u^* \leqslant U$ a.e. in $(0,T)$ and

$$\int_0^T u^*(t)\,dt = \lim_{n\to+\infty} \int_0^T u_n(t)\,dt = \lim_{n\to+\infty} \langle u_n, 1\rangle_{L^\infty,L^1} \leqslant C.$$

We thus infer that $u^* \in \mathcal{U}_{T,C,U}$.

Next, we consider $(p_n)_{n\in\mathbb{N}}$ where $p_n$ solves $p_n' = f(p_n) + u_n g(p_n)$ in $(0,T)$ with $p_n(0) = 0$. Using the fact that $f$ and $g$ are continuous in $[0,1]$ and since $0 \leqslant p_n \leqslant 1$ in $[0,T]$, we deduce that $(p_n')_{n\in\mathbb{N}}$ is bounded in $L^\infty(0,T)$. Hence, $p_n$ is bounded in $W^{1,\infty}([0,T])$ and according to the Ascoli-Arzelá theorem, $(p_n)_{n\in\mathbb{N}}$ converges in $\mathcal{C}^0([0,T])$ to $p^* \in W^{1,\infty}(0,T)$ up to a subsequence. Now, let $\varphi \in H^1(0,T)$. One has

$$p_n(T)\varphi(T) - \int_0^T p_n(t)\varphi(t)\,dt = \int_0^T (f(p_n) + u_n g(p_n))\varphi$$

for all $n \in \mathbb{N}$. According to the previous considerations, extracting adequately subsequences and letting then $n$ tend to $+\infty$ shows that

$$p^*(T)\varphi(T) - \int_0^T p^*(t)\varphi(t)\,dt = \int_0^T (f(p^*) + u^* g(p^*))\varphi.$$

Therefore, a standard variational analysis yields that $p^*$ satisfies $p'^* = f(p^*) + u^* g(p^*)$ in $(0,T)$ with $p^*(0) = 0$.

Finally, in order to assure the existence of solutions, it remains to prove that

$$\lim_{n\to\infty} J_\alpha(u_n) \geqslant J_\alpha(u^*). \tag{A.1}$$

By convexity of $j_1$, the functional

$$\mathcal{U}_{T,C,U} \ni u \mapsto \int_0^T j_1\left(u(t)\right) dt$$

is convex. Furthermore, it is easy to see that the functional $L^2(0,T;[0,U]) \ni u \mapsto \int_0^T j_1\left(u(t)\right) dt$ is continuous for the strong convergence of $L^2(0,T;[0,U])$ (indeed, this follows from the fact that the strong convergence in $L^2$ implies pointwise one and from the dominated convergence theorem). Now, using that a convex function on a real locally convex space is lower semicontinuous if and only if it is weakly lower semicontinuous, we infer that

$$\liminf_{n\to\infty} \int_0^T j_1\left(u_n(t)\right) dt \geqslant \int_0^T \liminf_{n\to\infty} j_1\left(u^*(t)\right) dt.$$

Up to a subsequence, $(p_n(T))_{n\in\mathbb{N}}$ converges to $p^*(T)$ and it follows by assumption on $j_2$ that up to a subsequence, $\liminf_{n\to+\infty} j_2(T,p_n(T)) \geqslant j_2(T,p^*(T))$, whence (A.1). This concludes the proof. □

## A.2 Existence for Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$ in the case where $j_1$ is concave

The concave case is a bit more intricate than the convex one. Indeed, we strongly used the convexity of $j_1$ to prove the lower semicontinuity of the integral term in the definition of $J_\alpha$. We overcome this difficulty by introducing an auxiliary problem where only bang-bang control functions with a finite number of switches are considered.

**Proposition A.2.** *Let us assume that $j_1(\cdot)$ and $j_2(\cdot)$ satisfy $(\mathcal{H}')$. Let $\alpha \in (0,1]$, $T>0$, $U>0$, $C>0$ and let us assume that $j_1$ is concave. Then, Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$ has a solution which is necessarily bang-bang, equal a.e. to 0 or $U$ and with at most two switches.*

*Proof.* To deal with the concave case, we introduce the set

$$\mathcal{U}_N := \{u \in \mathcal{U}_{T,C,U}, u \text{ bang-bang equal a.e. to 0 or } U \text{ and having at most } N \text{ switches}\}.$$

Let $N \in \mathbb{N}^*$ be given and consider the auxiliary problem

$$\begin{cases} \inf_{u\in\mathcal{U}_N} J_\alpha(u) \\ p' = f(p) + ug(p) \quad , \ p(0)=0. \end{cases} \tag{$\mathcal{P}^N$}$$

We first claim that Problem $(\mathcal{P}^N)$ has a solution. Indeed, note first that $\mathcal{U}_N$ is compact for the strong topology of $L^1(0,T)$ (since a sequence of switching points converges up to a subsequence in $[0,T]$ according to the Bolzano-Weierstrass lemma). Let $(u_{N,n})_{n\in\mathbb{N}}$ denote a minimizing sequence for Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$. Up to a subsequence, $(u_{N,n})_{n\in\mathbb{N}}$ converges to some element $u_N$ in $L^1(0,T)$. Since $j_1(\cdot)$ is locally Lipschitz as a concave function, there exists $K>0$ such that

$$\left|\int_{(0,T)} j_1(u_{N,n}) - \int_{(0,T)} j_1(u_N)\right| \leqslant \int_0^T |j_1(u_{N,n}) - j_1(u_N)| \leqslant K\|u_{N,n}-u_N\|_{L^1(0,T)}.$$

Finally, dealing similarly as in the proof of Lemma A.1 with the term $j_2(T, p_{N,n}(T))$, where $p_{N,n}$ stands for the solution to $p' = f(p) + u_{N,n}g(p)$ and $p(0)=0$, enables us to show that (A.1) still holds true in that case. It follows that Problem $(\mathcal{P}^N)$ has a solution $u_N$.

Let us now show that $u_N$ has at most two switches. Let $u_N \in \mathcal{U}_N$ solving Problem $(\mathcal{P}^N)$. Let $0 \leqslant \xi_1 < ... < \xi_{N_0} \leqslant T$ denote the distinct switching points of $u_N$ with $N_0 \leqslant N$, with the convention that $\xi_1 = 0$ if, and only if, $u_N = U$ in a neighborhood of $t=0$ and that $x_{N_0} = T$ if, and only if, $u_N = U$ in a neighborhood of $t=T$. We have to distinguish between two cases: there exist three distinct switching points $\xi_{k-1}$, $\xi_k$ and $\xi_{k+1}$ such that (a) $\xi_{k-1}>0$ and $u=U$ on $(\xi_k,\xi_{k+1})$, or (b) $\xi_{k+1}<T$ and $u=U$ on $(\xi_{k-1},\xi_k)$. In what follows, we will only deal with the case (a), the study of the case (b) being exactly similar.

Let us first write $J_\alpha(u_N)$ as a function of the $\xi_k$ as

$$J_\alpha(u_N) := J^\xi_\alpha(\xi_1,\dots,\xi_{N_0}) := (1-\alpha)j_1(U) \sum_{\substack{j\in[\![1,N_0]\!] \\ j \text{ odd}}} (\xi_{j+1}-\xi_j) + \alpha j_2(T, p_N(T)),$$

where $p_N$ denotes the solution to the Cauchy problem $p' = f(p) + u_N g(p)$ with $p(0)=0$.

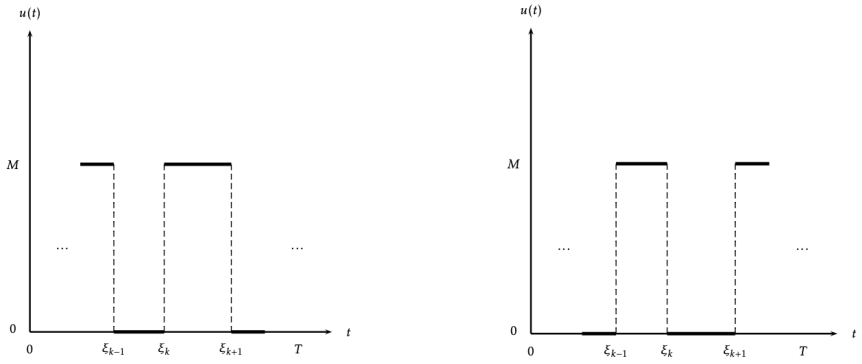


Figure A.1 – Left: case (a). Right: case (b).

Hence, one can rewrite Problem $(\mathcal{P}^N)$ as

$$\begin{cases} \inf_{\xi_1<\cdots<\xi_{N_0}} J_\alpha^\xi(\xi_1,\ldots,\xi_{N_0}), \\ \displaystyle\sum_{\substack{j\in[\![1,N_0]\!] \\ j \text{ odd}}} (\xi_j - \xi_{j-1}) \leqslant C/U, \\ \xi_j - \xi_{j+1} < 0 \ , \ j = 1,\ldots,N_0-1 \end{cases}$$

Notice that this problem is equivalent to Problem $(\mathcal{P}^N)$ and has therefore a solution. We write $p_N(T)$ in terms of the $\xi_k$ as

$$p_N(T) = \sum_{\substack{j\in[\![1,N_0]\!] \\ j \text{ odd}}} \int_{\xi_j}^{\xi_{j+1}} (f(p_N(t)) + Ug(p_N(t)))\ dt.$$

Let $k$ denote the integer satisfying the conditions of the case (a). Applying the Karush Kuhn-Tucker theorem to the optimization problem above in order to obtain the optimality conditions yields the existence of a Lagrange multiplier $\mu \in \mathbb{R}_+$ such that

$$\mu \left( \sum_{\substack{k\in[\![1,N_0]\!] \\ k \text{ odd}}} (\xi_k - \xi_{k-1}) - C/U \right) = 0 \qquad \text{(slackness condition)}$$

and

$$\begin{cases} (-1)^k(1-\alpha)j_1(U) + (-1)^k\alpha\frac{\partial j_2}{\partial p}(T,p_N(T))Mg(p_N(\xi_k)) + (-1)^k\mu M = 0 \\ (-1)^{k+1}(1-\alpha)j_1(U) + (-1)^{k+1}\alpha\frac{\partial j_2}{\partial p}(T,p_N(T))Mg(p_N(\xi_{k+1})) + (-1)^{k+1}\mu M = 0. \end{cases}$$

Therefore, adding these two equations, we get

$$\alpha U \frac{\partial j_2}{\partial p}(T,p_N(T))(g(p_N(\xi_k)) - g(p_N(\xi_{k+1}))) = 0.$$

Since $\alpha > 0$, $\frac{\partial j_2}{\partial p}(T, p_N(T)) < 0$ and $p \mapsto g(p)$ is strictly decreasing we reach a contradiction. It follows that $u_N$ has at most two switches and we infer that

$$\inf_{u\in\mathcal{U}_N} J_\alpha(u) = \min_{v\in\mathcal{U}_2} J_\alpha(v) \tag{A.2}$$

To conclude, one needs to investigate the links between Problems $(\mathcal{P}^N)$ and $(\mathcal{P}^{2,\alpha}_{T,C,U})$. One important ingredient is the following lemma, whose proof is postponed to the end of this section for the sake of readability.

**Lemma A.1.** *Let $u$ be an element of $\mathcal{U}_{T,C,U}$ such that $u$ is bang-bang. Then, there exists $u^N$ in $\mathcal{U}_N$ such that*

$$\lim_{N\to+\infty} u^N(t) = u(t) \quad \textit{for a.e. } t \in (0,T).$$

Let $u \in \mathcal{U}_{T,C,U}$. It is well-known that the set $\{v \in \mathcal{U}_{T,C,U} \mid v \text{ is bang-bang, equal a.e. to } 0 \text{ or } U\}$ is dense into $\mathcal{U}_{T,C,U}$ for the weak-star topology topology of $L^\infty(0,T)$. Hence, there exists $(u_k)_{k\in\mathbb{N}} \in \mathcal{U}^{\mathbb{N}}_{T,C,U}$ converging weakly-star to $u$ in $L^\infty(0,T)$.

By concavity of $j_1$ in $\mathbb{R}$, the mapping

$$\mathcal{U}_{T,C,U} \ni u \mapsto \int_0^T j_1\left(u(t)\right) dt$$

is concave. Mimicking the argument used at the end of the proof of Proposition A.1, one shows the upper semicontinuity property:

$$\limsup_{k\to+\infty} \int_{(0,T)} j_1(u_k) \leqslant \int_{(0,T)} j_1(u)$$

Now, according to Lemma A.1, there exists $u^N_k \in \mathcal{U}_N$ such that

$$\lim_{N\to+\infty} u^N_k(t) = u_k(t) \quad \text{for a.e. } t \in (0,T).$$

The dominated convergence theorem thus yields

$$\lim_{N\to+\infty} \int_{(0,T)} j_1(u^N_k) = \int_{(0,T)} j_1(u_k).$$

According to the convergence results above, we infer that, $\varepsilon > 0$ being given, there exists $N_0 \in \mathbb{N}$ such that

$$N \geqslant N_0 \Longrightarrow \limsup_{k\to+\infty} \int_{(0,T)} j_1(u^N_k) - \varepsilon \leqslant \limsup_{k\to+\infty} \int_{(0,T)} j_1(u_k) \leqslant \int_{(0,T)} j_1(u).$$

Dealing with the term involving $j_2$ is easier. Indeed, by using the approximation results above and mimicking the reasoning in the proof of Proposition A.1, one gets

$$\lim_{N,k\to+\infty} j_2(T, p^N_k(T)) = j_2(T, p(T))$$

where $p^N_k$ (resp. $p$) denotes the solution to the Cauchy problem $p' = f(p) + u^N_k g(p)$ and $p(0) = 0$ (resp. $p' = f(p) + ug(p)$ and $p(0) = 0$). The combination of the convergence results above yields

the existence of $\hat{N}_0 \in \mathbb{N}$ such that

$$N \geqslant \hat{N}_0 \Longrightarrow \limsup_{k\to+\infty} J_\alpha(u_k^N)) - \varepsilon \leqslant J_\alpha(u).$$

Since $\varepsilon$ has been chosen arbitrarily, and since $J_\alpha(u_k^N) \geqslant \min_{v\in\mathcal{U}_2} J_\alpha(v)$ according to (A.2), one gets

$$J_\alpha(u) \geqslant \min_{v\in\mathcal{U}_2} J_\alpha(v).$$

This concludes the proof: Problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$ has a solution which solves moreover Problem $(\mathcal{P}^2)$. □

*Proof of Lemma A.1.* Since $u$ is assumed to be bang-bang, let us write $u = U\mathbb{1}_I$ where $I$ denotes a measurable subset of $(0,T)$. Let $\varepsilon > 0$. By outer regularity of the Lebesgue measure, there exists un open subset of $(0,T)$ containing $I$ and such that $|I| \leqslant |O| \leqslant |I| + \varepsilon$. Let us write $O = \bigcup_{n\in\mathbb{N}}(\alpha_n, \beta_n)$ where the intervals $(\alpha_n, \beta_n)$ are disjoint and such that $|O| = \sum_{n\in\mathbb{N}}(\beta_n - \alpha_n)$. Let us introduce $u_n := U\mathbb{1}_{\bigcup_{p=0}^n(\alpha_p,\beta_p)}$. Writing $u = (u - U\mathbb{1}_O) + U\mathbb{1}_O$, one has

$$\begin{aligned}\int_0^T |u - u_n| &\leqslant U\int_0^T |\mathbb{1}_I - \mathbb{1}_O| + U\int_0^T |\mathbb{1}_O - \mathbb{1}_{\mathbb{1}_{\bigcup_{p=0}^n(\alpha_p,\beta_p)}}| \\ &\leqslant 2\varepsilon U + U\sum_{p=n+1}^{+\infty}(\beta_p - \alpha_p)\end{aligned}$$

Since $\varepsilon$ is arbitrary and since the series with general term $\beta_n - \alpha_n$ is convergent, it follows that $(u_n)_{n\in\mathbb{N}}$ converges to $u$ in $L^1(0,T)$ and thus also pointwise. This concludes the proof. □

## A.3 Existence results for Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$

**Proposition A.3.** *Let us assume that $\alpha \in (0,1]$, $p_T \in (0,1)$, (1.2) is true, and that $j_1(\cdot)$ and $j_2(\cdot)$ satisfy the assumptions of $(\mathcal{H}')$. Let us assume that $U > m^*(p_T)$ and*

$$C > C^{p_T}(U) \text{ if } p_T \leqslant \theta \qquad \text{and} \qquad C > C^\theta(U) \text{ otherwise.}$$

*Finally, let us also assume that for every $p_T$, $T \mapsto j_2(T, p_T)$ is lower semi-continuous in $\mathbb{R}_+$. Then, Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ has a solution.*

*Proof.* To avoid working on a variable domain, let us make the following change of variables: we define $\tilde{p}(s) := p(Ts)$ and $\tilde{u}(s) := u(Ts)$, with $s \in [0,1]$. Then, Problem $(\mathcal{P}^{1,\alpha}_{p_T,C,U})$ rewrites

$$\left\{\begin{array}{l}\inf\limits_{(T,\tilde{u})\in\mathcal{D}^{p_T}} \tilde{J}_\alpha(T,\tilde{u}), \\ \tilde{p}'(s) = T\left(f(\tilde{p}(s)) + \tilde{u}(s)g(\tilde{p}(s))\right)\ ,\ \tilde{p}(0) = 0\ ,\ \tilde{p}(1) = p_T,\end{array}\right. \qquad (\tilde{\mathcal{P}}^{1,\alpha}_{p_T,C,U})$$

where $\tilde{J}(T,\tilde{u})$ is defined by

$$\tilde{J}(T,\tilde{u}) = (1-\alpha)\ T\int_0^1 j_1(\tilde{u}(s))ds + \alpha j_2(T,p_T).$$

and $\mathcal{D}^{p_T}$ is the set of admissible controls

$$\mathcal{D}^{p_T} = \{(T, \tilde{u}) \in \mathbb{R}_+ \times \mathcal{U}_{1,C,U} \times [0,1] \mid \tilde{p}(1) = p_T\}.$$

Let us first prove that $\mathcal{D}^{p_T}$ is non-empty. To this aim, let us define

$$T^{p_T}(U) := \int_0^{p_T} \frac{d\nu}{f(\nu) + Ug(\nu)} \tag{A.3}$$

and look for controls of the form $u_\xi(t) = U\mathbb{1}_{[0,\xi]}$ belonging to this set, where

$$\xi = \begin{cases} 1 & \text{if } UT^{p_T} \leqslant C \\ \frac{C}{UT^{p_T}} & \text{if } UT^{p_T} > C. \end{cases} \tag{A.4}$$

Let us introduce $\tilde{p}_\xi$ solving $\tilde{p}'_\xi = T\left(f(\tilde{p}_\xi) + \tilde{u}_\xi g(\tilde{p}_\xi)\right)$ in $(0,1)$ and $\tilde{p}_\xi(0) = 0$. By integrating both sides of the differential equation, we get that the time $T_\xi$ taken by $p_\xi$ to reach the final state $p_T$ reads

$$T_\xi = \int_0^{p_\xi(\xi)} \frac{d\nu}{f(\nu) + Ug(\nu)} + \int_{p_\xi(\xi)}^{p_T} \frac{d\nu}{f(\nu)}.$$

Note that in case $p_\xi(\xi) \leqslant \theta$ the second integral does not converge unless $\xi = 1$, in which case it vanishes. This expression gives a lower bound on $C$ depending on $p_T$. If $p_T \leqslant \theta$ we must have $\xi = 1$, concluding that $p_\xi(\xi) = p_T$ and $C \geqslant UT^{p_T} = C^{p_T}$, with $C^{p_T}$ as defined in (1.19). Instead if $p_T > \theta$, then either $\xi = 1$ implying $C \geqslant C^{p_T}$ or $p_\xi(\xi) > \theta$ and therefore $C > U\int_0^\theta \frac{d\nu}{f(\nu)+Ug(\nu)} = C^\theta$. Since in this case $C^{p_T} > C^\theta$, the least restrictive condition is $C > C^\theta$. We conclude that under the hypothesis of this proposition $T_\xi < \infty$ and $\mathcal{D}^{p_T}$ is non-empty.

Let us consider a minimizing sequence $(T_n, \tilde{u}_n)_{n\in\mathbb{N}} \in (\mathcal{D}^{p_T})^{\mathbb{N}}$ and let $\tilde{p}_n$ be the solution of $\tilde{p}' = T\left(f(\tilde{p}) + \tilde{u}_n g(\tilde{p}_n)\right)$ in $(0,1)$ and $\tilde{p}_n(0) = 0$. By minimality, one has $\lim\limits_{n\to\infty} \tilde{J}_\alpha(T_n, \tilde{u}_n) < \infty$, i.e.

$$\lim_{n\to\infty} (1-\alpha)\, T_n \int_0^1 j_1(\tilde{u}_n(s))ds + \alpha j_2(T_n, p_T) < \infty.$$

Each term of the sum being bounded from below by 0, it follows that both of them are also bounded above. Since $\alpha > 0$ and $\lim_{n\to\infty} j_2(T_n, p_T) = +\infty$, it follows that $(T_n)_{n\in\mathbb{N}}$ is bounded, and therefore, up to a subsequence, $T_n \to \tilde{T} < \infty$ as $n \to +\infty$. By mimicking the arguments used for problem $(\mathcal{P}^{2,\alpha}_{T,C,U})$, one shows that, up to a subsequence, $(\tilde{u}_n)_{n\in\mathbb{N}}$ converges to $\tilde{u}^* \in \mathcal{U}_{\tilde{T},C,U}$ weakly-star in $L^\infty(0,1;[0,U])$. Moreover,$(\tilde{p}_n)_{n\in\mathbb{N}}$ converges to $\tilde{p}^*$ in $\mathcal{C}^0([0,\tilde{T}])$, where $\tilde{p}^*$ solves the equation

$$(\tilde{p}^*)' = \tilde{T}(f(\tilde{p}^*) + \tilde{u}^* g(\tilde{p}^*)) \quad \text{in } (0,\tilde{T})$$

and $\tilde{p}^*(0) = 0$. As a consequence, $(\tilde{J}_\alpha(T_n, \tilde{u}_n))_{n\in\mathbb{N}}$ converges to $\tilde{J}_\alpha(\tilde{T}, \tilde{u}^*)$, which concludes the proof. □

Appendix B

# Complementary material to Chapter 2

## B.1 Numerical exploration of the parameter space for Hypothesis $\mathcal{H}.2$

**Proposition B.1.** *Assuming $d_M \leqslant d_W \leqslant b_W^0 \leqslant b_M^0$ and $0 < \theta < 1$, then $f''$ admits a single zero in $(0,1)$.*

*Proof.* The existence of a zero of $f''$ is straightforward to prove: there holds $f(0) = f(\theta) = f(1) = 0$, thus from Rolle's theorem there exist two zeros of $f'$ in $(0,1)$. Then applying again Rolle's theorem we prove the existence of some zero $\theta_2$ of $f''$, lying in between the two zeros of $f'$, thus $\theta_2 \in (0,1)$ in all generality.

Let us now prove the uniqueness of the zero of $f''$ in $[0,1]$. By computing the rational function $f''$, we see that $\{f'' = 0\} = \{R = 0\}$ where, denoting $\kappa := 1 + s_h - \frac{b_2}{b_1} > 0$,

$$\begin{aligned} R(p) &:= (s_h - s_h^2\theta - \kappa^2 + \kappa s_h + \kappa s_h\theta)p^3 + 3(\kappa - s_h - s_h\theta)p^2 - 3(1 - s_h\theta)p + \theta - \kappa\theta + 1 \\ &= \bar{A}p^3 + \bar{B}p^2 + \bar{C}p + \bar{D} \end{aligned}$$

Thus to conclude, it is enough to prove that $R$ has a unique zero in $[0,1]$. Because $d_M \leqslant d_W \leqslant b_W^0 \leqslant b_M^0$ holds, we find that

$$\bar{A} > 0, \qquad \bar{B} \leqslant 0, \qquad \bar{C} < 0, \qquad \bar{D} > 0.$$

Then, using Descarte's rule of sign, we find that $R$ has zero or two positive roots. However, since $f''$ has at least one zero in $(0,1)$, so does $R$, so that $R$ admits exactly two positive roots. Meanwhile, applying the rule to $p \mapsto R(-p)$ implies that $R$ has one negative root.

Now, we set $S(p) = R(p+1)$. In particular, the leading coefficient of $S$ is $\bar{A} > 0$ while one can prove that

$$S(0) = \bar{A} + \bar{B} + \bar{C} + \bar{D} < 0.$$

Clearly $S$ has three real roots, and their product is given by $-\frac{S(0)}{\bar{A}} > 0$. However, $S$ has at least one negative root since $R$ does. Since the product of all three roots of $S$ is positive, $S$ has exactly two negative roots and one positive root. As a result, $R$ has exactly one root in $[0,1]$, and the conclusion follows.

□

This section is devoted to a numerical exploration of the space of parameters, in order to establish the validity of Hypothesis ($\mathcal{H}.2$). For the exploration, we normalize the parameters assuming $b_M^0 = 1$. The results are presented in Figures B.1 and B.2. To produce these images fo a given pair of values $(s_h, b_W)$, two random values for $d_W$ and $d_M$ are chosen, such that $d_M \leqslant d_W \leqslant b_W^0 \leqslant b_M^0 = 1$. If the randomly generated set of parameters are such that $\theta \notin (0, 1)$, the set is discarded. If indeed $0 < \theta < 1$, then the Hypothesis ($\mathcal{H}.2$) is tested. In blue, are the values of the parameters for which Hypothesis ($\mathcal{H}.2$) is satisfied. In red, the values for which is not.

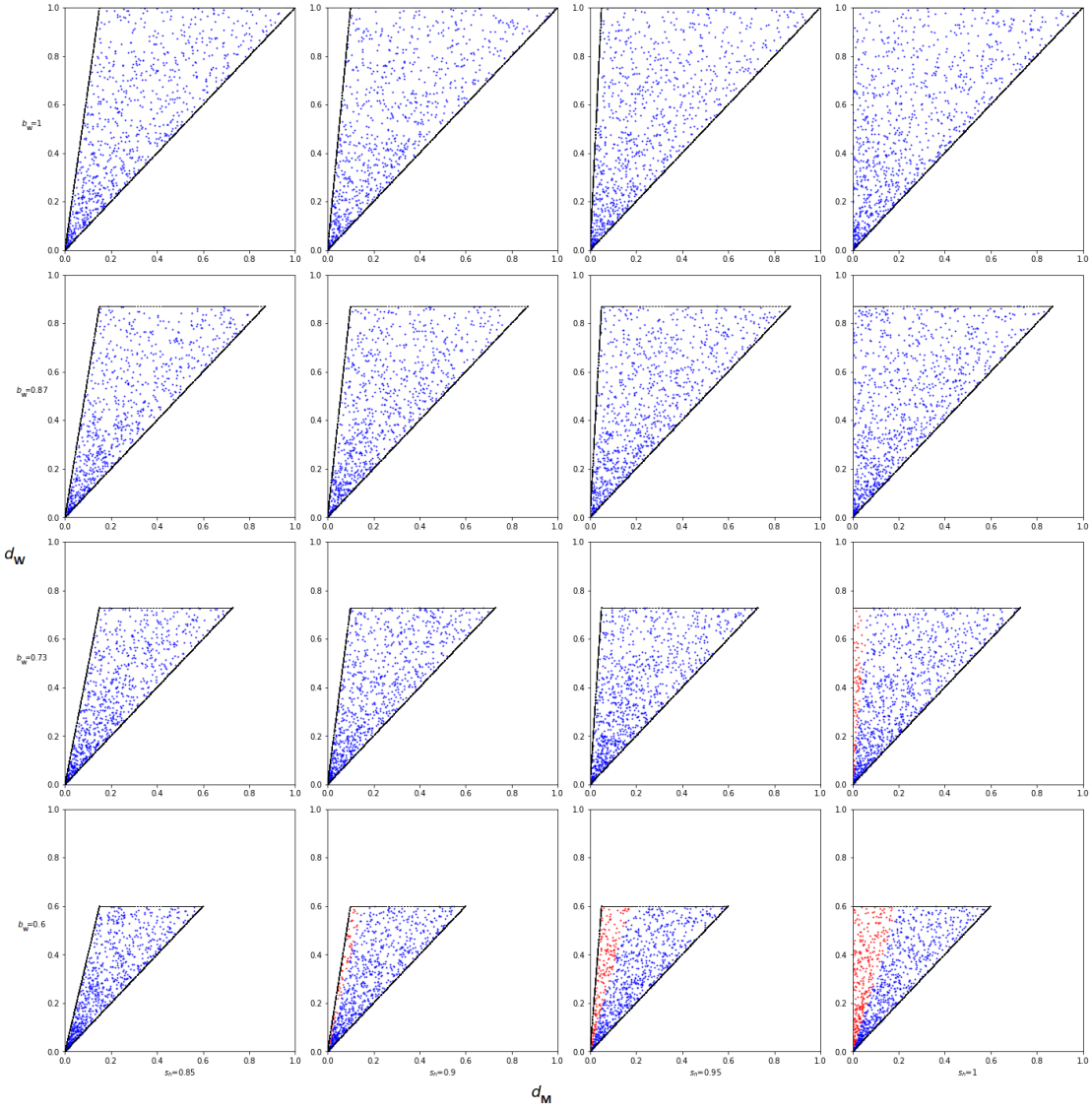


Figure B.1 – Hypothesis ($\mathcal{H}.2$) tested for different parameter values. All pictures have $d_M$ in the $x$-axis and $d_W$ in the $y$-axis. In this image, $s_h \in \{0.5, 0.67, 0.83, 1\}$ increases from left to right and $b_W \in \{0.6, 0.73, 0.87, 1\}$ decreases from top to bottom. Blue dots mean Hypothesis ($\mathcal{H}.2$) is satisfied for those parameters, while red dots mean it is not.

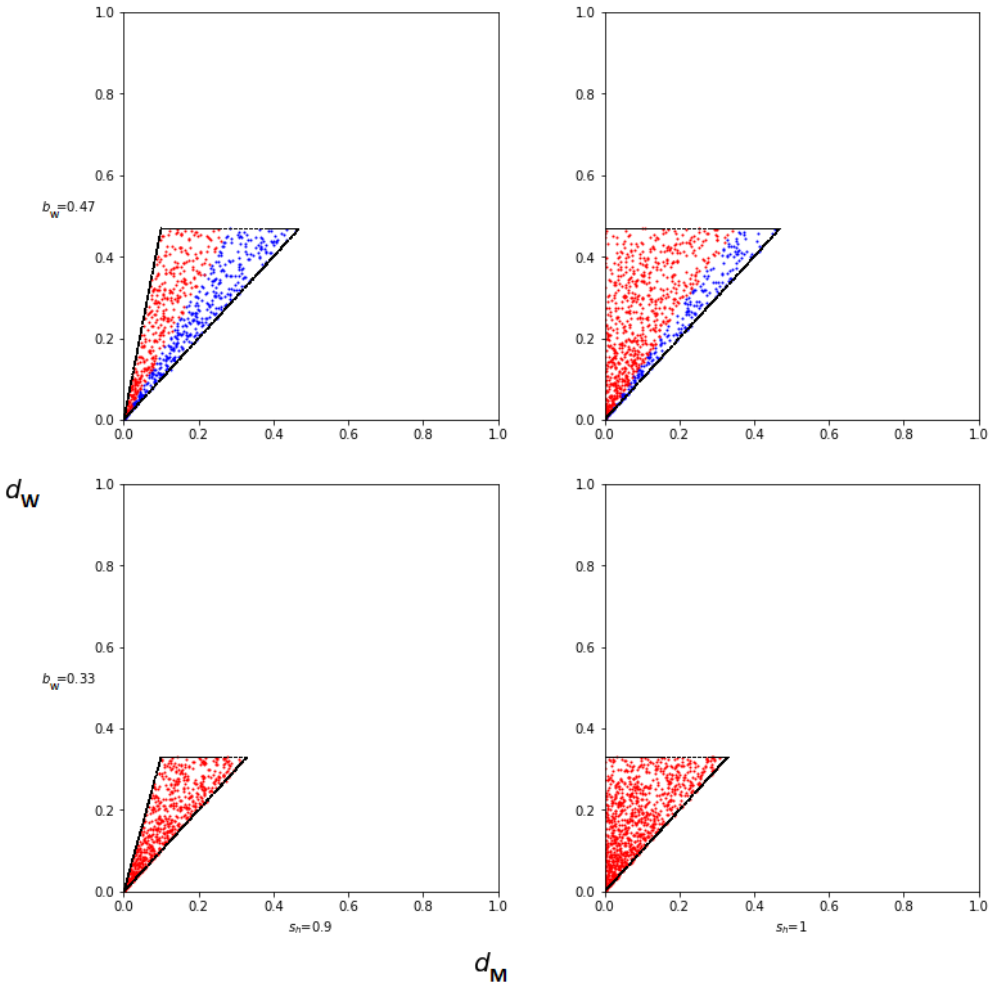


Figure B.2 – Hypothesis ($\mathcal{H}.2$) tested for small values of $b_W$ and high values of $s_h$. All pictures have $d_M$ in the $x$-axis and $d_W$ in the $y$-axis. In this image, $s_h \in \{0.9, 1\}$ increases from left to right and $b_W \in \{0.33, 0.47\}$ decreases from top to bottom.

The condition $\theta \in (0, 1)$ can be written in terms of the other parameters,

$$0 < \theta < 1 \Leftrightarrow 0 < 1 - \frac{d_M b_W^0}{d_W b_M^0} < s_h \Leftrightarrow 1 > \frac{d_M b_W^0}{d_W b_M^0} > 1 - s_h \Leftrightarrow \frac{d_W}{d_M} > \frac{b_W^0}{b_M^0} > \frac{d_W}{d_M}(1 - s_h).$$

Since $b_W^0 \leqslant b_M^0$ and $d_M \leqslant d_W$, this means that if $b_W \leqslant 1 - s_h$, necessarily $\theta > 1$, thus these values can be excluded from the exploration. Indeed, the black lines wrapping the dots in Figures B.1 and B.2 are $d_W = d_M$, $b_W^0 = 1$ and $b_W^0 = 1 - s_h$.

As we can see in Figure B.1 and B.2, Hypothesis $\mathcal{H}.2$ is satisfied by most of the parameters of the parameter space. For high values of $b_W$ is always satisfied (also for those values not shown in Figure B.1). As $b_W$ decreases, red dots appear for high values of $s_h$ and $d_W >> d_M$. Only for high values of $s_h$ and small values of $b_W$ the red dots dominate the picture. In a realistic scenario, based on the values for the parameters found in te literature [10, 46] we expect a high

value of $s_h$ and $b_W^0$ and smaller values of $d_W$ and $d_M$, for which hypothesis ($\mathcal{H}.2$) is satisfied. The values of the parameters not satisfying Hypothesis ($\mathcal{H}.2$) would represent a particular strain of *Wolbachia* that, in a certain variety of mosquito, would produce a high CI rate and a big penalty on their fertility, which, a priori, is not impossible.

## B.2 Existence of solutions for problem $(\mathcal{P}_{p_0})$ for piecewise constant $K(\cdot)$ in 1D

We devote this section to the study of the existence of minimizers for problem $(\mathcal{P}_{p_0})$. We present here a partial result, settling the existence in 1D for the case where $K(\cdot)$ is piecewise constant. This proof, nevertheless, cannot be straightforwardly extended for the fully general case.

**Proposition B.2.** *Let $K$ be a piecewise constant function, with $x \in \Omega \subset \mathbb{R}$. Then there exists $p_0^* \in \mathcal{P}_{0,C,U}$ solving problem $(\mathcal{P}_{p_0})$.*

*Proof.* Let us write $K(x) = \sum_{i=1}^{n} K_i \mathbb{1}_{[x_{i-1},x_i]}$. We place ourselves in one of the intervals $[x_{i-1}, x_i]$, where $K(\cdot)$ is constant.

Let us consider any function $p_0 \in \mathcal{P}_{0,C,U}$ in this interval. We claim there exists a monotonic (decreasing or increasing) rearrangement of $p_0$, that we will denote $\hat{p}_0$ such that $\hat{p}_0 \in \mathcal{P}_{0,C,U}$. To define this rearrangement, let us introduce, in a given interval $[x_{i-1}, x_i]$,

$$\mu(s) := \left|\{x \in [x_{i-1}, x_i] \ : \ p_0(x) > s\}\right|.$$

Then, we define $\hat{p}_0$ in that interval as

$$\hat{p}_0(x) := \inf\{s \in [0,1] \ : \ \mu(s) \leqslant x\}.$$

The fact that such a rearrangement will respect $0 \leqslant \hat{p}_0 \leqslant G^{-1}\left(U/K(x)\right)$ is trivial since rearranging a function does not change its maximums or minimums (see [118]). Suppose $\int_\Omega K(x)G(p_0(x))\,dx \leqslant C$, then

$$\int_\Omega K(x)G(\hat{p}_0(x))\,dx = \int_{\Omega\setminus[x_{i-1},x_i]} K(x)G(p_0(x))\,dx + K_i \int_{x_{i-1}}^{x_i} G(\hat{p}_0(x))\,dx$$

for every $i \in \{1, \dots, n\}$. $G$ is a continuous function, hence it is measurable. Therefore, since $G$ is non-negative and measurable we have

$$\int_{x_{i-1}}^{x_i} G(p_0(x))\,dx = \int_{x_{i-1}}^{x_i} G(\hat{p}_0(x))\,dx$$

by equimeasurability of the rearrangement.

This implies that if $\int_\Omega K(x)G(p_0(x))\,dx \leqslant C$, then $\int_\Omega K(x)G(\hat{p}_0(x))\,dx \leqslant C$. These reasoning can be easily extended to all of the subintervals. Therefore we have proved that $\mathcal{P}_{0,C,U}$ is stable under rearrangements.

Let us define now

$$\hat{\mathcal{P}}_{0,C,U} := \{\hat{p}_0 \in \mathcal{P}_{0,C,U} \mid \hat{p}_0 \text{ is monotonic in } [x_{i-1}, x_i], i = 1, \dots, n\}.$$

Observe that

$$\min_{p_0 \in \mathcal{P}_{0,C,U}} J^0(p_0) = \min_{\hat{p}_0 \in \hat{\mathcal{P}}_{0,C,U}} J^0(\hat{p}_0),$$

with $J^0$ defined by (2.8). Indeed, if $p_0^*$ is minimizer of $J^0$ in $\mathcal{P}_{0,C,U}$, then

$$\int_\Omega K(x)^2(1-\hat{p}(T,x))^2\,dx = \int_{\Omega\setminus[x_{i-1},x_i]} K(x)^2(1-p(T,x))^2\,dx + K_i^2\int_{x_{i-1}}^{x_i}(1-\hat{p}(T,x))^2\,dx,$$

for every $i \in \{1,\dots,n\}$, where we are denoting by $\hat{p}(t,x)$ the solution to equation (2.10) with initial condition $\hat{p}_0(x)$.

We can follow the same reasoning as before to prove that

$$\int_{x_{i-1}}^{x_i}(1-p(T,x))^2\,dx = \int_{x_{i-1}}^{x_i}(1-\hat{p}(T,x))^2\,dx$$

for every $i \in \{1,\dots,n\}$. To see this clearly we can write $p(t,x)$ as a function of its initial condition by realising that $p(t,x)$ can be written as

$$\frac{\partial}{\partial t}p(t,x) = f(p(t,x)) \Rightarrow \int_0^p \frac{d\nu}{f(\nu)} = \int_0^t ds = t.$$

Defining $F(p)$ as the primitive of $1/f(p)$ vanishing at 0, $F(p) := \int_0^p \frac{d\nu}{f(\nu)}$, we can write

$$F(p(T,x)) = F(p_0(x)) + T \Rightarrow p(T,x) = F^{-1}\left(F(p_0(x)) + T\right). \tag{B.1}$$

Both $F$ and its inverse are continuous functions and thus, so it is its composition. Therefore $p(T,\cdot)$ is also a measurable function of $p_0(x)$ and since it is non-negative both integrals are equal.

This implies that, if there exists a solution monotonic by intervals, $\hat{p}_0^* \in \hat{\mathcal{P}}_{0,C,U}$ there must also exist a solution in $\mathcal{P}_{0,C,U}$. Thus, we restrict our analysis to the first kind of functions.

Let us consider a minimizing sequence $(\hat{p}_0^n)_{n\in\mathbb{N}} \in \hat{\mathcal{P}}_{0,C,U}$ for problem $(\mathcal{P}_{p_0})$. We know it exists since $\hat{\mathcal{P}}_{0,C,U}$ is non-empty. Due to the fact that for all $n \in \mathbb{N}$, $0 \leqslant \hat{p}_0^n(x) \leqslant G^{-1}(U/K(x))$ a.e. in $\Omega$ and using the monotonicity of $\hat{p}_0^n$ on each interval $(x_{i-1}nx_i)$, we deduce from Helly's selection theorem (see [126]) that $(\hat{p}_0^n)_{n\in\mathbb{N}}$ converges pointwisely to an element $\hat{p}_0^*$, up to a subsequence.

Basic properties of pointwise convergence lead us to conclude that $0 \leqslant \hat{p}_0^*(x) \leqslant G^{-1}(U/K(x))$ a.e. in $\Omega$. Moreover, according to the Lebesgue dominated convergence theorem, one has

$$\int_\Omega K(x)G\left(\hat{p}_0^*(x)\right)\,dx = \lim_{n\to\infty}\int_\Omega K(x)G\left(\hat{p}_0^n(x)\right)\,dx = \lim_{n\to\infty}\left\langle K(x)G\left(\hat{p}_0^n(x)\right),1\right\rangle_{L^\infty,L^1} \leqslant C.$$

Indeed, we recall that $K(\cdot)$ is piecewise constant and thus it does not affect the convergence properties of the sequence under the integral. Therefore, $\hat{p}_0^* \in \hat{\mathcal{P}}_{0,C,U}$.

A similar reasoning shows that the sequence $\left(F^{-1}\left(F(\hat{p}_0^n(x)) + T\right)\right)_{n\in\mathbb{N}}$ converges almost everywhere in $\Omega$ and therefore, we have

$$\lim_{n\to\infty} J^0\left(\hat{p}_0^n(x)\right) = J^0\left(\hat{p}_0^*(x)\right),$$

according to (B.1). It follows that $\hat{p}_0^*$ is indeed a solution to problem $(\mathcal{P}_{p_0})$.

□

Appendix C

# Complementary material for Chapter 3

## C.1 $R_0$ computations

We detail in this section the computations of $R_0^M$ and $R_0^W$ defined in section 3.2. To compute the value of these quantities we follow the lines of [44]. The relevant compartments for these computations are only the infected ones. As [44] points out, this distinction is determined from the epidemiological interpretation of the model and cannot be deduced from the structure of the equations alone. The infected compartments in our case are those in which there are individuals carrying the dengue virus. For model (3.1) these are $E_H$,$I_H$,$E_M$ and $I_M$.

We need then to separate the changes in the compartments due to new infections from the rest. We write system (3.1) in the following way $\mathbf{x} = (E_H, I_H, E_M, I_M, S_H, S_M)$,

$$\dot{\mathbf{x}} = \mathcal{F}(\mathbf{x}) - \mathcal{V}(\mathbf{x}),$$

where $\mathcal{F}$ contains the rate of appearance of new infections in each compartment and $\mathcal{V}$ the rate of transfer of individuals into the compartments by all other means.

Let's see the decomposition of the first equation, $E_H'$, as an example:

$$E_H' = \underbrace{\frac{\beta_M}{H} I_M S_H}_{\mathcal{F}_1(\mathbf{x})} - \underbrace{(\gamma_H E_H + b_H E_H)}_{\mathcal{V}_1(\mathbf{x})}.$$

Doing this decomposition for all the equations we obtain

$$\mathcal{F}(\mathbf{x}) = \left(\frac{\beta_M}{H} I_M S_H, 0, \frac{\beta_M}{H} S_M I_H, 0, 0, 0\right)$$

and $\mathcal{V}(\mathbf{x})$ containing all the other terms.

Then we construct the matrices

$$F = \left(\frac{\partial \mathcal{F}_i}{\partial x_j}(\mathbf{x_0})\right)_{i,j} \quad \text{and} \quad V = \left(\frac{\partial \mathcal{V}_i}{\partial x_j}(\mathbf{x_0})\right)_{i,j} \quad , \quad i,j = 1,\ldots,4$$

where $\mathbf{x_0}$ represents the equilibrium for which we compute the $R_0$, i.e., the disease-free equilibrium $\mathbf{x_0} = (0,0,0,0,H,K^*)$. The values taken by $i$ and $j$ are given by the fact we labeled the

infected compartments 1 to 4. These matrices for our model read

$$F = \begin{pmatrix} 0 & 0 & 0 & \beta_M \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_M}{H}K^* & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \gamma_H + b_H & 0 & 0 & 0 \\ -\gamma_H & \sigma_H + b_H & 0 & 0 \\ 0 & 0 & \gamma_M + d_M & 0 \\ 0 & 0 & -\gamma_M & d_M \end{pmatrix}.$$

In [44] is shown that $R_0 = \rho(FV^{-1})$, where $\rho$ denotes the spectral radius of the resulting matrix, namely

$$R_0^M = \rho(FV^{-1}) = \beta_M \sqrt{\frac{K^* \gamma_M \gamma_H}{H d_M (b_H + \sigma_H)(\gamma_M + d_M)(\gamma_H + b_H)}}.$$

In the case of system $(WB')$, where also mosquitoes with *Wolbachia* are present, there are six infected compartments and two relevant $R_0$, one at the disease-free/ *Wolbachia*-free equilibrium and one at the disease-free/full invasion equilibrium. We follow, step by step, the same procedure, adapting it to the new system for each of the $R_0$. We define $\mathbf{x} = (E_H, I_H, E_M, I_M, E_W, I_W, S_H, p)$ and we write the system as $\dot{\mathbf{x}} = \mathcal{F}(\mathbf{x}) - \mathcal{V}(\mathbf{x})$, where

$$\mathcal{F}(\mathbf{x})^\top = \begin{pmatrix} \frac{\beta_M}{H} I_M S_H + \frac{\beta_{WH}}{H} I_W S_H \\ 0 \\ \frac{\beta_M}{H}(K(1-p) - E_M - I_M) I_H \\ 0 \\ \frac{\beta_{HW}}{H}(Kp - E_W - I_W) I_H \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

and $\mathcal{V}(\mathbf{x})$ contais the rest of the terms.

The two relevant equilibria are both disease-free, one is the *Wolbachia*-free equilibrium, $\mathbf{x_0^M} = (0, 0, 0, 0, 0, 0, H, 0)$ and the other the full invasion equilibrium, $\mathbf{x_0^W} = (0, 0, 0, 0, 0, 0, H, 1)$. Matrix $V$ is the same in both cases, namely

$$V = \begin{pmatrix} \gamma_H + b_H & 0 & 0 & 0 & 0 & 0 \\ -\gamma_H & \sigma_H + b_H & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_M + d_M & 0 & 0 & 0 \\ 0 & 0 & -\gamma_M & d_M & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma_W + d_W & 0 \\ 0 & 0 & 0 & 0 & -\gamma_W & d_W \end{pmatrix}.$$

On the other hand, $F$ has a different value at each equilibrium, namely

$$F_M = \begin{pmatrix} 0 & 0 & 0 & \beta_M & 0 & \beta_{WH} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_M}{H}K & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad F_W = \begin{pmatrix} 0 & 0 & 0 & \beta_M & 0 & \beta_{WH} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_{HW}}{H}K & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Although computed differently, we recover the value of $R_0^M$ obtained in system (3.1) (keep in mind that in the high birth limit $K = K^*$). As for the value of $R_0^W$ we obtain

$$R_0^W = \rho(F_W V^{-1}) = \sqrt{\frac{\beta_{HW}\beta_{WH}K\gamma_W\gamma_H}{Hd_W(b_H+\sigma_H)(\gamma_W+d_W)(\gamma_H+b_H)}}.$$

## C.2 Proof of Theorem 3.1

Let us fix $p^* = 0$, the remaining cases can be dealt analogously. First of all we assume $R_{p^*} > 1$ and apply [55, Theorem 1] in order to obtain our persistence result. The set of initial conditions which we refer in the theorem is

$$\left\{(S_H, E_H, I_H, E_M, I_M, E_W, I_W, p) \in \mathbb{R}^7_{+0} \times [0, \theta[\right\}.$$

Note that it is an immediate consequence of the equations that if one of the latent or of the infectious classes is nonempty then it will remain always nonempty. Moreover we know that if $p(0) < \theta$ then $p(t) \to p^*$. Hence in order to prove persistence in our set we can consider a $0 < \zeta < \theta$ and prove persistence in

$$\left\{(S_H, E_H, I_H, E_M, I_M, E_W, I_W, p) \in \mathbb{R}^7_{+0} \times [0, \theta - \zeta]\right\}.$$

Notice that we assumed the human population constant and equal to $H$ and that the mosquito population satisfies a logistic growth. Taking this into account there exists a constant $\bar{K} > 0$ such that the set

$$\mathcal{K} = \left\{(S_H, E_H, I_H, E_M, I_M, E_W, I_W, p) \in \mathbb{R}^7_{+0} \times [0, \theta - \zeta] : S_H + E_H + I_H + E_M + I_M + E_W + I_W \leq \bar{K}\right\}$$

is a positively invariant compact set and each solution of system $(WB')$ with initial condition in $\mathbb{R}^7_{+0} \times [0, \theta - \zeta]$ enters in $\mathcal{K}$. For each $x_0 = (S_H^0, E_H^0, I_H^0, E_M^0, I_M^0, E_W^0, I_W^0, p^0) \in \mathcal{K}$ there exists exactly one solution $x(t; x_0)$ of system $(WB')$ defined in $\mathbb{R}_{0+}$ and such that $x(0; x_0) = x_0$ and $x(t; x_0) \in \mathcal{K}$ for all $t \geq 0$. We have that $x_0 \to x(t; x_0)$ is a semi-dynamical system in $\mathcal{K}$.

Consider the set

$$\mathcal{S} = \{(S_H, E_H, I_H, E_M, I_M, E_W, I_W, p) \in \mathcal{K} : E_H + I_H + E_M + I_M + E_W + I_W = 0\}.$$

We have that the set $\mathcal{K} \setminus \mathcal{S}$ is invariant by the remark above about the latent and the infectious

classes. As we have $R_{p^*} > 1$ we can consider $\delta_1 > 0$ and $\eta > 0$ such that

$$\begin{aligned}\left(\frac{\gamma_M\beta_M^2}{Hd_M(\gamma_M+d_M)} - \frac{(1+\delta_1)(\gamma_H+b_H)(\sigma_H+b_H)}{\gamma_H}\right)(K(1-p^*)-2\eta)+\\ +\left(\frac{\gamma_W\beta_{HW}\beta_{WH}}{Hd_W(\gamma_W+d_W)} - \frac{(1+\delta_1)(\gamma_H+b_H)(\sigma_H+b_H)}{\gamma_H}\right)(Kp^*-2\eta)>0.\end{aligned} \tag{C.1}$$

We consider $\xi$ and $\delta_2$ such that $0 < \delta_2 < \xi < \delta_1$ and define in $\mathcal{K}$ the map

$$P(S_H, E_H, I_H, E_M, I_M, E_W, I_W) =$$

$$(1+\xi)E_H + \frac{(1+\delta_1)(\gamma_H+b_H)}{\gamma_H}I_H + \frac{\gamma_M\beta_M}{d_M(\gamma_M+d_M)}E_M + \frac{(1+\delta_2)\beta_M}{d_M}I_M + \frac{\gamma_W\beta_{WH}}{d_W(\gamma_W+d_W)}E_W + \frac{(1+\delta_2)\beta_{WH}}{d_W}I_W.$$

Let us consider also for sufficiently small $\varepsilon$ the neighbourhood of $\mathcal{S}$

$$\mathcal{U} = \{x \in \mathcal{K} : \ P(x) < \varepsilon\}.$$

We have that

$$P(x) = 0 \Longleftrightarrow x \in S.$$

Moreover let us assume, in order to arrive to a contradiction, that:

$$\exists x_0 \in \mathcal{U} \setminus \mathcal{S} \text{ such that } P(x(t;x_0)) < \varepsilon \text{ for all } t > 0. \tag{C.2}$$

Let $\phi(t) = P(x(t;x_0))$, we are going to prove that there exists $k > 0$ such that

$$\phi'(t) \geq k\phi(t) \tag{C.3}$$

for large $t$. In fact, taking into account (C.2), we obtain that there exists $\varepsilon^* > 0$ such that $\liminf_{t\to+\infty} S_H(t) > \frac{b_H H}{\varepsilon^*+b_H}$ and this $\varepsilon^* > 0$ can be chosen sufficiently small if we choose $\varepsilon$ small. We assume that $\varepsilon$ is chosen in order to imply $\dfrac{\varepsilon^*+b_H}{b_H}(1+\delta_2) < 1+\xi$ and also that the latent and infected mosquitoes classes are smaller then $\eta$ for $t > 0$ (this will be useful after and is possible by (C.2)). Then we evaluate $\phi'(t)$ and recall that $p(t) \to p^*$ when $t \to +\infty$. We obtain

$$\begin{aligned}\phi'(t) &= \left(\frac{b_H}{\varepsilon^*+b_H}(1+\xi) - (1+\delta_2)\right)(\beta_M I_M + \beta_{WH} I_W)\\ &+ (\delta_1-\xi)(\gamma_H+b_H)E_H + \delta_2\left(\frac{\beta_M\gamma_M}{d_M}E_M + \frac{\beta_{WH}\gamma_W}{d_W}E_W\right)\\ &+ \left(\left(\frac{\gamma_M\beta_M^2}{Hd_M(\gamma_M+d_M)} - \frac{(1+\delta_1)(\gamma_H+b_H)(\sigma_H+b_H)}{\gamma_H}\right)(K(1-p) - E_M - I_M)\right.\\ &+ \left.\left(\frac{\gamma_W\beta_{HW}\beta_{WH}}{Hd_W(\gamma_W+d_W)} - \frac{(1+\delta_1)(\gamma_H+b_H)(\sigma_H+b_H)}{\gamma_H}\right)(Kp - E_W - I_W)\right)I_H.\end{aligned}$$

We have that $p(t) \to p^*$ and hence by (C.1) we have that for sufficiently large $t$ the coefficient of $I_H$ in the last expression is positive. The existence of $k > 0$ satisfying (C.3) follows and this contradicts (C.2). We conclude that $\mathcal{S}$ is an uniform repeller and the result for $R_{p^*} > 1$ follows.

The case $R_{p^*} < 1$ can be obtained in the spirit of the previous one constructing this time a function $\phi^*$ for which there exists $k^* < 0$ such that for each $t > 0$

$$\phi^{*\prime}(t) \leq -k^*\phi^*(t). \tag{C.4}$$

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