Feedback Control Principles for Biological Control of Dengue Vectors
Pierre-Alexandre Bliman

To cite this version:
Pierre-Alexandre Bliman. Feedback Control Principles for Biological Control of Dengue Vectors. European Control Conference ECC19, Jun 2019, Naples, Italy. pp.6. hal-01944958v2

HAL Id: hal-01944958
https://inria.hal.science/hal-01944958v2
Submitted on 5 Mar 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
Feedback Control Principles for Biological Control of Dengue Vectors*

Pierre-Alexandre Bliman*

Abstract—Controlling diseases such as dengue fever, chikungunya and zika fever by introduction of the intracellular parasitic bacterium Wolbachia in mosquito populations which are their vectors, is presently quite a promising tool to reduce their spread. While description of the conditions of such experiments has received ample attention from biologists, entomologists and applied mathematicians, the issue of effective scheduling of the releases remains an interesting problem for Control theory. Having in mind the important uncertainties present in the dynamics of the two populations in interaction, we attempt here to identify general ideas for building release strategies, which should apply to several models and situations. These principles are exemplified by two interval observer-based feedback control laws whose stabilizing properties are demonstrated when applied to a model retrieved from [1]. Crucial use is made of the theory of monotone dynamical systems.

I. INTRODUCTION

Already a major issue in southern countries since decades, the control of vector-borne diseases transmitted by mosquitoes recently became an important concern for northern countries too, due to the geographical dissemination of the vectors favored by climate change, urbanization and increasing international travel. When no vaccine or curative treatment exists, traditional control measures focus on reducing the vector population in order to reduce the pathogen transmission. Mechanical control methods by preventive actions and removal of breeding sites are invaluable, but costly and difficult to implement efficiently. Chemical control by insecticides has been quite popular, but on top of its negative impacts on humans and animals, it experiences Decreasing efficiency due to resistance generation. Recently, various biological control methods have been proposed and tested as alternative or complementary strategies, typically by the release of transgenic or sterile mosquitoes [2], [3]. A new promising strategy based on the use of the bacterium Wolbachia, is being developed to control the spread of dengue fever and other diseases transmitted by species of the genus Aedes (chikungunya, zika fever, yellow fever). It is grounded in the fact that Wolbachia severely reduces the insect vectorial ability, indirectly by reducing lifespan and fertility, and directly by reducing the virus ability to proliferate within the organism [4], [5], [6], [7].

The dynamics resulting from the introduction of Wolbachia-infected mosquitoes in wild populations has been abundantly considered, even in the absence of spatial aspects; see [8], [9], [10], [11], [12], [13], [14], [15], [1], [16], and [17], [18], [19] for the effects induced on a dengue epidemics. Field sampling methods allow to evaluate population density [20], [21], and such operations are commonly performed during experimental campaigns. Also, the presence of the bacterium in the captured sample may be investigated by polymerase chain reaction (PCR) method [6]. Theoretically, this opens up the possibility to assess the released quantities on the basis of the observed population, and to benefit from the multiple advantages of closed-loop methods. Most papers analyze only the effect of a unique, initial, release. By contrast, [11] considers continuous releases and [12] impulsive releases (with no analytical results), both with constant release amplitude, while [1] provides linear control-law and [14], [15], [22] optimal control approach. However these stabilization results are highly dependent upon the setting, and their generalization is in no way straightforward. Our aim here is to identify simple control principles, based on the understanding of the biological phenomena involved, and to test them on the model introduced in [1]. More specifically, we propose two control laws achieving complete infestation, respectively through the introduction of infected adults and larvae. Their implementation necessitates the construction of an interval observer [23], [24], [25] for the considered system.

The content of the paper is as follows. The characteristics of the compartmental model developed in [1] are recalled in Section [II] together with some analysis results. Section [III] proposes a class of interval observers for this model. The main results (Theorems [II] and [III]) are exposed and proved in Section [IV] Numerical simulations are shown in Section [V] and some concluding remarks are given in Section [VI]. All proofs are omitted and may be found in [26].

Notations. The following notations are used for the positive, resp. negative, parts of a real number \(z\): \(|z|_+ := \max\{z, 0\}\), \(|z|_- := -\min\{z, 0\}\). Both are nonnegative, and

\[
\forall z \in \mathbb{R}, \quad z = |z|_+ - |z|_- .
\]  

(1)

The usual order relation \(\geq\) in \(\mathbb{R}\) is employed, and the same notation is extended to vectors and matrices by the product order: \((x_1, x_2) \geq 0\) if and only if \(x_1 \geq 0\) and \(x_2 \geq 0\). It is similarly extended to locally integrable functions taking on values in one of these ordered spaces, with the evident meaning. In all cases, the symbol \(>\) is used as usual to mean “at most

* The author acknowledges the financial support of the Franco-Columbian program ECOS-Nord, through the project C17M01. This work benefited from fruitful discussions with Y. Dumont (CIRAD, University of Pretoria) within the framework of the Phase 2 SIT feasibility project against Aedes albopictus in Reunion Island, jointly funded by the Regional Council of La Reunion and the European Regional Development Fund (ERDF) under the 2014-2020 Operational Program.

* Pierre-Alexandre Bliman is with Sorbonne Université, Université Paris-Diderot SPC, Inria, CNRS, Laboratoire Jacques-Louis Lions, équipe Mamba, F-75005 Paris, France; e-mail: pierre-alexandre.bliman@inria.fr

\[\text{"Feedback Control Principles for Biological Control of Dengue Vectors"} \]

Pierre-Alexandre Bliman*

Abstract—Controlling diseases such as dengue fever, chikungunya and zika fever by introduction of the intracellular parasitic bacterium Wolbachia in mosquito populations which are their vectors, is presently quite a promising tool to reduce their spread. While description of the conditions of such experiments has received ample attention from biologists, entomologists and applied mathematicians, the issue of effective scheduling of the releases remains an interesting problem for Control theory. Having in mind the important uncertainties present in the dynamics of the two populations in interaction, we attempt here to identify general ideas for building release strategies, which should apply to several models and situations. These principles are exemplified by two interval observer-based feedback control laws whose stabilizing properties are demonstrated when applied to a model retrieved from [1]. Crucial use is made of the theory of monotone dynamical systems.

I. INTRODUCTION

Already a major issue in southern countries since decades, the control of vector-borne diseases transmitted by mosquitoes recently became an important concern for northern countries too, due to the geographical dissemination of the vectors favored by climate change, urbanization and increasing international travel. When no vaccine or curative treatment exists, traditional control measures focus on reducing the vector population in order to reduce the pathogen transmission. Mechanical control methods by preventive actions and removal of breeding sites are invaluable, but costly and difficult to implement efficiently. Chemical control by insecticides has been quite popular, but on top of its negative impacts on humans and animals, it experiences decreasing efficiency due to resistance generation. Recently, various biological control methods have been proposed and tested as alternative or complementary strategies, typically by the release of transgenic or sterile mosquitoes [2], [3]. A new promising strategy based on the use of the bacterium Wolbachia, is being developed to control the spread of dengue fever and other diseases transmitted by species of the genus Aedes (chikungunya, zika fever, yellow fever). It is grounded in the fact that Wolbachia severely reduces the insect vectorial ability, indirectly by reducing lifespan and fertility, and directly by reducing the virus ability to proliferate within the organism [4], [5], [6], [7].

The dynamics resulting from the introduction of Wolbachia-infected mosquitoes in wild populations has been abundantly considered, even in the absence of spatial aspects; see [8], [9], [10], [11], [12], [13], [14], [15], [1], [16], and [17], [18], [19] for the effects induced on a dengue epidemics. Field sampling methods allow to evaluate population density [20], [21], and such operations are commonly performed during experimental campaigns. Also, the presence of the bacterium in the captured sample may be investigated by polymerase chain reaction (PCR) method [6]. Theoretically, this opens up the possibility to assess the released quantities on the basis of the observed population, and to benefit from the multiple advantages of closed-loop methods. Most papers analyze only the effect of a unique, initial, release. By contrast, [11] considers continuous releases and [12] impulsive releases (with no analytical results), both with constant release amplitude, while [1] provides linear control-law and [14], [15], [22] optimal control approach. However these stabilization results are highly dependent upon the setting, and their generalization is in no way straightforward. Our aim here is to identify simple control principles, based on the understanding of the biological phenomena involved, and to test them on the model introduced in [1]. More specifically, we propose two control laws achieving complete infestation, respectively through the introduction of infected adults and larvae. Their implementation necessitates the construction of an interval observer [23], [24], [25] for the considered system.

The content of the paper is as follows. The characteristics of the compartmental model developed in [1] are recalled in Section [II] together with some analysis results. Section [III] proposes a class of interval observers for this model. The main results (Theorems [II] and [III]) are exposed and proved in Section [IV] Numerical simulations are shown in Section [V] and some concluding remarks are given in Section [VI]. All proofs are omitted and may be found in [26].

Notations. The following notations are used for the positive, resp. negative, parts of a real number \(z\): \(|z|_+ := \max\{z, 0\}\), \(|z|_- := -\min\{z, 0\}\). Both are nonnegative, and

\[
\forall z \in \mathbb{R}, \quad z = |z|_+ - |z|_- .
\]  

(1)

The usual order relation \(\geq\) in \(\mathbb{R}\) is employed, and the same notation is extended to vectors and matrices by the product order: \((x_1, x_2) \geq 0\) if and only if \(x_1 \geq 0\) and \(x_2 \geq 0\). It is similarly extended to locally integrable functions taking on values in one of these ordered spaces, with the evident meaning. In all cases, the symbol \(>\) is used as usual to mean “at most

* The author acknowledges the financial support of the Franco-Columbian program ECOS-Nord, through the project C17M01. This work benefited from fruitful discussions with Y. Dumont (CIRAD, University of Pretoria) within the framework of the Phase 2 SIT feasibility project against Aedes albopictus in Reunion Island, jointly funded by the Regional Council of La Reunion and the European Regional Development Fund (ERDF) under the 2014-2020 Operational Program.

* Pierre-Alexandre Bliman is with Sorbonne Université, Université Paris-Diderot SPC, Inria, CNRS, Laboratoire Jacques-Louis Lions, équipe Mamba, F-75005 Paris, France; e-mail: pierre-alexandre.bliman@inria.fr
equal to, but not equal’. As an example, for locally integrable functions \( f, g \) defined on a common domain, ‘\( f > g \)’ is equivalent to ‘\( f \geq g \) and \( f > g \) on a nonzero-measured set’. Also, we use the notation \( \ll \) for ‘much less than’. Whenever the sign \( \pm \) is used, it means that the relevant formula is valid for + and for −. Last, usual matrix notations are employed: \( I_n, 0_n \) denote respectively the identity and null square matrices of order \( n \), \( n \in \mathbb{N} \), \( ^\top \) denotes transposition.

### II. Modeling

#### A. Model equations

The compartmental model in [1] focuses on the main effects pertinent for control purposes. It contains two life phases: a preliminary phase which gathers the early, aquatic, stages (egg, larva and pupa), subject to competition for food and space; and an adult, aerial, mature phase. The corresponding state variables are respectively denoted \( L \) (‘larvae’) and \( A \) (‘adults’), and the uninfected and Wolbachia-infected populations are distinguished by indices \( U \) and \( W \). Assuming in first approximation that the sex ratio is stationary and the mortality is sex-independent, these variables represent indifferently the quantities of males or females, up to constant ratio. After normalization, the 4-dimensional population model used in the present paper is the following [1]:

\[
\begin{align*}
\dot{L}_U &= \gamma_U R_0^U \frac{A_U}{A_U + A_W} A_U - (1 + L_U + L_W) L_U \quad (2a) \\
\dot{A}_U &= L_U - \gamma_U A_U \quad (2b) \\
\dot{L}_W &= \gamma_W R_0^W A_W - (1 + L_U + L_W) L_W + u_L(t) \quad (2c) \\
\dot{A}_W &= L_W - \gamma_W A_W + u_A(t) \quad (2d)
\end{align*}
\]

The quantities \( \gamma_U, \gamma_W \) are (normalized) mortality rates, while \( R_0^U, R_0^W \) are the basic offspring numbers [27], [28] associated to each population. They represent the average number of mosquitoes born to each adult mosquito during its entire lifespan.

The signal \( u_L \) (resp. \( u_A \)) represents the infected larvae (resp. adults) released per time unit in order to infect the wild population. By construction both have nonnegative values. Using \( x := (L_U, A_U, L_W, A_W) \), \( u := (u_L, u_A) \) as state and input variables, the previous controlled system writes compactly:

\[
\dot{x} = f(x) + Bu, \quad y = Cx, \quad (3)
\]

where the function \( f \) is easily expressed from (2), and the input matrix \( B \) is given by

\[
B := \begin{pmatrix}
0 & 0 & 1 & 0 \\
0 & 0 & 0 & 1
\end{pmatrix}^\top.
\]

The output matrix \( C \) is used to define which are the available measurements, it is specified in Section [III].

Well-posedness of the Cauchy problem for system (2) does not present specific difficulty, e.g. for locally integrable input \( u \) with nonnegative values almost everywhere. As a result of this and of the fact that \( (f(x))_i \geq 0 \) if \( x \geq 0 \) and \( x_i = 0 \), \( i = 1, \ldots, 4 \), the set \( \mathbb{R}_+^4 \) is forward invariant for the flow.

#### B. Phenomenological hypotheses on the infection dynamics

The main phenomenological assumptions contained in the previous infection model are the following.

- 1. The Wolbachia infection in Aedes mosquito leads to lifespan shortening through adult mortality increase [4], [29] and fecundity rate reduction [30]. This is accounted for by the following inequalities between normalized constants:

\[
0 < \gamma_U < \gamma_W, \quad R_0^U > R_0^W > 1. \quad (4)
\]

The variations of larval development time and mortality are regarded as limited and are not modeled here.

- 2. The density-dependent mortality is a major component of larval dynamics [31], [32], rendered here by quadratic competition terms in the immature phase dynamics. Accounting for restricted food and space in the breeding sites, it acts evenly on the immature infected and uninfected population, with a rate proportional to its global size \( L_U + L_W \).

- 3. The Wolbachia transmission occurs only vertically, from mother to offspring. It is accompanied by a phenomenon called cytoplasmic incompatibility, which provides a reproduction advantage to infected females against uninfected ones and facilitates the spread of the bacterium. Cytoplasmic incompatibility is characterized by the fact that an uninfected female only produces offspring when mating with an uninfected male [33], [4], [29], [34]. On the contrary when an infected female mated, the outcome is infected independently of whether the male is infected or not. The probability of a male being uninfected is \( \frac{A_U}{A_U + A_W} \), and the nonlinear birth term \( \frac{A_U}{A_U + A_W} A_W \) in (2a) accounts for such encounters. By contrast, the birth term for infected in (2c) is simply proportional to the corresponding population \( A_W \).

#### C. Analysis of the uncontrolled model [1]

In order to understand the meaning of the basic offspring numbers, consider the following auxiliary system:

\[
\dot{L} = \gamma R A - (1 + L) L, \quad \dot{A} = L - \gamma A, \quad (5)
\]

with \( \gamma > 0, R > 0 \). System (5) is monotone [35]. When \( R < 1, 0_2 \) is the unique (extinction) equilibrium and is globally asymptotically stable; while when \( R > 1 \) it is unstable, and the nonzero equilibrium \( (R - 1, 0_2) \) appears, which is asymptotically stable and limit point of every nonzero trajectory. The relevance of this comes from the following fact, which may be easily checked: when initially one of the two populations (infected or uninfected) is absent from (2), then the other one evolves alone according to system (5).

Transposing this remark discloses immediately the existence, under hypothesis (4), of two equilibria for system (2) with zero input \( u \), characterized by the state values \( (L_U^*, A_U^*, 0, 0) \) and \( (0, 0, L_W^*, A_W^*) \), where:

\[
L_U^* := R_0^U - 1, \quad A_W^* := \frac{L_W^*}{\eta}, \quad \eta = U, W.
\]

They correspond respectively to disease-free and complete infestation situations. Under hypothesis (4), both are locally asymptotically stable: this assumption ensures the sustainability of each of the two isolated populations, with a greater
basic offspring number for the uninfected population, in accordance with the fact that Wolbachia globally reduces the fitness of the infected mosquitoes.

Two other equilibria exist, which correspond to extinction and coexistence, and are both unstable. System (2) presents bistability, and the control purpose is typically to pass from the disease-free situation to the complete infestation.

A structural property, central to analyze the behavior of system (2), is monotonicity [35]. It will be instrumental in the sequel. We first introduce a specific order relation defined in the space $\mathbb{R}^4$.

**Definition 1:** The ordering induced in the space $\mathbb{R}^4$ by the cone $\mathbb{R}_- \times \mathbb{R}_- \times \mathbb{R}_+ \times \mathbb{R}_+$ is denoted $\succeq$: by definition,

$$ x \succeq x' \iff x_i \leq x_i', \quad i = 1, 2 \text{ and } x_i \geq x_i', \quad i = 3, 4 \quad (6) $$

The following results is borrowed from [1].

**Theorem 1:** System (2) with zero input $u$ is strongly order-preserved [35, p. 2] in $\mathbb{R}_+^4$ for the order induced by (6).

### III. Upper and lower state estimates

In order to study control synthesis in Section IV upper and lower estimates of the state variables will be needed. Notice that using monotonicity and the fact that the input variable $u$ takes on nonnegative values, one may show e.g. that the solutions of (2) fulfill, for any initial condition, the properties:

- $0 \leq \lim_{t \to +\infty} L_U(t) \leq \lim_{t \to +\infty} L_U(t) \leq L_U^*$,
- $0 \leq \lim_{t \to +\infty} A_U(t) \leq \lim_{t \to +\infty} A_U(t) \leq A_U^*$,

The use of such rough estimates is possible, but may yield uselessly costly control laws. On the other hand, it is important to stress here that the stabilisation results that we present below in Section IV do not require any convergence property from the used observers.

We assume the availability of, say, $p$ measurements, and introduce the output variable $y = Cx$ for some fixed matrix $C \in \mathbb{R}^p \times 4$. Typically $y$ contains measurement on the values of $L_U(t), L_W(t)$ and $A_U(t), A_W(t)$, depending upon the information monitored in the field.

In order to take into account measurement uncertainties, one assumes that are available two (locally integrable, nonnegative-valued) auxiliary signals $y_-(t), y_+(t)$ bounding (componentwise) the exact, but unknown, value $y(t)$: for (almost) any $t \geq 0$, $0 \leq y_-(t) \leq y(t) \leq y_+(t)$.

As a quite easy consequence of the monotonicity of the model (see Theorem 1), one has the following result.

**Theorem 2:** (Interval observer design). For $x$ evolving according to (3), let the evolution of the variables

$$ x_- := \begin{pmatrix} L_U^* \\ A_U^* \\ L_W^* \\ A_W^* \end{pmatrix}, \quad x_+ := \begin{pmatrix} L_U^* \\ A_U^* \\ L_W^* \\ A_W^* \end{pmatrix} \quad (7) $$

be defined by

$$ \dot{x}_- = f(x_-(t)) + Bu + K_-(x_-(t))(y_-(t) - Cx_-(t)) \quad (8a) $$

$$ \dot{x}_+ = f(x_+(t)) + Bu + K_+(x_+(t))(y_+(t) - Cx_+(t)) \quad (8b) $$

for gain matrices $K_-(\cdot), K_+(\cdot) \in \mathbb{R}^{4 \times p}$ depending continuously upon the state. Assume that

$$ \text{diag}\{ -I_2; I_2 \} K_+ \circ \geq 0 \quad (9a) $$

$$ \text{diag}\{ -I_2; I_2 \} K_- \circ C \text{ diag}\{ -I_2; I_2 \} \leq 0 \quad (9b) $$

and that the $i$-th line of $K_-(\cdot)$ (resp. $K_+(\cdot)$) is null whenever the $i$-th component of its argument is null, $i = 3, 4$ (resp. $i = 1, 2$). If

$$ x_-(t) \leq x(t) \leq x_+(t) \quad \text{and} \quad 0 \leq x_-(t), x(t), x_+(t) \quad (10) $$

for $t = 0$, then the same holds true for any $t \geq 0$.

Recall that $f$ in the previous statement is the function that allows to write (2) as (3). Theorem 2 provides sufficient conditions under which, if $0 \leq L_U^*(t) \leq L_W^*(t)$, $0 \leq A_U^*(t) \leq A_W^*(t)$, $\eta = U, W$, for $t = 0$, then the same holds true for any $t \geq 0$. In addition, it is easy to show that if $x(t) = x(t)$, say for $t = 0$, then the same is true for any $t \geq 0$. System (2) therefore constitutes an interval observer [23, 24, 25] for $f$ but not an asymptotic observer, as previously mentioned.

Coming back to the definition of the order $\succeq$ in (6), conditions (9a)-(9b) appear as rephrasings of the conditions:

$$ \forall y, y' \in \mathbb{R}^p, \quad y \leq y' \quad \Rightarrow \quad K_- \circ y \leq K_- \circ y', \quad K_+ \circ y \leq K_+ \circ y' \quad (11a) $$

$$ \forall x, x' \in \mathbb{R}^4, \quad x \leq x' \quad \Rightarrow \quad K_- \circ Cx \leq K_- \circ Cx', \quad K_+ \circ Cx \leq K_+ \circ Cx' \quad (11b) $$

**Remark 1:** Notice that (9b) comes as a consequence of (9a) when e.g.

$$ C \text{ diag}\{ -I_2; I_2 \} \leq 0 \quad . \quad (9c) $$

When for example measurements of the two larval populations $L_U(t), L_W(t)$ are available, then $p = 2$ and one may take $C = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 0 & -1 & 0 \end{pmatrix}$, in accordance with (9c).

Condition (9a) then says that the first two rows of the admissible gain matrices $K_-(\cdot), K_+(\cdot)$ must be nonpositive, and their last two rows nonnegative.

**Remark 2:** A simple way to fulfill the last assumption on the matrix gain lines is to introduce a smoothed Heaviside function for the corresponding components; namely to take the $i$-th line of $M_{\pm}(x_{\pm})$ equal to the $i$-th line of a constant matrix $M_{\pm}$ fulfilling (11), multiplied by the function $\max\{ \min\{x_{\pm}, \varepsilon\}, 0\}$, for some $0 < \varepsilon < 1$.

### IV. Feedback control principles and observer-based stabilization

Due to the uncertainty inherent to the models of population dynamics, it seems valuable to propose feedback control strategies obeying general, ‘model-free’, principles. We propose in the sequel two such approaches, related to control by release of adult mosquitoes and of larvae.

---

1 Notice however that this does not mean that the estimates are bounded, as according to the input u, the state x itself may grow unbounded.
A. Control by release of adult mosquitoes

First, it is clear that, if the inter-species competition induced by the presence of infected mosquitoes is sufficient to make unviable the uninfected population, then the latter disappears. Adults do not directly interact, as shown by equations (25) and (24). However, they participate centrally to the natality. With this in mind, assume that, due to releases of adults through the input \( u_A \) in (24), the fractional term responsible in (25) for the cytoplasmic incompatibility, is kept smaller than the \( 1/R_0 \), where \( R_0 \) is the basic offspring number of the uninfected population. Under such conditions, the uninfected population evolves sensibly as in equation (5) — however with a subcritical ‘apparent’ basic offspring number, as \( R_0 U \times 1/R_0 = 1 \). This suggests that targeting the cytoplasmic incompatibility term may be a way to realize eradication of the uninfected population. This general principle underpins the following result.

Theorem 3: (Sufficient conditions for successful introduction via release of adults). Assume available upper and lower state estimates \( x_\pm \) for the solution of (2), according to (10) and (7). Then \( \lim_{t \to +\infty} \left( L_U(t), A_U(t) \right) = (0,0), \lim_{t \to +\infty} \left( L_W(t), A_W(t) \right) \geq \left( L_U^*, A_U^* \right) \) holds for given constants \( k > 0, k_U > R_0 U \). Then

\[
\lim_{t \to +\infty} \begin{pmatrix} L_U(t) \\ A_U(t) \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \liminf_{t \to +\infty} \begin{pmatrix} L_W(t) \\ A_W(t) \end{pmatrix} \geq \begin{pmatrix} L_U^* \\ A_U^* \end{pmatrix}
\]

Formula (A) is displayed on top of the next page. The goal of the control is to steer the system to the complete infestation equilibrium \((0,0, L_U^*, A_U^*)\). Notice that when it succeeds, the lower bound of \( u_A \) in (A) may vanish asymptotically only if \( k = \gamma_W \). In this case, the second inequality in (A) becomes in view of (25)

\[
u_A \geq \left( k_U \cdot k_U (\gamma_W - \gamma_U) - 1 \right) \begin{pmatrix} L_U^* \\ A_U^* \end{pmatrix} \quad \text{on } [T, +\infty)
\]

expression in which the three useful components of the estimator pertain to \( x_- \), see (7).

B. Control by release of larvae

We now examine a control approach based on release of larvae. This method amounts to acting on the input term \( u_L \) in (25). The only hindrance to the growth of the infected population lies on the competition term in the previous equation. Therefore, if the rate of introduction of infected larvae is sufficient to compensate for the competition effect, then the infected population should reach the complete infestation equilibrium and induce collapse of the uninfected population, through the competitive pressure term in (25).

This is evidenced by the following result.

Theorem 4: (Sufficient conditions for successful introduction via release of larvae). Assume available upper and lower state estimates \( x_\pm \) for the solution of (2), according to (10) and (7). Then (12) holds if for some \( T \geq 0 \),

\[
u_L > L_U^* L_W^+, \quad u_A \geq 0 \quad \text{on } [T, +\infty).
\]

V. Numerical simulations

Numerical simulations of the controlled system have been achieved for the control laws designed in Theorems 3 and 4 (using the stiff option of the ode function of the free open-source software Scilab). Numerical values from [1] have been used: \( \gamma_U = 0.79365, \gamma_W = 0.92907, R_0 U = 45, R_0 W = 34.2, \) so that \( L_U^* = 44.0, A_U^* = 55.4, L_W^* = 33.2, A_W^* = 33.5. \)

The initial state is taken at the disease-free equilibrium \((L_U^*, A_U^*, 0, 0)\) and observer is initialized with quite conservative estimates: \((L_U^*(0), A_U^*(0), L_W^*(0), A_W^*(0)) = (0,0,0,0), (L_U^*(0), A_U^*(0), L_W^*(0), A_W^*(0)) = (2 L_U^*, 2 A_U^*, 0.05 L_W^*, 0.05 A_W^*). \)

Noisy measurement is considered, with \( y = y + 20\% y \).

The choice of the gains present no specific difficulty, as the conditions on the observer gains stated in Theorem 1 are not hard to meet. The output gain \( C \) is taken as the example in Remark 1, while the observer gains \( K_\pm(\cdot) \) are chosen as explained in Remark 2 with

\[
\varepsilon = 10^{-5}, \quad M_- = M_+ = 0.1 \begin{pmatrix} -1 & -1 & 1 & 1 \\ -1 & -1 & 1 & 1 \end{pmatrix}^T.
\]

In these conditions, all assumptions of Theorem 2 are fulfilled. The simulations show, as expected and in spite of precise initial state estimation and measurement, convergence of the controlled system towards the complete infestation equilibrium \((0,0, L_W^*, A_W^*)\), in dashed line in the Figures.

a) Release of adult mosquitoes (Theorem 2). The control \( u := (u_L, u_A) \) is defined by taking equalities in the formulas in (A). One chooses \( k_U = 1.1(R_0 U - 1) \) and \( k = \gamma_W \). The control \( u_A \) is then linear in the right-hand side of (13). As noticed after the statement of Theorem 3 only \( x_- \) is used for the control synthesis. The results are shown in Figure 1. The green curves represent the ‘true’ values (components of \( x \)), while the blue ones show the evolution of the components of \( L_U^*, A_U^*, L_W^*, A_W^* \) of \( x_+ \).

b) Release of larvae (Theorem 2). The control \( u := (u_L, u_A) \) is defined here by taking equalities in (L). Notice that the strict inequity in (L) is obtained thanks to a nonzero initialization of \( L_U^* \). The results are shown in Figure 2. The green curves represent the components of \( x_- \) (resp. \( x_+ \)).

VI. Concluding remarks

Two release strategies have been proposed, allowing to realize complete infestation of a population of Aedes mosquitoes by a population artificially infected by the bacterium Wolbachia, which reduces their ability as vectors of several important diseases. The efficiency of the approach has been demonstrated analytically and tested numerically. Its main force is to be expressed in general terms, giving rise to potential extensions to other models in the literature, e.g. those in [8], [9], [17], [10], [18], [19], [11], [12], [13].

2 More precisely: \( u_A = \begin{pmatrix} k_U \\ k_U (\gamma_W - \gamma_U) - 1 \end{pmatrix} \begin{pmatrix} L_U^* \\ A_U^* \end{pmatrix}. \)
\[ u_L \geq 0, \ u_A \geq K \begin{pmatrix} L^U_L \\ A^U_L \\ A^W_L \\ A^W \\ \end{pmatrix} \text{ on } [T, +\infty), \quad K := \begin{pmatrix} k_U & k_U |k - \gamma_U| + & k_U |k - \gamma_U| - & -1 & |\gamma_W - k| + & |\gamma_W - k| - \end{pmatrix} \] (A)

Fig. 1. Release of adult mosquitoes: evolution of the uninfected (top) and Wolbachia-infected (bottom), as function of time. The larvae appear on the left column, the adults on the right one. The components of the state \( x \) (resp. of the estimate \( x^- \)) appear in green (resp. in blue).

Fig. 2. Release of larvae: evolution of the uninfected (top) and Wolbachia-infected (bottom), as function of time. The larvae appear on the left column, the adults on the right one. The components of the state \( x \) (resp. of the estimates \( x^- \), \( x^+ \)) appear in green (resp. in blue, in red).
[16], due to their monotonicity. Being based on monotone system properties, it is believed to be a good way to ensure robust behavior with respect to unmodeled dynamics and parameter uncertainties, with no need of precise knowledge of the boundary between the basins of attraction of the two locally asymptotically stable equilibria. Future works include the consideration of measurement delays. Also, further study is needed in order to reduce the peaking effect apparent with the first method. Last, extensions to non monotone systems should be considered, as well as more realistic impulsive periodic releases, much in the spirit of [36] in the context of Sterile Insect Techniques.

REFERENCES


3 One may check that the underlying entomological models are all monotone, assuming where appropriate complete cytoplasmic incompatibility, zero delay and possibly after merging of some male/female compartments.