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VECTOR CONTROL FOR THE CHIKUNGUNYA DISEASE

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Abstract. We previously proposed a compartmental model to explain the outbreak of Chikungunya disease in Réunion Island, a French territory in Indian Ocean, and other countries in 2005 and possible links with the explosive epidemic of 2006. In the present paper, we asked whether it would have been possible to contain or stop the epidemic of 2006 through appropriate mosquito control tools. Based on new results on the Chikungunya virus, its impact on mosquito life-span, and several experiments done by health authorities, we studied several types of control tools used in 2006 to contain the epidemic. We present an analysis of the model, and we develop a new nonstandard finite difference scheme to provide several simulations with and without mosquito control. Our preliminary study shows that an early use of a combination of massive spraying and mechanical control (like the destruction of breeding sites) can be efficient, to stop or contain the propagation of Chikungunya infection, with a low impact on the environment.

1. **Introduction.** In 2004, 2005, and 2006, epidemics of Chikungunya [40] hit Indian Ocean islands like Comoros, Réunion Island, and Mauritius [35], and more recently India [28]. In Europe, a few cases were reported in summer 2007 in Italy [37, 44, 11, 41]. It is now recognized that *Aedes albopictus* [20] was the principal vector of transmission for the Chikungunya in Réunion Island [36] and even in some parts of India [38], for instance, in Kerala where the outbreak was particularly dramatic [26]. *Aedes albopictus*, also known as the *Asian tiger* mosquito, is found in Southeast Asia, the Pacific and Indian Ocean islands, and up north through China and Japan. It recently was found in Europe [29], USA, and Australia [5]. It appeared in Réunion Island one century ago and is now well established on the island [10].

The symptoms of Chikungunya appear between 2 and 4 days after a bite by an infected mosquito: high fever and headache, with arthritis affecting multiple joints (like ankle and wrist). Symptoms can persist several weeks or months (see [34] for further information). Infected people can be treated with drugs, but the efficacy

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of the treatment varies greatly from one person to another [34]. Finally, in the absence of a vaccine, the main preventive measures to reduce the transmission of the Chikungunya virus are individual protection against mosquito bites and mosquito control.

Through research conducted in France and India, we are better able to explain what happened in 2006 (see also [40] for an overview about Chikungunya). Till the huge episode of 2006, no model was explicitly developed for Chikungunya, in contrast to many models for other vector-borne diseases (see [1, 14, 16, 17, 22] and references therein). Since then, a few models have been proposed [4, 13, 35].

The present paper considers the L-SEIR model proposed in [13], but we now take into account recent results obtained on the virus [43] and the life-span of the infected mosquitoes [15]. In particular, we show that mosquito life-span in the different compartments has a direct impact on the existence or not of an endemic equilibrium. Moreover, we added additional terms in the model related to the different control tools we intend to study. Then, we computed the basic reproduction number $\mathcal{R}_0$ (see [1, 14, 21, 22]) for the largest cities in Réunion Island, Saint-Denis and Saint-Pierre.

We focused on the type of control tool for containing or stopping the epidemic. Indeed, during the epidemic, the DRASS (a French government agency for disease prevention and vector control) conducted several interventions, including:

- massive spraying using a chemical adulticide, Deltamethrin, to reduce the number of adult mosquitoes. Note that Deltamethrin is the only authorized adulticide in the European Union. Because Réunion Island has chaotic landscapes, most people live in the coastal lowlands, and thus, only truck-mounted sprayers can be used to disperse the adulticide. This is done at night (between 2 am and 5 am). The problem is that this type of intervention can be very detrimental to the environment [18]. In particular, the high toxicity and the lack of specificity of Deltamethrin prevent spraying it near rivers or sources. Yet, the population of *Aedes albopictus* in Réunion Island is sensitive to Deltamethrin, which is not the case everywhere. For instance, in Martinique, another French overseas department, located in the French West Indies, 60% of the *Aedes* are Deltamethrin-resistant. Massive spraying is not efficient in this case.
- localized treatment using a chemical larvicide, *Bti* (*Bacillus thuringensis israelensis*), targeting the larvae in their breeding habitat before they mature. Unfortunately, the impact of *Bti* seems not as efficient as that of adulticides. In laboratory conditions the killing rate is good at least the first few days, but in real conditions, i.e. in natural breeding sites, recent results show that it is not so good [27].
- mechanical control (like "Kass'Moustik", see [25]) to reduce the number of breeding sites. This effective means consists in eliminating standing water in rain gutters, old tires, buckets, plastic covers, tree holes, or any other container where mosquitoes can breed. It requires the help of the local population and permanent work to maintain the number of breeding sites as low as possible.

Based on these three control tools, we wanted to determine whether it would have been possible to contain or stop the epidemic. In particular, we compared the efficiency of each control tool to choose the best one, having in mind that chemical control tools may not be specific enough and that they may impact endemic species.

Remember that Réunion Island is one of the 35 hot spots of endemicity in the world and thus, during massive spraying, it is necessary to conduct appropriate controls to protect this endemic heritage and at the same time to reduce the mosquito population. In mid-February 2006, an estimated 45,000 persons were infected by the Chikungunya virus in Réunion Island. Thus, the French health authorities decided to use mechanical control, massive adulticide spraying, and localized larvicide treatment on the whole island. They estimated that only one third of the population became sick. This result is far from the prevalence obtained in Comoros in 2006: 63% of the population was infected by the virus. Thus, we can suppose that either more people were infected in Réunion Island, leading to a phenomenon of global "resistance", or that the combination of the different control tools helped to stop the epidemic, or that other factors, like the impact of the virus on mosquito life-span [15], have limited the spreading of the disease. The previous assumptions could partly explain why no more outbreaks have appeared since the middle of 2006, just isolated cases till March 2007.

The outline of the paper is as follows. Section two presents the compartmental L-SEIR model and some theoretical results: existence of a solution, existence of disease-free equilibrium, existence of an endemic equilibrium, and stability and instability properties of the disease-free equilibrium associated to the basic reproduction number $\mathcal{R}_0$. In section three, based on the work of Kamgang and Sallet [24] and recent works by Anguelov et al. [2], we propose a new nonstandard finite difference scheme. Section four presents several simulations according to the different control tools used in Réunion Island in 2006. The last section concludes the paper.

2. The compartmental model for the Chikungunya disease: equilibrium, basic reproduction number, global asymptotic stability.

The Chikungunya epidemiological cycle is like that of other vector-borne diseases (see Figure 1, page 316). The so-called L-SEIR model [13] is a compartmental model that classifies hosts (the humans) into four epidemiological states: susceptible (or non-immune), S_h; exposed, E_h; infectious, I_h; and resistant (or immune), R_h. As a first approach, we assume that the total population N_h is constant, because we are mainly interested in the years following the beginning of the epidemic.

Female mosquitoes are also classified into four epidemiological states: susceptible, S_m; exposed, E_m; infectious, I_m; and aquatic, A_m. The aquatic state includes the eggs, larvae, and pupae. Both humans and mosquitoes are assumed to be born susceptible. The exposed (or incubating) states, E_h and E_m, reflect the viral intrinsic and extrinsic incubation periods, $\frac{1}{\nu_h}$ days and $\frac{1}{\eta_m}$ days, respectively. The extrinsic incubation period is the time necessary for the virus to follow a cycle that brings it from the mosquito's stomach to its salivary gland. This incubation period can vary greatly depending, for example, on the temperature. For humans, the intrinsic incubation period or latent period is the period from the onset of infection to the beginning of infectiousness. An infected human is infectious during $\frac{1}{\eta_h}$ days, called the viremic period, and then becomes resistant or immune.

Cross-infection between humans and vectors is modeled by the mass-action principle normalized by the total population of humans. Every day, each mosquito bites, on average, B times. β_{mh} is the probability that a bite will lead to host infection, which implies that $B\beta_{mh}$ represents the contact rate between infectious mosquitoes

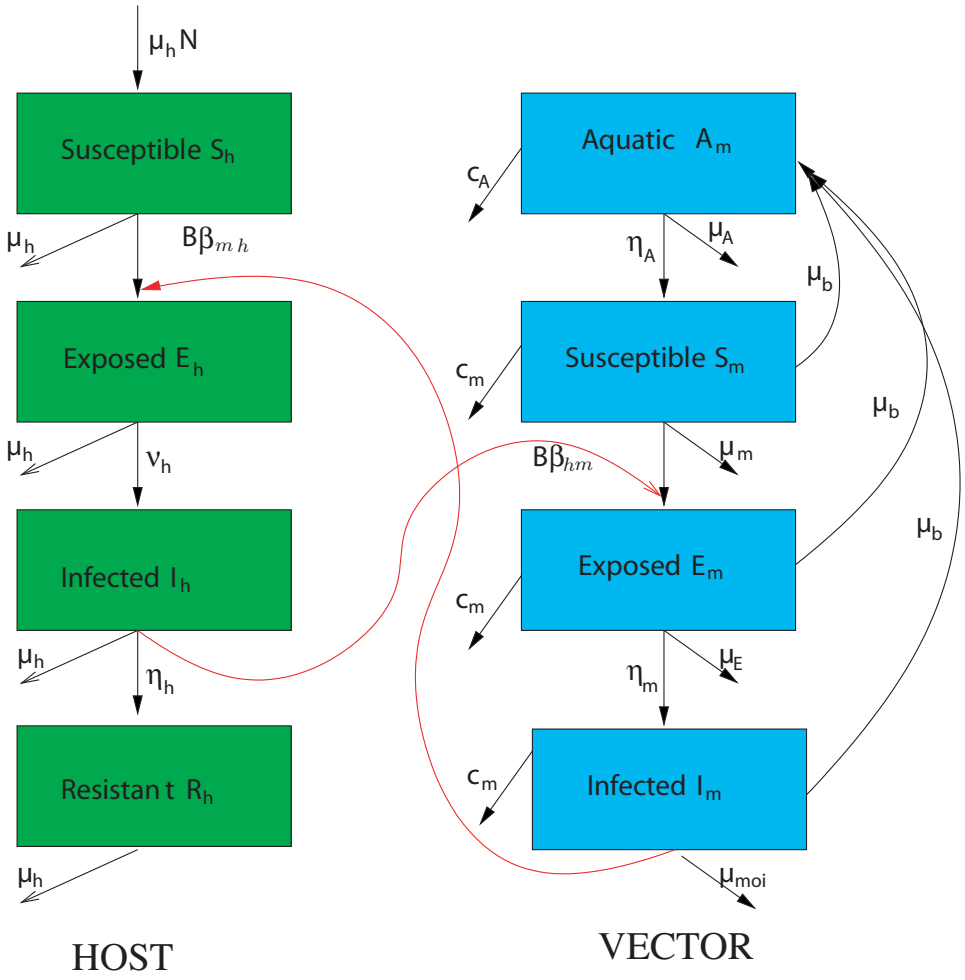

FIGURE 1. A compartmental model for the Chikungunya disease

and susceptible hosts. Similarly, $B\beta_{hm}$ is the contact rate between infectious hosts and susceptible mosquitoes.

K is the carrying capacity of breeding sites. The average lifespan for susceptible mosquitoes is $1/\mu_m$, the average lifespan of the exposed mosquitoes is $1/\mu_E$ days, while the average adult lifespan for infected mosquitoes is $1/\mu_{moi}$. The last two assumptions are new in the modeling of vector-borne diseases. Indeed, for other vector-borne diseases it has never been observed that the virus influences the lifespan of an infected mosquito. But in Réunion Island, it was recently proven that the lifespan of the infected mosquito is almost halved, which influences the dynamic of the disease [15]. Thus $1/\mu_{moi} \leq 1/\mu_E \leq 1/\mu_m$.

Vertical transmission was not taken into account because it was very recently shown that vertical transmission of Chikungunya has not played a key role in the maintenance of the virus in Réunion Island [45].

Then, we add new terms in the model to assess the different control tools studied: c_A is the additional mortality rate due to the larvicide, c_m is the additional mortality rate due to the adulticide, and α is the parameter associated with the efficacy of the mechanical control.

Estimates of the parameters are given in Table 1, page 324.

From the aforementioned, we obtain the following systems of equations

$$\begin{cases} \frac{dS_h}{dt}(t) &= \mu_h N_h - B\beta_{mh}\frac{I_m}{N_h}S_h - \mu_h S_h \\ \frac{dE_h}{dt}(t) &= B\beta_{mh}\frac{I_m}{N_h}S_h - \nu_h E_h - \mu_h E_h \\ \frac{dI_h}{dt}(t) &= \nu_h E_h - \eta_h I_h - \mu_h I_h \\ \frac{dR_h}{dt}(t) &= \eta_h I_h - \mu_h R_h \end{cases} \tag{1}$$

and

$$\begin{cases} \frac{dA_m}{dt}(t) &= \mu_b\left(1-\frac{A_m}{\alpha K}\right)(S_m+E_m+I_m) - (\eta_A+\mu_A)A_m - c_A A_m, \\ \frac{dS_m}{dt}(t) &= -B\beta_{hm}\frac{I_h}{N_h}S_m - (\mu_m+c_m)S_m + \eta_A A_m, \\ \frac{dE_m}{dt}(t) &= B\beta_{hm}\frac{I_h}{N_h}S_m - (\mu_E+c_m)E_m - \eta_m E_m, \\ \frac{dI_m}{dt}(t) &= \eta_m E_m - (\mu_{moi}+c_m)I_m, \end{cases} \tag{2}$$

with the following initial conditions $(N_h - 1, 0, 1, 0, \alpha K, mN_h, 0, 0)$, where m is a positive integer. In the forthcoming computations and numerical simulations, we will consider $K = kN_h$, where k is a positive integer.

Using the fact that $S_h + E_h + I_h + R_h$ is constant, equal to N_h, system (1)-(2) can be rewritten in the following way:

$$\frac{dX}{dt} = \mathcal{A}(X)X + F \tag{3}$$

with $X = (S_h, E_h, I_h, A_m, S_m, E_m, I_m)^T$, $\mathcal{A}(X) =$

$$\begin{pmatrix} -B\beta_{mh}\frac{I_m}{N_h}-\mu_h & 0 & 0 & 0 & 0 & 0 & 0 \\ B\beta_{mh}\frac{I_m}{N_h} & -\nu_h-\mu_h & 0 & 0 & 0 & 0 & 0 \\ 0 & \nu_h & -\eta_h-\mu_h & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -A_{44} & \mu_b & \mu_b & \mu_b \\ 0 & 0 & 0 & \eta_A & -B\beta_{hm}\frac{I_h}{N_h}-\mu_m-c_m & 0 & 0 \\ 0 & 0 & 0 & 0 & B\beta_{hm}\frac{I_h}{N_h} & -\mu_E-\eta_m-c_m & 0 \\ 0 & 0 & 0 & 0 & 0 & \eta_m & -\mu_{moi}-c_m \end{pmatrix}$$

such that $A_{44} = (c_A + \mu_A + \eta_A + \mu_b\frac{S_m+E_m+I_m}{\alpha K})$, and $F = (\mu_h N_h, 0, 0, 0, 0, 0, 0)^T$. Note that $\mathcal{A}(X)$ is a Metzler Matrix, i.e. a matrix such that off-diagonal terms are nonnegative for all $X \in \mathbb{R}^7_+$. Thus, using the fact that $F \geq 0$, system (3) is positively invariant in $\mathbb{R}^7_+$, which means that any trajectory of the system starting from an initial state in the positive orthant $\mathbb{R}^7_+$ remains forever in $\mathbb{R}^7_+$. The right-hand side is Lipschitz continuous: there exists a unique maximal solution.

Let $\mathcal{G} = \{(S_h, E_h, I_h, A_m, S_m, E_m, I_m) \in \mathbb{R}^7_+ / A_m \leq \alpha k N_h, S_h + E_h + I_h \leq N_h \text{ and } S_m + E_m + I_m \leq mN_h\}$. Since $m \geq \frac{\eta_A}{\mu_m+c_m}\alpha k$, it can be verified that $\mathcal{G}$ is positively invariant with respect to (3). Thus, from now on, we suppose that m and k are choosen such that

$$m \geq \frac{\eta_A}{\mu_m + c_m}\alpha k \tag{4}$$

and we set

$$\mathcal{N} = \frac{\mu_b \eta_A}{(\mu_m + c_m)(c_A + \eta_A + \mu_A)}.$$

Then, we prove

Proposition 2.1.
- *If $\mathcal{N} \leq 1$, then, system (1)-(2) has only one Trivial (Disease Free) Equilibrium $TE = (N_h, 0, 0, 0, 0, 0, 0, 0)$.*
- *If $\mathcal{N} > 1$, then, system (1)-(2) has a biologically Realistic Disease-Free Equilibrium, called hereafter $RDFE$, $(N_h, 0, 0, 0, A_{m0}, S_{m0}, 0, 0)$, with*

$$\begin{array}{ll} A_{m0} & = \left(1 - \frac{1}{\mathcal{N}}\right) \alpha k N_h, \\ S_{m0} & = \left(1 - \frac{1}{\mathcal{N}}\right) \frac{\eta_A}{\mu_m + c_m} \alpha k N_h. \end{array}$$

Proof: Appendix A

Remark 2.2. The first steady state TE, the "Trivial Equilibrium", corresponds to a human population free of mosquitoes, while the second one, $RDFE$, is the steady state of a human population in the presence of mosquitoes.

Then, following [42], we prove

Proposition 2.3. *If $\mathcal{N} > 1$, then, the basic reproduction number associated to (1)-(2) is*

$$\mathcal{R}_0^2 = \frac{\eta_m \nu_h B^2 \beta_{hm} \beta_{mh}}{(\nu_h + \mu_h)(\eta_h + \mu_h)(\mu_{moi} + c_m)(\mu_E + \eta_m + c_m)} \left(1 - \frac{1}{\mathcal{N}}\right) \frac{\eta_A}{\mu_m + c_m} \alpha k. \quad (5)$$

$RDFE$ is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Proof. see Appendix B. □

Remark 2.4. Without control, following the parameters given in Table 1, page 324, we have $\mathcal{N} > 1$. Thus, the only possible disease-free equilibrium is $RDFE$. Even if we consider a mechanical control, i.e $0 < \alpha < 1$, $RDFE$ still exists. This is no longer true when we consider chemical control tools, i.e. when we choose c_A, and c_m such that $\mathcal{N}$ becomes less than 1. In that case, the only disease-free equilibrium is TE.

We now turn to the existence of an endemic equilibrium. We prove the following

Proposition 2.5. *Let $\mathcal{N} > 1$, $\mu_m \leq \mu_E \leq \mu_{moi}$, and $\mathcal{R}_0^2 > 1$. There exists a unique endemic equilibrium.*

Proof. see Appendix C. □

2.1. **Global asymptotic stability of TE and $RDFE$.** Let us denote by $\gamma(A)$ the stability modulus of A, i.e. $\gamma(A) = \max_{\lambda \in Sp(A)} \mathcal{R}e(\lambda)$. Then, following $\mathcal{G}$, defined on page 5, we now consider the bounded set $\mathcal{D}$:

$\mathcal{D} = \{(S_h, R_h, A_m, S_m, E_h, I_h, E_m, I_m) \in \mathbb{R}_+^8 / A_m \leq \alpha k N_h, S_h + E_h + I_h + R_h = N_h$ and $S_m + E_m + I_m \leq m N_h\}$. First, we prove the following

Proposition 2.6. *If $\mathcal{N} < 1$, then, TE is globally asymptotically stable.*

Proof. From the previous proposition, if $\mathcal{N} \leq 1$, we know that there exists a unique equilibrium TE. Now, setting $Y = X - TE$, we can rewrite (3) in the following manner

$$\frac{dY}{dt} = \mathcal{B}(Y)Y \quad (6)$$

with $\mathcal{B}(Y) =$

$$\begin{pmatrix} -B\beta_{mh}\frac{Y_8}{N_h}-\mu_h & 0 & 0 & 0 & 0 & 0 & 0 & -B\beta_{mh} \\ B\beta_{mh}\frac{Y_8}{N_h} & -\nu_h-\mu_h & 0 & 0 & 0 & 0 & 0 & B\beta_{mh} \\ 0 & \nu_h & -\eta_h-\mu_h & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \eta_h & -\mu_h & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -B_{44} & \mu_b & \mu_b & \mu_b \\ 0 & 0 & 0 & 0 & \eta_A & -B\beta_{hm}\frac{Y_3}{N_h}-\mu_m-c_m & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & B\beta_{hm}\frac{Y_3}{N_h} & -\mu_E-\eta_m-c_m & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \eta_m & -\mu_{moi}-c_m \end{pmatrix},$$

and $B_{44} = (c_A+\mu_A+\eta_A+\mu_b\frac{Y_6+Y_7+Y_8}{\alpha K})$. It is clear that $TE_Y = (0,0,0,0,0,0,0,0)$ is the only equilibrium. Then, it suffices to consider the following Lyapunov function $V(Y) =< W, Y >$, with $W = (1,1,1,1,\frac{1}{\mu_b},\frac{1}{\mu_m+c_m},\frac{1}{\mu_m+c_m},\frac{1}{\mu_m+c_m}) >> 0$. Thus, we have $V(Y) > 0$ except for $Y = TE_Y$. Straightforward computations show that

$$\begin{aligned} \dot{V}(Y) &= < W, \mathcal{B}(Y)Y > \\ &= \left(1-\frac{Y_5}{\alpha K}\right)(Y_6+Y_7+Y_8) - \frac{\mu_A+\eta_A+c_A}{\mu_b}Y_5 - \mu_h(Y_1+Y_2+Y_3+Y_4) \\ &\quad + \frac{\eta_A}{\mu_m+c_m}Y_5 - Y_6 - \frac{\mu_E+c_m}{\mu_m+c_m}Y_7 - \frac{\mu_{moi}+c_m}{\mu_m+c_m}Y_8. \end{aligned}$$

Thus,

$$\begin{aligned} \dot{V}(Y) &= -\frac{Y_5}{\alpha K}(Y_6+Y_7+Y_8) - Y_5(1-\mathcal{N})\frac{\mu_A+\eta_A+c_A}{\mu_b} \\ &\quad -\mu_h(Y_1+Y_2+Y_3+Y_4) - \left(\frac{\mu_E+c_m}{\mu_m+c_m}-1\right)Y_7 - \left(\frac{\mu_{moi}+c_m}{\mu_m+c_m}-1\right)Y_8. \end{aligned} \tag{7}$$

Then, using the fact that $\mu_m \leq \mu_E \leq \mu_{moi}$, we deduce that $\frac{\mu_E+c_m}{\mu_m+c_m} \geq 1$ and $\frac{\mu_{moi}+c_m}{\mu_m+c_m} \geq 1$, which implies that $\dot{V}(Y) \leq 0$ if $\mathcal{N} < 1$. Moreover, the maximal invariant set contained in $\{V|\dot{V}(Y) = 0\}$ is TE_Y. Thus, from Lyapunov theory, we deduce that TE_Y and thus, TE is GAS if $\mathcal{N} < 1$. □

Proving that $RDFE$ is globally asymptotically stable is a very difficult task. Also, there is no general result for epidemiological problem apart [7, 24]. Following [23, 24] and [13], we prove that $RDFE$ is globally asymptotically stable under a certain threshold condition. Using the approach of Chavez et al. [7], it is possible to rewrite (1)-(2) in the following manner

$$\begin{cases} \dot{x}_S &= A_1(x)(x_S - x_{RDFE,S}) + A_{12}(x)x_I, \\ \dot{x}_I &= A_2(x)x_I, \end{cases} \tag{8}$$

where x_S is the vector representing the state of different compartments of non-transmitting individuals (e.g. susceptible, immune) and the vector x_I represents the state of compartments of different transmitting individuals (e.g. infected, exposed). Here, we have $x_S = (S_h, R_h, A_m, S_m)^T$, $x_I = (E_h, I_h, E_m, I_m)^T$, and $x_{RDFE,S} = (N_h, 0, A_{m0}, S_{m0})^T$, with

$$A_1(x) = \begin{pmatrix} -\mu_h & 0 & 0 & 0 \\ 0 & -\mu_h & 0 & 0 \\ 0 & 0 & -(c_A+\mu_A+\eta_A+\mu_b\frac{S_m}{\alpha K}) & \mu_b(1-\frac{A_{m0}}{\alpha K}) \\ 0 & 0 & \eta_A & -(\mu_m+c_m) \end{pmatrix},$$

$$A_{12}(x) = \begin{pmatrix} 0 & 0 & 0 & -B\beta_{mh}\frac{S_h}{N_h} \\ 0 & \eta_h & 0 & 0 \\ 0 & 0 & \mu_b\left(1-\frac{A_m}{\alpha K}\right) & \mu_b\left(1-\frac{A_m}{\alpha K}\right) \\ 0 & -B\beta_{hm}\frac{S_m}{N_h} & 0 & 0 \end{pmatrix}$$

and

$$A_2(x) = \begin{pmatrix} -(\nu_h+\mu_h) & 0 & 0 & B\beta_{mh}\frac{S_h}{N_h} \\ \nu_h & -(\eta_h+\mu_h) & 0 & 0 \\ 0 & B\beta_{hm}\frac{S_m}{N_h} & -(\mu_E+\eta_m+c_m) & 0 \\ 0 & 0 & \eta_m & -(\mu_{moi}+c_m) \end{pmatrix}$$

A direct computation shows that the eigenvalues of $A_1(x)$ are real and negative. Thus, the system $\dot{x}_S = A_1(x)(x_S - x_{RDFE,S})$ is GAS at $x_{RDFE,S}$. Note also that $A_2(x)$ is a Metzler matrix. We set

$$\mathcal{R}_G^2 = \frac{\eta_m \nu_h B^2 \beta_{hm}\beta_{mh}}{(\nu_h+\mu_h)(\eta_h+\mu_h)(\mu_{moi}+c_m)(\mu_m+\eta_m+c_m)} m. \tag{9}$$

Let us recall the general result proved in [23, 24]:

Theorem 2.7. *Let $\mathcal{D} \subset \mathbb{R}^4_+ \times \mathbb{R}^4_+$, the compact subset defined in page 6. The system (8) is of class C^1, defined on $\mathcal{U}$. If*

1. *$\mathcal{D}$ is positively invariant relative to (8);*
2. *The system $\dot{x}_S = A_1(x_S, 0)(x_S - x_{RDFE,S})$ is GAS at $x_{RDFE,S}$;*
3. *For any $x \in \mathcal{D}$, the matrix $A_2(x)$ is Metzler irreducible;*
4. *There exists a matrix $\overline{A}_2$, which is an upper bound of the set $\mathcal{M} = \{A_2(x) \in \mathbb{R}^{4\times 4} | x \in \mathcal{D}\}$, with the property that if $\overline{A}_2 \in \mathcal{M}$, for any $\overline{x} \in D$, such that $A_2(\overline{x}) = \overline{A}_2$, then, $\overline{x} \in \mathbb{R}^4 \times \{0\}$;*
5. *The stability modulus of $\overline{A}_2$ satisfies $\gamma(\overline{A}_2) \leq 0$.*

Then, RDFE is GAS in $\mathcal{D}$.

Finally, using the same reasoning and computations as in [13], we show that $\gamma(\overline{A}_2) \leq 0$ if $\mathcal{R}_G \leq 1$, which leads to the following

Theorem 2.8. *If $\mathcal{N} > 1$ and $\mathcal{R}_G \leq 1$, then, RDFE is globally asymptotically stable in $\mathcal{D}$.*

Remark 2.9. Following (4), we have

$$\mathcal{R}_G^2 = \left(\frac{m}{\alpha k}\frac{\mu_m + c_m}{\eta_A}\right)\frac{\mathcal{N}}{\mathcal{N}-1}\mathcal{R}_0^2 > \mathcal{R}_0^2,$$

showing that $\mathcal{R}_G^2$ is not necessarily an optimal threshold parameter.

Remark 2.10. The previous results are of utmost importance, because they show that if at any time, through appropriate interventions (e.g. destruction of breeding sites, massive spraying....), we are able to lower $\mathcal{N}$ or $\mathcal{R}_0$ and $\mathcal{R}_G$ to less than 1 for a sufficiently long period, then the disease can disappear (see the simulations hereafter).

Remark 2.11. Instead of considering the compact subset $\mathcal{D}$, it is possible to consider the particular compact subset $\mathcal{D}_{Sm_0} = \{(S_h, R_h, A_m, S_m, E_h, I_h, E_m, I_m) \in \mathbb{R}^8_+ / A_m \leq \alpha k N_h, S_h + E_h + I_h + R_h = N_h \text{ and } S_m + E_m + I_m \leq S_{m0}\}$ in Theorem 2.7. Then, using the same computations, it is possible to show that DFE is GAS in $\mathcal{D}_{Sm0}$ if $\mathcal{N} > 1$ and $\mathcal{R}_0 \leq 1$.

After the huge episode of 2006, the DRASS carried out several interventions, like the destruction of breeding sites, and these can partly explain why no more outbreaks appeared. Only a few cases were reported from time to time but none since March 2007.

3. **Construction of a dynamically consistent scheme.** Numerical simulations are crucial in the study of deterministic models. But not all numerical methods are suitable for solving an epidemiological model (see for instance [3]). Nonstandard finite difference schemes have shown their great potential in many areas of research (for an overview, see [31, 33]). In [13], the authors have presented a nonstandard finite difference scheme [30, 32] that preserves the positivity of the solutions as well as the relation $S_h + E_h + I_h + R_h = N_h$ and the local asymptotic stability of $RDFE$ since $\mathcal{R}_0 < 1$.

Here, we propose a new nonstandard finite difference scheme, that preserves the previous properties and in particular the global asymptotic stability property of $RDFE$. Thus, following Mickens' rules [30, 32], we approximate the nonlinear terms in a nonlocal way and the linear terms in an explicit way. Moreover, instead of considering the classical denominator Δt, we consider a time step function $\phi(\Delta t)$ such that $\phi(\Delta t) = \Delta t + O(\Delta t^2)$. Thus, using a suitable time-step function, we obtain a scheme that preserves the equality $S_h + E_h + I_h + R_h = N_h$, the positivity of the solution as well as the equilibria and the stability/instability property associated to the Realistic Disease-Free Equilibrium, $RDFE$ (see [2]), for all $\Delta t > 0$, when $\mathcal{N} > 1$. In fact, to construct our discrete scheme, we consider equation (8) instead of equation (3). Let X^n be an approximation of $X(t_n)$, where $t_n = n\Delta t$, $n \in \mathbb{N}$ and $\Delta t > 0$. Thus, a nonstandard approximation for system (1)-(2) is given by

$$\begin{cases} \dfrac{X_S^{n+1} - X_S^n}{\phi(\Delta t)} = A_1(X^n)\left(X_S^n - X_{RDFE,S}\right) - D_{12}(X_I^n)X_S^{n+1} + B_{12}(X^n)X_I^n, \\ \dfrac{X_I^{n+1} - X_I^n}{\phi(\Delta t)} = A_2\left(X_S^{n+1}\right)X_I^n \end{cases} \tag{10}$$

such that

$$-D_{12}(X_I)X_S + B_{12}(X)X_I = A_{12}(X)X_I, \tag{11}$$

with

$$D_{12}(X_I) = \begin{pmatrix} B\beta_{mh}\frac{I_m}{N_h} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & B\beta_{hm}\frac{I_h}{N_h} \end{pmatrix},$$

and

$$B_{12}(X) = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & \eta_h & 0 & 0 \\ 0 & 0 & \mu_b\left(1 - \frac{A_m}{\alpha K}\right) & \mu_b\left(1 - \frac{A_m}{\alpha K}\right) \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

which implies that the scheme is consistant with formulation (8).

Remark 3.1. The matrix formulation seems to be quite complicated relative to the system formulation, but it permits us to prove several results in a very efficient way.

Summing lines 1, 2, 5, and 6 in (10) shows that $S_h^{n+1} + E_h^{n+1} + I_h^{n+1} + R_h^{n+1} = S_h^n + E_h^n + I_h^n + R_h^n$ for all $n \geq 0$ and all $\Delta t > 0$. Thus, using the fact that $S_h^0 + E_h^0 + I_h^0 + R_h^0 = N_h$, we deduce that $S_h^n + E_h^n + I_h^n + R_h^n = N_h$ for all $n \geq 0$.

The scheme (10) can also be rewritten in the following way:

$$\begin{cases} \mathcal{A}_n X^{n+1} = b_n \\ X^0 \geq 0, \end{cases} \tag{12}$$

with

$$\mathcal{A}_n = \begin{pmatrix} Id + \phi(\Delta t) D_{12}(X_I^n) & 0 \\ 0 & Id \end{pmatrix}$$

and

$$b_n = \begin{pmatrix} X_S^n + \phi(\Delta t) \left(A_1(X^n) \left(X_S^n - X_{RDFE,S} \right) + B_{12}(X^n) X_I^n \right), \\ \left(Id + \phi(\Delta t) A_{22}(X_S^{n+1}) \right) X_I^n \end{pmatrix}.$$

Noticing that $\mathcal{A}_n$ is a diagonal matrix, (12) leads to the following numerical scheme:

$$\left\{ \begin{array}{ll} X_S^{n+1} = & \left(Id + \phi(\Delta t) \left(D_{12}(X_I^n) \right) \right)^{-1} \left(X_S^n + \phi(\Delta t) \left(A_1(X^n) \left(X_S^n - X_{RDFE,S} \right) + \right. \right. \\ & \left. \left. + B_{12}(X^n) X_I^n \right) \right) \\ X_I^{n+1} = & \left(Id + \phi(\Delta t) A_2(X_S^{n+1}) \right) X_I^n. \end{array} \right. \tag{13}$$

The Kamgang-Sallet approach used for (10) ensures that $RDFE$ is a fixed point of (10), as well as is TE. Using special matrices arguments [6, 19], it is possible to show the following:

Lemma 3.2. *The scheme (12) is positively stable for all* $\Delta t > 0$.

Proof. We suppose $X^n \geq 0$. $\mathcal{A}_n$ is a positive diagonal matrix and thus, $\mathcal{A}_n^{-1} \geq 0$. It suffices to show that $b_n \geq 0$. B_{12} is a positive matrix and a direct computation shows that $-A_1(X)(X_{RDFE,S}) \geq 0$. Finally, it suffices to choose $\phi(\Delta t)$ such that

$$Id + \phi(\Delta t) A_1(X) \geq Id + \phi(\Delta t) \underline{\mathrm{A}}_1 \geq 0,$$
$$Id + \phi(\Delta t) A_2(X_S) \geq Id + \phi(\Delta t) \underline{\mathrm{A}}_2 \geq 0,$$

for all $X \in \mathcal{D}$, where $\underline{\mathrm{A}}_1$ and $\underline{\mathrm{A}}_2$ are lower bounds for the sets $\{X \in \mathcal{D} | A_1(X)\}$ and $\{X \in \mathcal{D} | A_2(X)\}$ respectively. Then, considering the following time-step function

$$\phi(\Delta t) = \frac{1 - \exp(-M \Delta t)}{M}, \tag{14}$$

with

$$M \geq \max \left(\mu_h + \nu_h, \mu_h + \eta_h, \mu_E + \eta_m + c_m, \mu_{moi} + c_m, \mu_A + \eta_A + c_A + \mu_b \frac{m}{\alpha k} \right).$$

implies that $b_n \geq 0$. Altogether we have proved that $X^n \geq 0$ implies $X^{n+1} \geq 0$. Hence, by induction, the result is true for all n. □

Equation (13) can be rewritten in the following formulation

$$\left\{ \begin{array}{l} X_S^{n+1} = g(X_S^n, X_I^n), \\ X_I^{n+1} = A(X_S^n, X_I^n) X_I^n, \end{array} \right. \tag{15}$$

for $n \geq 0$ with

$$A(X_S, X_I) = Id + \phi(\Delta t) A_2(X_S).$$

In [2], we have showed the following result:

Theorem 3.3. [2] *Let system (15) satisfy the following conditions:*

- *D1 the system is dissipative on* $\mathcal{D}$;
- *D2 the subsystem* $X_S^{k+1} = g(X_S^k, \mathbf{0})$ *is globally asymptotically stable at the equilibrium* $X_{RDFE,S}$ *on* $\mathcal{D}_1 = \{X_S \in \mathbb{R}^{n_1} : (X_S, \mathbf{0}) \in \mathcal{D}\}$;
- *D3* $A(X_S, X_I)$ *is nonnegative for all* $(X_S, X_I)^T \in \mathcal{D}$;
- *D4 there exists an upper bound* $\overline{A}$ *of the set* $\mathcal{M} = \{A(X_S, X_I) : A(X_S, X_I) \in \mathcal{D}\}$ *and* $\overline{A}$ *is irreducible;*

D5 either (D5.1) $\rho(\overline{A}) < 1$
or (D5.2) $\rho(\overline{A}) = 1$ *and* $A(X) >> 0$, $X \in \mathcal{D}$,
and $(A(X_S, X_I) = \overline{A} \Longrightarrow X_I)$ *has a zero coordinate).*
Then, $(X_{RDFE,S}, 0)$ *is a GAS equilibrium of (15) on* $\mathcal{D}$.

In some sense, our theorem is an extension of the result from Kamgang and Sallet to discrete systems (see (13)). Finally, using the previous theorem, we show the following important result:

Proposition 3.4. *If* $\mathcal{N} > 1$ *and* $\mathcal{R}_G < 1$, *then, RDFE is a GAS equilibrium of (15), for all* $\Delta t > 0$.

Proof. see Appendix D. □

Remark 3.5. This result is very important. In general, even if an equilibrium of the continuous problem is globally asymptotically stable, it is not necessary that this property holds for the numerical scheme. Actually, it is very difficult to find or to construct a numerical scheme that handles this global asymptotic stability property. Here, we show that the nonstandard finite difference method can be very helpful to construct such a scheme. In that sense our scheme is superior to the scheme proposed in [13] and, it is said to be dynamically consistent, irrespective of the values of the time step size.

4. **Numerical simulations and control.** We now present some simulations for the two largest cities of the Réunion Island: Saint-Denis, the capital, located in the North, and Saint-Pierre, in the South-West. These cities are at sea-level. Moreover, we compare our simulations with real data, corresponding to declared cases, recorded (with corrections) since the beginning of the outbreak by the DRASS in cooperation with the CIRE (both French government health authorities) through a sentinel network. The major difference between our simulations and the simulations given in [13] is that here we consider the evolution of infected humans (and not only the new cases) per week. Indeed, using the fact that the average viremic period is 3 days, we use the data recorded in 2005 to obtain the number of infected people per week, which can be compared with the simulated I_h.

4.1. **Parameters and simulations.** In Table 1, page 324, and Table 2, page 325, we give the parameters used in the computations. We have included new knowledge on the virus and *Aedes albopictus*. In this Table, some parameters can change from place to place. Most of the values were obtained from entomologists and are related to experiments on *Aedes albopictus* conducted by Dr. H. Delatte (CIRAD, France) (see [8, 9]) and Dr. A. Failloux (Institut Pasteur, France) (see [43]), or obtained through an adjustment of the numerical results to the data recorded during the epidemic of 2005.

4.2. **Simulations without vector control.** We first consider that $c_A = c_m = 0$ and $\alpha = 1$. These values correspond to the period of the first peak in 2005 when there was no control policy. At time $t = 0$, we assume that one human is infectious, i.e. $I_h(0) = 1$. In the following computations (see Figures 2 and 3, page 325), we consider only the two largest cities in Réunion Island: Saint-Denis and Saint-Pierre. We suppose that at the beginning of each episode ($t = 0$ in our Figures), there are m female mosquitoes per human, i.e. the whole population of female mosquitoes is

Parameters	Description	average value, range of values
B	average daily biting (per day)	1
β_{mh}	transmission probability from I_m (per bite)	≈ 0.375
β_{hm}	transmission probability from I_h(per bite)	≈ 0.375
$1/\mu_h$	average lifespan of humans (in days)	78×365
$1/\eta_h$	average viremic period (in days)	3
$1/\mu_m$	average lifespan of adult mosquitoes (in days)	11
$1/\mu_E$	average lifespan of exposed mosquitoes (in days)	10
$1/\mu_{moi}$	average lifespan of infected mosquitoes (in days)	5
μ_b	nbr of eggs at each deposit per capita (per day)	6
μ_A	natural mortality of larvae (per day)	[3; 5]
η_A	maturation rate from larvae to adult (per day)	≈ 0.08
$1/\eta_m$	extrinsic incubation period (in days)	2
$1/\nu_h$	intrinsic incubation period (in days)	3

TABLE 1. Epidemiological and entomological parameters.

thus $S_m(0) = m \times N_h$. In the same way, for the maximal capacity K, we consider a number k of larvae per human. K is given by $K = k \times N_h$ and we choose $A_m(0) = k \times N_h$. In Table 2, page 325, we summarize the initial values used in the computations for each city. Note that k and m verify assumption (4).

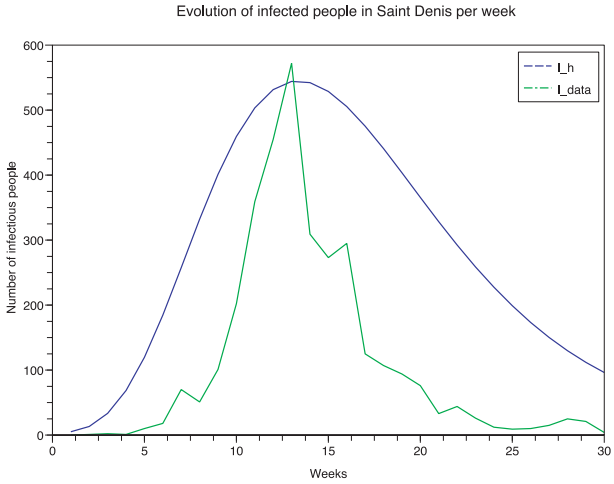

FIGURE 2. Evolution of the infected population per week in Saint-Denis in 2005; comparison of simulated data (blue) with real data (green).

Remark 4.1. We begin our simulations in March 2005. This is the end of the rainy season in Réunion Island. According to entomologists, the number of mosquitoes is maximal in the end of the rainy season in Réunion Island. This is why we consider a high number of susceptible mosquitoes at the begining of our simulations. This

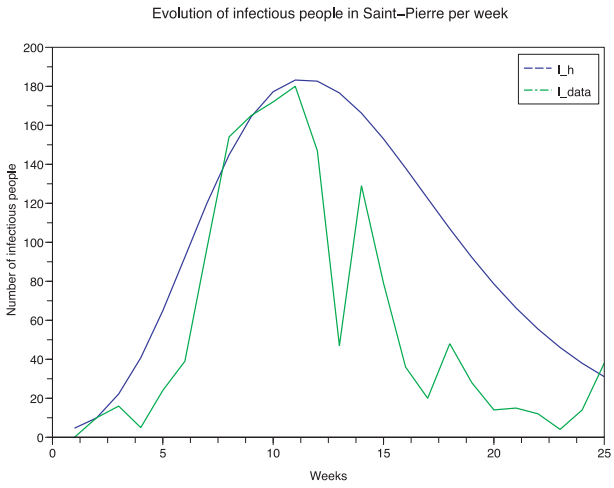

FIGURE 3. Evolution of the infected population per week in Saint-Pierre in 2005 ; comparison of simulated data (blue) with real data (green).

city	N_h	m	k
Saint-Denis	130000	5	2
Saint-Pierre	73000	3	2

TABLE 2. Initial values for each city

fact explains partly why a small outbreak appeared in 2005, although the estimated basic reproduction number is less than 1.

In Table 3, page 325, we summarize the results obtained for $\mathcal{R}_0^2$ and $\mathcal{R}_G^2$. In

Towns	$\mathcal{R}_0^2$	$\mathcal{R}_G^2$
Saint-Denis	0.7	7.7
Saint-Pierre	0.57	4.6

TABLE 3. $\mathcal{R}_0^2$ and $\mathcal{R}_G^2$ for Saint-Denis and Saint-Pierre in May 2005

2005, our simulations show that $\mathcal{R}_0 < 1$, indicating a small outbreak with a fast decay to $RDFE$, as expected from the theory. In general, because Saint-Denis and Saint-Pierre are at sea-level, we obtain almost identical results . Also, recall that the model and the simulations give only a mean behavior of the time course of the disease; hence, it is impossible to fit the real values. According to the model, the disease should have disappeared after a while in 2005, but this did not happen.

Indeed, the disease survived the dry period and rose again in December 2005-January 2006, at the beginning of the rainy season. Many assumptions have been made to explain the sudden large outbreak in December 2005-May 2006. Because $\mathcal{R}_0$ was less than 1 in 2005, it should have been impossible to have an outbreak of such amplitude in 2006. Yet, it is known that mosquitoes are able to survive during

the dry period, which can explain why during this period (from June to October) some cases appeared from time to time in Réunion Island. Another important factor was pointed out by Vazeille et al. [43]: two strains of the virus were isolated in Réunion Island. The first one, strain 05.115, was isolated in May 2005, during the first outbreak, and the second one, strain 06.21, was isolated later, in November 2005. Vazeille et al. proved that strain 06.21 had a larger rate of transmission from human to mosquito. In fact, through several experiments, they showed that β_{hm} increased from 0.37 for the first strain (May 2005) to 0.95 for the second strain (November 2005). This implies new values for $\mathcal{R}_0$, see Table 4. In particular the basic reproduction number becomes greater than 1, which could explain the renewal of the epidemic in December 2005 (see Figs. 4 and 5) (see also [13] for further explanations and simulations).

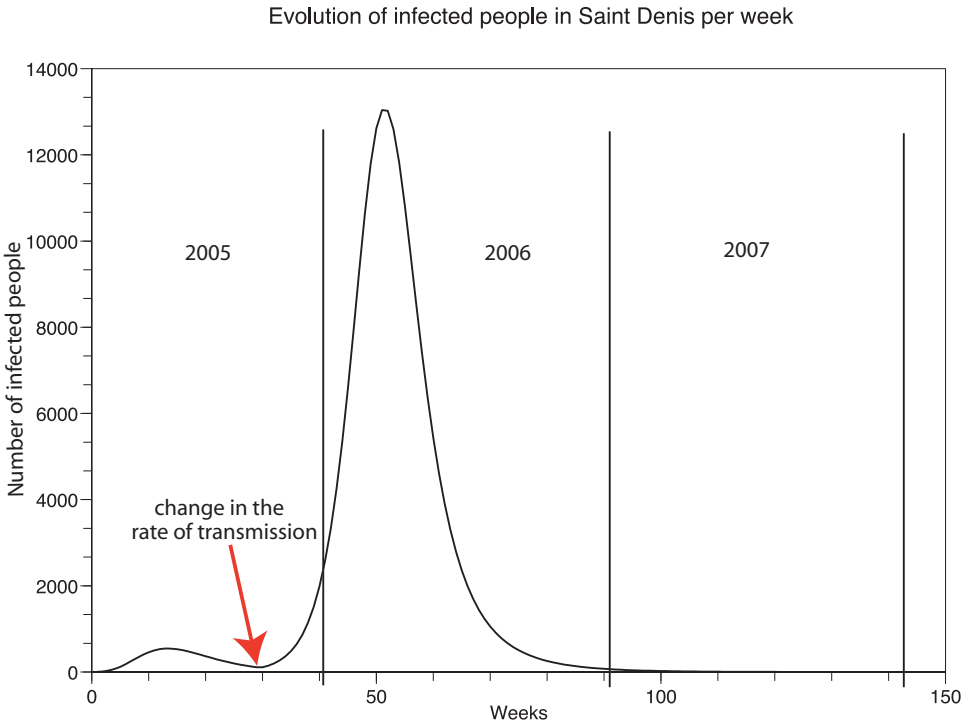

FIGURE 4. Simulation of the evolution of the infected population per week in Saint-Denis from 2005 till 2008

Of course, this is not the only way to explain the amplitude of the outbreak of 2006, but it seems that this "optimal" rate of transmission, associated to a small extrinsic incubation period (only two days! [15]), gives a perfect combination for a wide and fast spread of the disease, no matter what the number of mosquitoes was. Indeed, recent models have considered a periodic amplitude in the mosquito population for vector-borne diseases and this assumption seems to be realistic for such diseases, like Dengue, for which the extrinsic incubation time is far longer. But for the special case of Chikungunya, it appears that only a minimal number of mosquitoes, with an optimal rate of transmission, could be sufficient to spread the epidemic.

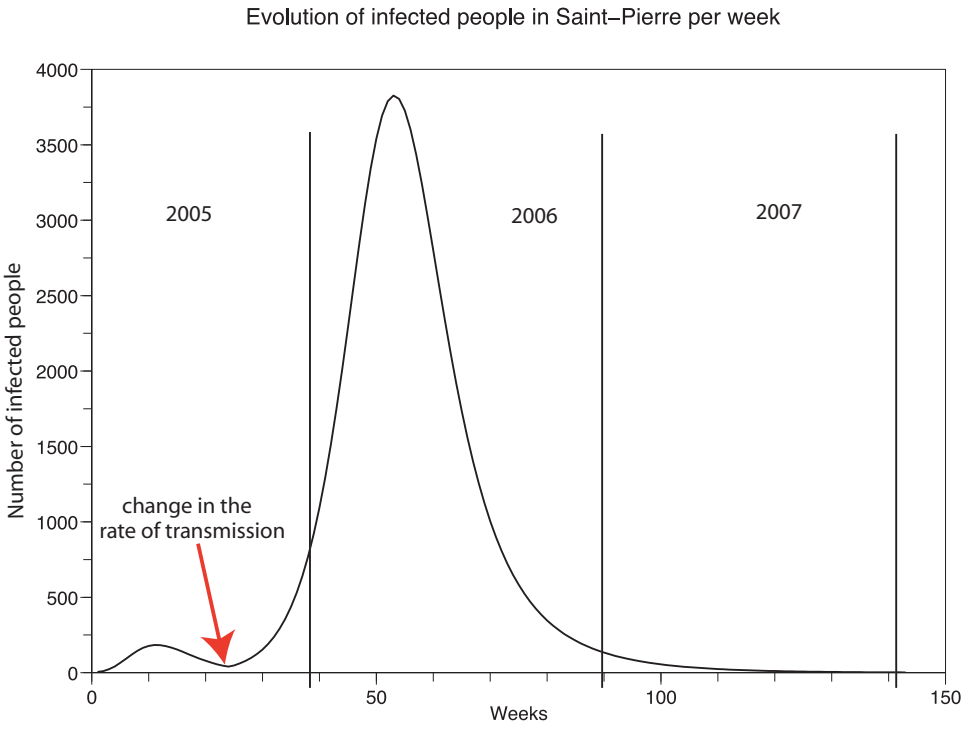

FIGURE 5. Simulation of the evolution of the infected population per week in Saint Pierre from 2005 till 2008

Towns	$\mathcal{R}_0^2$	$\mathcal{R}_G^2$
Saint-Denis	1.78	19.58
Saint-Pierre	1.46	9.64

TABLE 4. $\mathcal{R}_0^2$ and $\mathcal{R}_G^2$ for the Saint-Denis and Saint-Pierre in November 2005

These results about the variation of $\mathcal{R}_0$ are important because they show that, in some places, interventions for vector control must be immediate and strong. At the beginning of an epidemic, it is important to localize places where the basic reproduction number has a good chance of being large [13].

Tables 3 and 4 indicate clearly that $\mathcal{R}_G^2$ is only of theoretical interest, because, practically, it seems quite difficult to get values less than 1. The different simulations showed that the the parameter to be used is still the basic reproduction number $\mathcal{R}_0$, even if we only proved a local stability result for $RDFE$.

In particular, in February 2006 and after, the DRASS conducted several interventions to reduce the number of breeding sites or adult mosquitoes. Thus, considering recent information on the evolution of virus virulence, we wanted to know if the epidemic could have been controlled through fast and early interventions, like "Kass'Moustic" or chemical control tools.

In the next section, we present various simulations to assess the efficacy of control tools to reduce the mosquito population.

4.3. **Assessing the efficacy of mosquito control tools.** In this section, we consider several control tools that could stop, contain, or eradicate the disease: an adulticide, Deltamethrin; a larvicide, *Bti*; a mechanical control; and combinations of these. Here, we focus only on Saint-Denis, the capital.

To measure the efficacy of the control tools, we compare the cumulative number of infected humans, i.e. $C_H = \sum_{n=0}^{N} I_h^n$, over a certain period $[0, T]$, with and without control. Thus, we consider the following fraction:

$$F_0^c = 100 \frac{C_H^c}{C_H^0},$$

where C_H^0 and C_H^c are the cumulative numbers of infected humans without and with control respectively. Hence, F_0^c indicates the efficacy of the control tools to reduce the number of infected humans over a certain period: the lower F_0^c is, the better the control tool is.

Remark 4.2. In the following simulations, we assume that the disease is eradicated as soon as the number of infected humans per week is less than 0.75. It is possible to consider another threshold, like 0.5 or 0.25. We have verified that our simulations are not sensitive to the choice of the threshold, i.e. whatever the threshold, we obtained the same kind of results.

4.3.1. *Adulticide only.* The peak of the epidemic was in mid-February 2006, and one may wonder whether massive spraying was effective and whether it was begun early enough? In 2005, there was an episode of Chikungunya and thus, maybe, it would have been preferable to plan massive spraying before the beginning of the rainy season and just after the episode of 2005. When sprayed in an open environment, Deltamethrin seems to be effective only during a couple of hours [18].

Several numerical simulations were run to test different possible scenarios to control or eradicate the disease. In particular, we considered three important parameters:

- the periodicity of the treatment, τ: we assume that the spraying is done every τ days, with $\tau = 15$, 30, and 60 (the treatment is not efficient for longer periods). Note also that 30 days is the minimal time for the DRASS agency to conduct massive spraying in different large places. But, sometimes, when the epidemic is highly localized, it is possible to plan a 15-day treatment.
- the start date of the treatment, t_i, corresponds to the time lag between the emergence of the first case, in March 2005 in Saint-Denis, and the beginning of the treatment. We mainly consider two start dates, namely $t_i = 100$ days, which corresponds to a couple of days after the peak of the outbreak of 2005, and $t_i = 200$ days, which corresponds approximately to the beginning of the rainy season. Sometimes we consider $t_i = 300$, which corresponds to January 2006.
- the adulticide killing rate, c_m: we considered different rates, i.e. $c^* = 0.2$, 0.5, and 0.8. In the laboratory, the killing rate is about 1 but in real conditions it is not; a DRASS study in 2006 showed that the mortality of the mosquitoes after spraying varied between 20% and 80%, depending on parameters like the distance from the truck-mounted sprayer and the weather.

This is why it is necessary to consider various killing rates in the simulations. Moreover, Deltamethrin has a very short residual action [18]. From the entomologists' point of view, it is also not realistic to consider that an adulticide, like Deltamethrin, can be efficient no more than one day. Thus, we will consider that the adulticide is active only one day. The parameter c_m can be defined as follows

$$c_m(t) = \begin{cases} c^*, & \text{if } t = t_i + j\tau \\ 0, & \text{elsewhere,} \end{cases}$$

where j depends on the duration of the treatment. Thus, in the case of massive spraying, we consider in fact "pulse control", i.e. the control is not continuous in time but is effective only one day every τ days. This control is what happened in real conditions. Our aim is to consider simulations that are as close as possible from real experiments.

Remark 4.3. Our "pulse" adulticide control can be compared to "pulse vaccination" strategy considered in SIR and SEIR epidemic models (see [12, 39], for instance).

We ran simulations for a period of 600 weeks, which corresponds approximately to 11 years. After some runs, two important facts appeared clearly: the periodicity and the start date are of utmost importance in the control of the epidemic. Clearly, the sooner the interventions begin, the quicker the outbreak will stop or decrease.

We considered the start date $t_i = 100$ and a treatment duration of 150 days. Figure 6(a) shows the evolution of F_0^c (the level lines) with respect to the adulticide killing rate and the periodicity of the treatment. If the adulticide killing rate is between 0.5 and 0.8, and the periodicity is 15 days, then, the number of infected humans is decreased by 95%, i.e. $F_0^c \approx 5\%$. Note also, that for entomologists, the adulticide killing rate in field experiments is expected to be in the interval $[0.2; 0.5]$ [18]. Thus, with the previous treatment, the decay in the infected human population should vary between 0% and 80%, depending on the periodicity of the spraying.

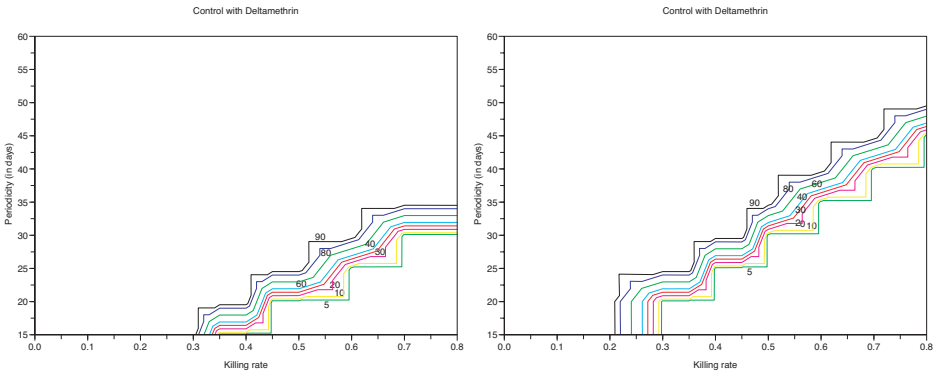

FIGURE 6. Evolution of F_0^c with respect to the killing rate and the periodicity of the treatment . The start date of the adulticide treatment is 100, and the duration of the treatment equal to: (a) 150 days; (b) 300 days

If the duration of the treatment is 300 days (Figure 6(b)), then, the number of infected humans can decrease by 95% even if the adulticide rate is about 0.3.

Note that the treatment and the way to use it can have severe drawbacks: if we increase the number of sprayings or the duration of the treatment, we can obtain a delay of the epidemic or a kind of periodic behavior during the years following the begining of the epidemic. If the treatment duration is not sufficiently long, an epidemic can rise again. Thus, it appears clearly that this type of control tool should be used with care and the best way to have a large and "permanent" impact is to use it as a short periodic treatment, like 15 days, in particular if the adulticide killing rate is low. In fact, this is now the procedure in Réunion Island: very localized interventions with a 15-day periodicity. Since March 2007, there have been no new Chikungunya cases in Réunion Island, despite an estimated prevalence of about 37% (for epidemiologists, as long as the prevalence of the population, i.e. the percentage of the population infected by the virus, is less that $60-65\%$, a risk of a new epidemic exists).

In fact, the later the start date of the adulticide treatment is (for instance $t_i = 200, 300$), the higher the killing rate must be to give satisfactory results.

Another important factor is the reaction time needed to plan field interventions. Figure 6 shows that if the control in 2005 had been planned sufficiently early during the first episode of Chikungunya, then, then the huge epidemic of 2006 could have been avoided. Of course, this does not indicate that we are done with the Chikungunya virus. As long as a large fraction of the population is susceptible, a new outbreak can appear as soon as an infectious host or an infectious mosquito appears. Moreover, spraying can in some cases just delay the epidemic and not necessarily prevent the rise of a new outbreak several years later. This is why it is so important to develop a sentinel network to alert the authorities when new cases appear in order to focus land interventions against a localized outbreak.

After the peak of the epidemic of 2006, the treatment becomes unnecessary: first because a sufficient fraction of the population (more than half of the population) has become resistant, second because infected mosquitoes die quickly.

4.3.2. *Larvicide only.* Larvicide alone seems not to be as efficient as adulticide alone. Here, based on real experiments, we assume that the maximal rate is effective during the spraying time and the day after and then decreases over the next 13 days. The efficacy and the duration of a larvicide strongly depend on water quality, exposure, and even the type of breeding sites [27]. Thus, the duration can vary between a couple of days and two weeks. We suppose that r_A is defined as depicted in Figure 7, page 331, that is

$$r_A\left(t+t_i\right)=\begin{cases}1, & \text{with } 0\leq t\leq 1,\\ \frac{14-t}{13}, & \text{with } 1<t\leq 14,\\ 0, & \text{with } 14<t.\end{cases}$$

In Figure (8), we show the evolution of F_o^c with respect to the periodicity τ, for various start dates and various treatment durations. It is clear that the impact strongly depends on the start date and the duration of the treatment: for the start dates $t_i = 100$ and $t_i = 200$, the same kind of result is obtained. The treatment seems better when used later, i.e. since $t_i = 300$, during the explosive epidemic: in that case, the duration of the treatment has a real impact (compare the green lines in Figures (8)(a) and (b)). Actually, the dynamic of the system is very complicated because, during the computations, $\mathcal{N}(t_i)$ has values less or greater than 1 and, thus, the approximation will converge either to TE or to $RDFE$. It seems also

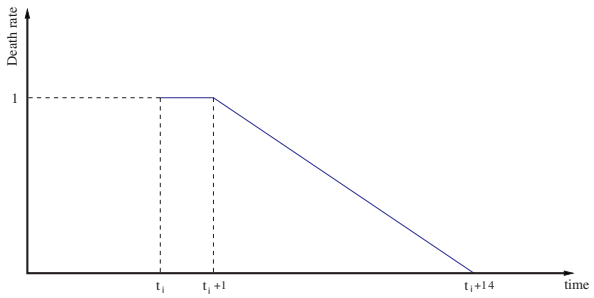

FIGURE 7. The larvicide killing rate.

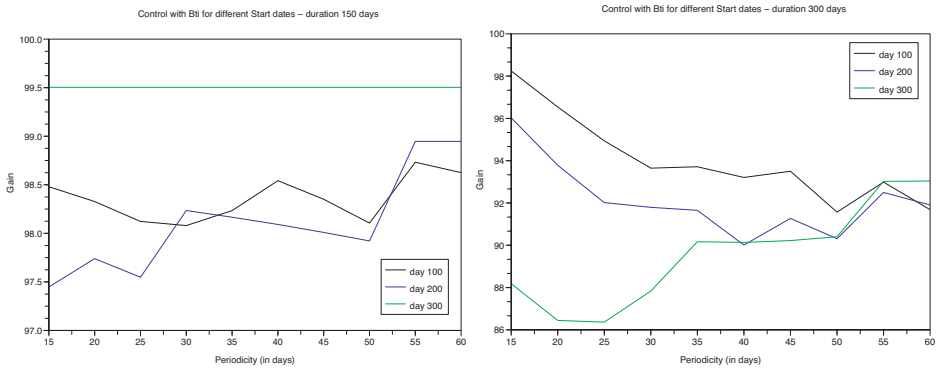

FIGURE 8. Efficacy of *Bti* with respect to the start date. The treatment duration is: (a) 150 days, (b) 300 days.

that significative results are obtained with the 300-day treatment, and for large periodicities.

Altogether, in comparison with the adulticide, the larvicide does not have a large impact on the epidemic: the intensity decreases only slightly. This is not surprising because only breeding sites are treated. And from land experiments, we know that most of the breeding sites are "small", like outdoor flower pots, bamboo holes, and bottles [9]. Thus, it seems that the larvicide should be used with an adulticide to optimize the treatment and to minimize the adulticide impact on the environment.

4.3.3. *Adulticide and larvicide.* We consider a Deltamethrin-*Bti* combination. We use the same values for the parameters c_A, c_m, τ, and t_i for various adulticide treatment durations. We consider two start dates for the adulticide treatment : $t_i = 100$, and $t_i = 300$. Of course, following the previous result, we only consider a larvicide treatment of 300 days. In Figure 9, we show that the Deltamethrin-*Bti* combination gives very interesting results: in comparison with the results obtained in Figure 6, page 329, the improvements are clear even for small adulticide killing rates and large periodicities. For instance, in Figure 9(b), with $c_m \approx 0.3$ and $\tau = 25$ days, the result is about 97% better than without treatment.

The best results are obtained when we consider a 300-day adulticide treatment (Figure 9(b)). Thus, with an early start date, i.e. $t_i = 100$, the adulticide-larvicide

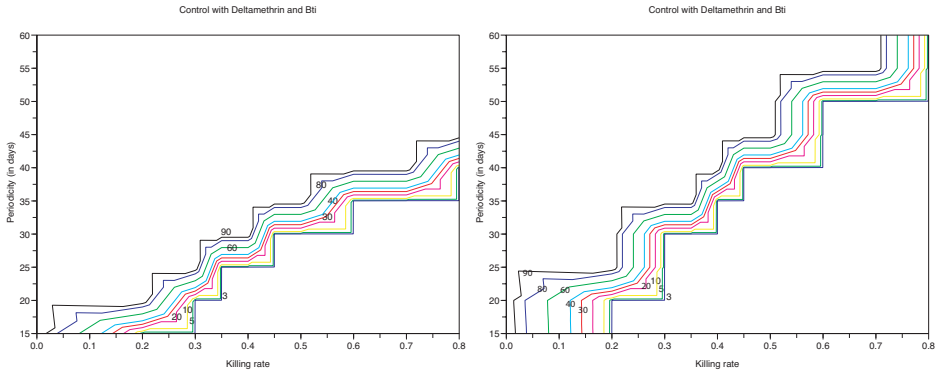

FIGURE 9. Combination of Deltamethrin-*Bti*. The start date is day 100 and the treatment durations are: (a) $150 - 300$ days, (b) $300 - 300$ days

combination provides an important improvement, indicating that the combination is very useful.

Finally, taking into account the improvement observed with the larvicide treatment (see Figure (8)(b), green line), we consider the start date $t_i = 300$. In Figure 10, we compare the adulticide treatment with the adulticide-larvicide combination. As expected, the combination clearly improves the results and it seems that the combination is a very interesting way to (partly) control the epidemic even if it is used "'too late"', i.e. after the begining of the explosive epidemic. This simulation showed that the campaign by the DRASS agency in February 2006 helped to stop the epidemic.

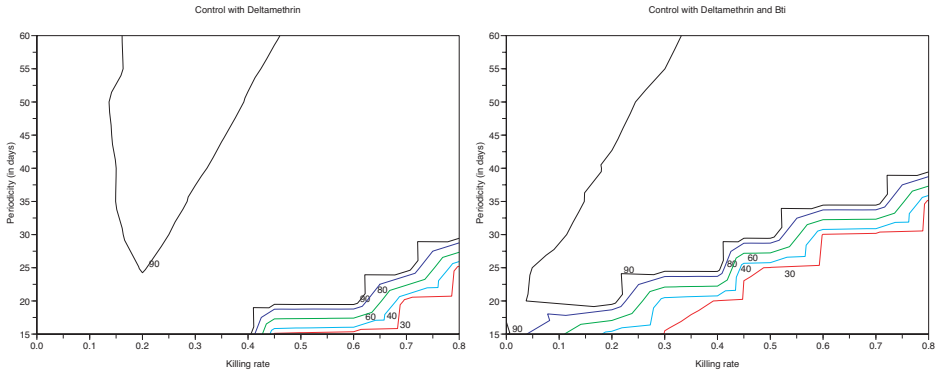

FIGURE 10. Comparison of (a) Deltamethrin and (b) combination of Deltamethrin-*Bti*. The start date is day 300 and the treament duration is 150 days for the adulticide, and 300 days for the larvicide.

4.3.4. *Mechanical control only.* This type of intervention was conducted in 2006 (it was called "Kass'Moustik"). It consists in reducing the number of breeding sites, at least near inhabited areas. Because of the amount of work, it is necessary to

involve the local population: the aim for inhabitants is to keep their gardens and neighborhood clean and in particular to reduce the number of breeding sites. It is now admitted that *Aedes albopictus* stays in the area of its birth place if it has suitable conditions to develop and to survive (blood and sugar meals).

Simulations show that the start date of the mechanical control tool is very important, as for the other control tools, as is the duration (see Figure 11). Clearly, if the

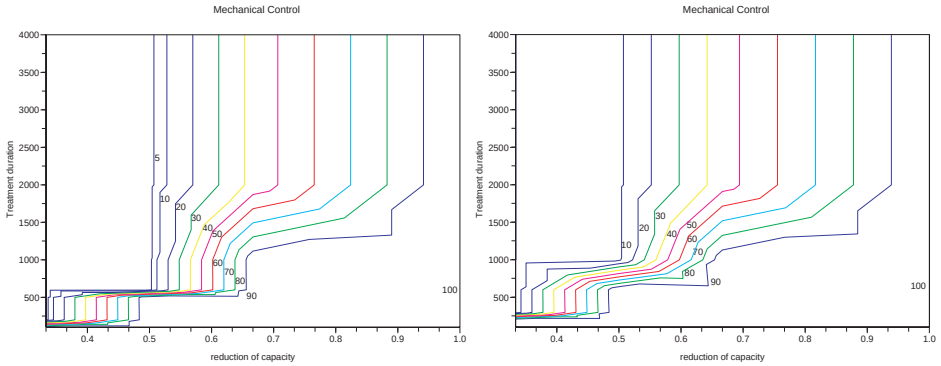

FIGURE 11. Efficacy of the mechanical control tool with respect to the efficacy of the control, the duration of the treatment, and with start dates: (a) $t_i = 100$, (b) $t_i = 200$.

larval capacity is not halved , i.e. $\alpha = 0.5$, there will be no impact on the disease. The best results are obtained with $\alpha = \frac{1}{3}$, which means that the larval capacity is reduced by 66%, but this seems unrealistic. Then, the duration of mechanical control is important too: there should be a long and permanent effort to maintain the capacity as low as possible but, in practice, this is not the case. Finally, as for the other control tools, the start date is important: the sooner the breeding sites are removed, the better the control is.

The final idea is to consider the combination of mechanical control tool with chemical control tools.

4.3.5. *Combining adulticide, larvicide, and mechanical control tools.* Following the results obtained in the previous sections, it seems that a combination of massive spraying and mechanical control should give interesting results. In Figure 12, we consider an adulticide-mechanical control combination with a start date at day 100 with two durations for the adulticide treatment and a 300-day treatment for the mechanical control. Considering that in real conditions the larval capacity can only be reduced by 25%, this leads to $\alpha = 0.75$ (Figure 12). We obtain even better results with the adulticide-mechanical control combination than with the adulticide-larvicide combination(compare also Figure 9 and Figure 12). Thus, for both mechanical control values, if the periodicity of the treament and the adulticide killing rate are low, then the number of infected humans is low.

In Figure 13, we consider the adulticide starts at day $t_i = 300$ and the mechanical control starts at day 100, with $\alpha = 0.75$. The results are very interesting, but this is possible only if we start the mechanical control as soon as possible.

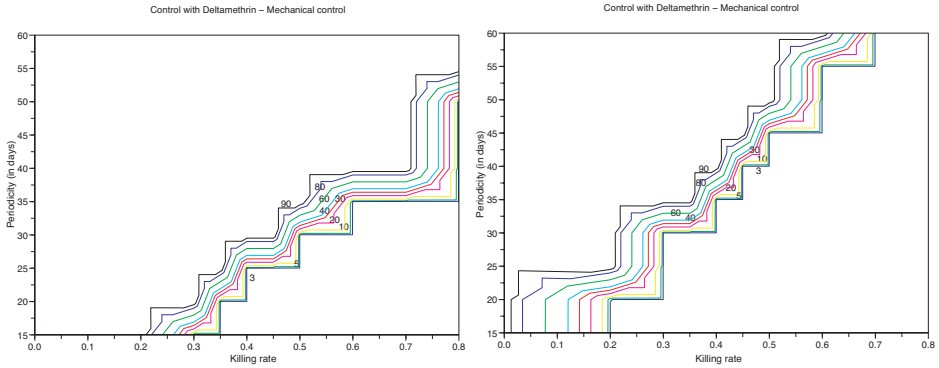

FIGURE 12. Combination of Deltamethrin and mechanical control with $\alpha = 0.75$. The start date is 100 days, and the duration of adulticide treatment is: (a) 150 days, (b) 300 days.

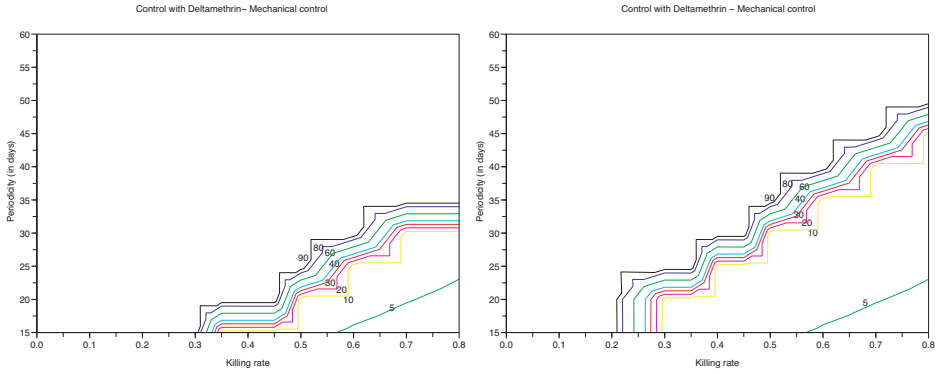

FIGURE 13. Combination of Deltamethrin and mechanical control with $\alpha = 0.75$. The start date of the adulticide treatment is day 300, the start date of mechanical control is day 100, and the duration of adulticide treatment is: (a) 150 days, (b) 300 days.

Finally, in Figures 14 and 15, we show simulations with the full combination of Deltamethrin, *Bti*, and mechanical control tools. Following the previous simulations, we consider that the mechanical control begins at day 100 with $\alpha = 0.75$, the larvicide control begins at day 300, with a duration of 300 days. Clearly, the addition of larvicide improves the previous results: compare Figure 12 with Figure 14, and Figure 13 with Figure 15.

It appears clearly that a suitable use of the different control tools with appropriate start dates and treatment durations can stop or contain the epidemic.

5. **Conclusion.** We have presented a study on various mosquito control tools that were used in Réunion Island during the explosive Chikungunya epidemic of 2006. It seems obvious that eradication is reached as soon as the reproduction number $\mathcal{R}_0$ is below unity. But, in fact, if $\mathcal{N}$ diminishes below unity and $\mathcal{R}_0 > 1$, then the disease

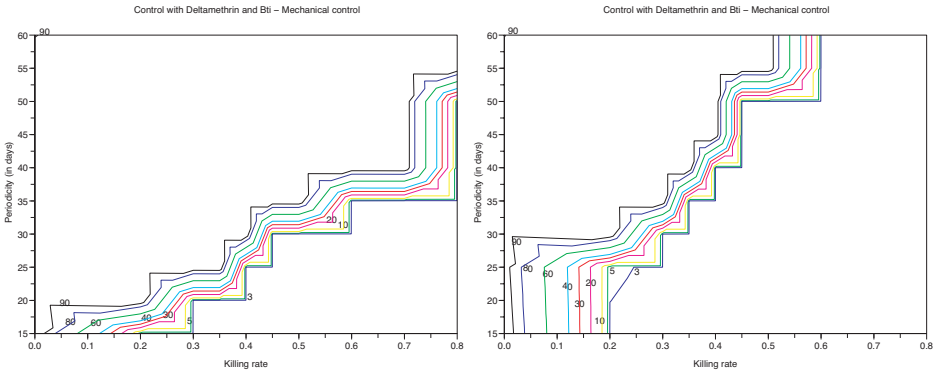

FIGURE 14. Combination of Deltamethrin, *Bti*, and mechanical control ($\alpha = 0.75$). The start date of the adulticide, and the mechanical control is day 100, the start date of the larvicide is day 300, and the duration of the adulticide treatment is: (a) 150 days, (b) 300 days.

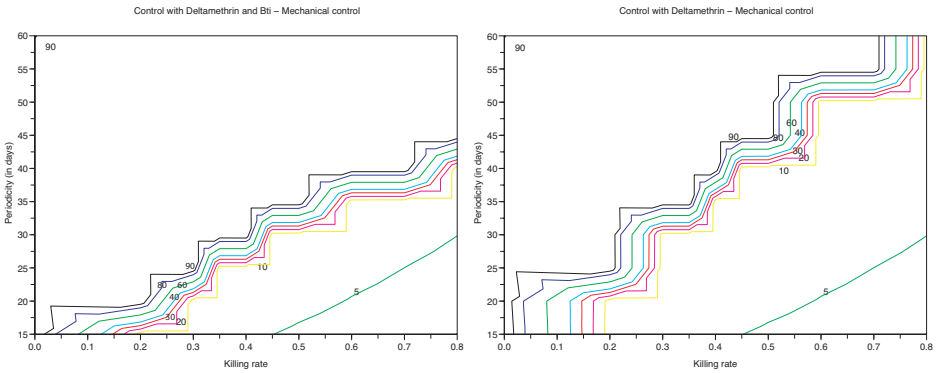

FIGURE 15. Combination of Deltamethrin, *Bti*, and mechanical control ($\alpha = 0.75$). The start dates of the adulticide and the larvicide are day 300, the start date of the mechanical control is day 100, and the duration of the adulticide treatment is: (a) 150 days, (b) 300 days.

can disappear, in other words, the system can converge to the Trivial Equilibrium, TE.

Some important elements appear:

- we have introduced new observations made by Dubrulle et al. [15] about the life-span of infected mosquitoes: the Chikungunya virus halves the lifespan of infected mosquito. In some sense, the virus has a "positive effect" because it kills the infected mosquito, which has less chance to propagate the virus. This is a very important result that can be helpful to explain the following fact: in 2006, the health authorities indicated that the estimated prevalence in the human population was (only) about 37%; i.e. 37% of the human population was infected by the virus. Surprisingly, the disease died out and apart from

some isolated cases no more (small) outbreaks appeared since the huge epidemic of 2006. Of course, all the control tools implemented since 2006 helped to prevent the rise of new epidemics, but the risk still exists because we are far away from an expected prevalence of $60-65\%$, like in Comoros, where the prevalence was estimated to be about 63%.

- a combination of several control tools seems to be the best way, from the ecological and environmental point of view, to stop or to contain an epidemic like the one in 2006.
- the adulticide-mechanical control combination gives satisfactory results but it seems better to use the full combination, i.e. combining larvicide, adulticide, and mechanical control. As we have showed, the impact of the larvicide is limited but seems more efficient if used later, i.e. with a start date $t_i = 300$. Moreover, the influence of the larvicide is very complicated to determine because *Bti* kills only the larval stage in the aquatic state. It might be better to split the differential equation associated to the aquatic state into three differential equations for the eggs, larvae, and pupae. Unfortunately, this complicates the model and can lead to serious mathematical difficulty. Moreover, we need more data about the larvicide killing rate for each sub-stage and for each type of breeding site [27].
- the start date of any treatment has a fundamental role and the sooner the authorities decide or plan land interventions, the more efficient the control tool is. In particular, it appears clearly that planning mechanical control as soon as possible can greatly improve the results.
- the duration of the treatment is important and it depends on the start date. If the duration is not long enough, then the epidemic will rise later or become periodic. Of course, the periodicity of the treatment is important too: it seems preferable to consider a 15-day treatment; this can be done in very localized areas. The start date, the duration, and the periodicity will determine the amount of adulticide and/or larvicide to use. Obviously, to preserve endemic species, only the smallest quantities of adulticide and/or larvicide should be used. As far as we know, the mosquito population in Réunion Island is sensitive to Deltamethrin (the only authorized adulticide in the European Union). Thus, it is necessary to use the adulticide as little as possible to avoid the emergence of resistant mosquitoes.
- Also, mechanical control, with the help of the local population, is a very good alternative: both "cheap" and sustainable. If it is done for a long time, it is efficient and then massive spraying can be used from time to time to prevent an "explosion" of the epidemic.

Of course, it is not possible to give a definitive answer. The previous examples show that vector control is a very complex problem and more real experiments are needed to measure the efficacy of the control tools. As a first attempt, the model could be improved by taking into account more biological factors or by considering delay differential equations.

Another improvement would be to take into account the periodicity in some of the parameters in the mosquito population. Indeed, in Réunion Island, the mean temperature during the dry season is about 21^oC at sea-level, where most of the cities are located. Yet, H. Delatte [8] showed adult survival is inversely correlated to the temperature: the highest survival rate is obtained at 15^oC, while the lowest

is obtained at 35^oC. Of course, humidity is an important factor too. The previous results indicate clearly that at sea-level, *Aedes albopictus* is able to survive the dry season and this explains why the virus Chikungunya survived from June to October 2005. Experiments are currently being conducted to estimate the evolution of the wild population according to the season and the weather parameters.

Temporal models assume homogeneity in the dispersal of the mosquitoes. Yet, this is untrue. Thus, another improvement, more difficult to achieve, would be to add spatial variables in the equations to take into account the fact that mosquitoes move to favorable environments, searching for breeding sites or blood meals.

Finally, it would be interesting to investigate a biological control like the release of sterile insects and to compare it with the control tools studied here.

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6. **Appendices.**

6.1. **Appendix A.**

We solve system (1), with $\frac{dS_h}{dt}(t) = 0 = \frac{dE_h}{dt}(t) = \frac{dI_h}{dt}(t) = \frac{dR_h}{dt}(t) = 0$, and we obtain the following relations

$$\begin{cases} E_h &= \frac{\mu_h+\eta_h}{\nu_h} I_h, \\ R_h &= \frac{\eta_h}{\mu_h} I_h, \\ S_h &= N_h - \frac{(\mu_h+\nu_h)(\mu_h+\eta_h)}{\mu_h \nu_h} I_h, \\ \frac{I_h}{N_h} &= \frac{\nu_h \mu_h B \beta_{mh} I_m}{(\mu_h+\nu_h)(\mu_h+\eta_h)(\mu_h N_h + B\beta_{mh} I_m)}. \end{cases} \tag{16}$$

Then, we solve system (2), with $\frac{dL_m}{dt}(t) = 0 = \frac{dS_m}{dt}(t) = \frac{dE_m}{dt}(t) = \frac{dI_m}{dt}(t) = 0$ and we obtain the following relations

$$\begin{cases} (\eta_A + \mu_A + c_A) A_m = \mu_b \left(1 - \frac{A_m}{\alpha K}\right) (S_m + E_m + I_m) \\ S_m = \frac{\eta_A}{\mu_m + c_m + B\beta_{hm} \frac{I_h}{N_h}} A_m, \\ E_m = \frac{B\beta_{hm}}{\mu_E + c_m + \eta_m} \frac{I_h}{N_h} S_m = \frac{B\beta_{hm}}{\mu_E + c_m + \eta_m} \frac{I_h}{N_h} \frac{\eta_A}{\mu_m + c_m + B\beta_{hm} \frac{I_h}{N_h}} A_m, \\ I_m = \frac{\eta_m}{\mu_{moi} + c_m} E_m = \frac{\eta_m}{\mu_{moi} + c_m} \frac{B\beta_{hm}}{\mu_E + c_m + \eta_m} \frac{I_h}{N_h} \frac{\eta_A}{\mu_m + c_m + B\beta_{hm} \frac{I_h}{N_h}} A_m. \end{cases} \tag{17}$$

In fact, there is a more simple relation: multiplying $(2)_2$ by $\frac{1}{\mu_m + c_m}$, $(2)_3$ by $\frac{1}{\mu_E + c_m}$ and $(2)_4$ by $\frac{1}{\mu_{moi} + c_m}$, setting $\frac{dS_m}{dt}(t) = \frac{dE_m}{dt}(t) = \frac{dI_m}{dt}(t) = 0$, and using the fact that $I_m = \frac{\eta_m}{\mu_{moi} + c_m} E_m$, and $B\beta_{hm} \frac{I_h}{N_h} S_m = (\mu_E + c_m + \eta_m) E_m$, we deduce

$$\begin{aligned} I_m + E_m + S_m &= \frac{\eta_A}{\mu_m + c_m} A_m + \eta_m E_m \frac{\mu_E - \mu_{moi}}{(\mu_{moi} + c_m)(\mu_E + c_m)} \\ &\quad - B\beta_{hm} \frac{I_h}{N_h} S_m \frac{\mu_E - \mu_m}{(\mu_E + c_m)(\mu_m + c_m)} -, \\ &= I_m \left(\frac{\mu_E - \mu_{moi}}{\mu_E + c_m} - \frac{(\mu_E - \mu_m)(\mu_E + c_m + \eta_m)(\mu_{moi} + c_m)}{\eta_m (\mu_m + c_m)(\mu_E + c_m)} \right) \\ &\quad + \frac{\eta_A}{\mu_m + c_m} A_m, \end{aligned}$$

that is

$$I_m + E_m + S_m = -I_m \left(\frac{\mu_{moi} - \mu_E}{\mu_E + c_m} + \frac{(\mu_E - \mu_m)(\mu_E + c_m + \eta_m)(\mu_{moi} + c_m)}{\eta_m(\mu_m + c_m)(\mu_E + c_m)} \right) + \frac{\eta_A}{\mu_m + c_m} A_m$$

Let us first compute the equilibrium without Disease, i.e. $I_m = I_h = 0$. Thus using (18), with $I_m = 0$, and $(17)_1$, we obtain

$$(\eta_A + \mu_A + c_A)A_m = \mu_b(1 - \frac{A_m}{\alpha K})\frac{\eta_A}{\mu_m + c_m} A_m.$$

We deduce that either $A_m = 0$ or $A_m = A_{m0} = \left(1 - \frac{1}{\mathcal{N}}\right) \alpha K$ if $\mathcal{N} > 1$.When $A_m = I_m = I_h = 0$, we easely deduce from (16) and (17) that $S_m = E_m = 0$, $E_h = R_h = 0$, and $S_h = N_h$. Thus, we recover the Trivial Equilibrium $TE = (N_h, 0, 0, 0, 0, 0, 0, 0)$.

Since $\mathcal{N} > 1$, and $A_m = A_{m0} = \left(1 - \frac{1}{\mathcal{N}}\right) \alpha K$, using (16) and (17), we deduce $S_{m0} = \frac{\eta_A}{\mu_m + c_m} A_{m0} = \frac{\eta_A}{\mu_m + c_m} \left(1 - \frac{1}{\mathcal{N}}\right) \alpha K$, $E_m = 0$, $E_h = R_h = 0$, and $S_h = N_h$. Thus, since $\mathcal{N} > 1$, there exists a non trivial Disease Free Equilibrium $RDFE = (N_h, 0, 0, 0, A_{m0}, S_{m0}, 0, 0)$.

6.2. **Appendix B.** We follow [42] and [13]. We consider only the terms in which the disease is in progression, which leads to the following subsystem

$$\begin{cases} \frac{dE_h}{dt}(t) &= B\beta_{mh}\frac{I_m}{N_h}S_h - (\nu_h + \mu_h)E_h \\ \frac{dI_h}{dt}(t) &= \nu_h E_h - (\eta_h + \mu_h)I_h \\ \frac{dE_m}{dt}(t) &= C\beta_{hm}\frac{I_h}{N_h}S_m - (\mu_E + \eta_m + c_m)E_m \\ \frac{dI_m}{dt}(t) &= \eta_m E_m - (\mu_{moi} + c_m)\, I_m \end{cases} \tag{18}$$

that can be rewritten as $\frac{dx}{dt} = \mathcal{F}(x) - \mathcal{V}(x)$, where $x^T = (E_h, I_h, E_m, I_m)$ and

$$\mathcal{F}(x_I) = \begin{pmatrix} B\beta_{mh}\frac{I_m}{N_h}S_h \\ 0 \\ C\beta_{hm}\frac{I_h}{N_h}S_m \\ 0 \end{pmatrix}, \qquad \mathcal{V}(x) = \begin{pmatrix} (\nu_h + \mu_h)E_h \\ -\nu_h E_h + (\eta_h + \mu_h)I_h \\ (\mu_m + \eta_m + c_m)E_m \\ -\eta_m E_m + (\mu_{moi} + c_m)\, I_m \end{pmatrix}$$

In [42], the authors showed that the general basic reproduction number is given by $\mathcal{R}_0 = \rho(J_{\mathcal{F}} J_{\mathcal{V}}^{-1})$, where $\rho(A)$ denotes the spectral radius of A. $J_{\mathcal{F}}$ and $J_{\mathcal{V}}$ are the Jacobian matrices associated with $\mathcal{F}$ and $\mathcal{V}$ and describe the linearization of the reduced system around $RDFE$.

We compute the Jacobian matrices associated with $\mathcal{F}$ and $\mathcal{V}$. A direct computation gives

$$J_{\mathcal{V}}(x) = \begin{pmatrix} \nu_h + \mu_h & 0 & 0 & 0 \\ -\nu_h & \eta_h + \mu_h & 0 & 0 \\ 0 & 0 & \mu_E + \eta_m + c_m & 0 \\ 0 & 0 & -\eta_m & \mu_{moi} + c_m \end{pmatrix}$$

and

$$J_{\mathcal{F}}(x) = \begin{pmatrix} 0 & 0 & 0 & B\beta_{mh}\frac{S_h}{N_h} \\ 0 & 0 & 0 & 0 \\ 0 & B\beta_{hm}\frac{S_m}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

Then, computing $J_{\mathcal{V}}^{-1}$, we deduce at x_{RDFE}: $J_{\mathcal{F}}(x_{RDFE})J_{\mathcal{V}}^{-1}(x_{RDFE}) =$

$$\begin{pmatrix} 0 & 0 & \frac{B\beta_{mh}\eta_m}{(\mu_{moi}+c_m)(\mu_E+\eta_m+c_m)} & \frac{B\beta_{mh}}{(\mu_{moi}+c_m)} \\ 0 & 0 & 0 & 0 \\ \frac{B\beta_{hm}\nu_h}{(\mu_h+\eta_h)(\mu_h+\nu_h)}\frac{S_{m0}}{N_h} & \frac{B\beta_{mh}}{\mu_h+\nu_h}\frac{S_{m0}}{N_h} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

We deduce the characteristic polynomial

$$p(\lambda) = \lambda^2\left(\lambda^2 - B\beta_{mh}\frac{\eta_m}{(\mu_{moi}+c_m)(\mu_E+\eta_m+c_m)}B\beta_{hm}\frac{\nu_h}{(\mu_h+\nu_h)(\mu_h+\eta_h)}\frac{S_{m0}}{N_h}\right)$$

which implies that $\rho(J_{\mathcal{F}}J_{\mathcal{V}}^{-1}) = \sqrt{\frac{\eta_m B^2\beta_{mh}\beta_{hm}\nu_h}{(\mu_{moi}+c_m)(\mu_E+\eta_m+c_m)(\mu_h+\nu_h)(\mu_h+\eta_h)}\frac{S_{m0}}{N_h}}$ and thus, we deduce

$$\mathcal{R}_0^2 = \frac{\eta_m B^2\beta_{mh}\beta_{hm}\nu_h}{(\mu_{moi}+c_m)(\mu_E+\eta_m+c_m)(\mu_h+\nu_h)(\mu_h+\eta_h)}\frac{S_{m0}}{N_h}.$$

or, equivalently

$$\mathcal{R}_0^2 = \frac{\eta_m B^2\beta_{mh}\beta_{hm}\nu_h\eta_A\alpha k}{(\mu_{moi}+c_m)(\mu_E+\eta_m+c_m)(\mu_h+\nu_h)(\mu_h+\eta_h)(\mu_m+c_m)}\left(1-\frac{1}{\mathcal{N}}\right).$$

6.3. **Appendix C.** Using (16) and (17), we now compute the endemic equilibrium, if any, i.e. we are looking for an equilibrium such that $I_h \neq 0$ and $I_m \neq 0$. In that case, we will have two cases to study. We assume that $\mathcal{N} > 1$ and $\mathcal{R}_0^2 > 1$.

1. If $\mu_m = \mu_E = \mu_{moi}$, then, from (18), we deduce

$$I_m + S_m + E_m = \frac{\eta_A}{\mu_m + c_m}A_m. \tag{19}$$

Thus, like before, we obtain the following equation in A_m

$$(\eta_A + \mu_A + c_A)A_m = \mu_b(1 - \frac{A_m}{\alpha K})\frac{\eta_A}{\mu_m + c_m}A_m, \tag{20}$$

from which we deduce that either $A_m = 0$ or $A_m = A_{m0} = \left(1 - \frac{1}{\mathcal{N}}\right)\alpha K$. Of course, we consider $A_m \neq 0$, otherwise we recover TE. Using $(17)_2$ and (19), we have

$$S_m = \frac{\eta_A}{\mu_m + c_m + B\beta_{hm}\frac{I_h}{N_h}}\left(1 - \frac{1}{\mathcal{N}}\right)\alpha K \tag{21}$$

$$I_m + S_m + \frac{\mu_{moi} + c_m}{\eta_m}I_m = \frac{\eta_A}{\mu_m + c_m}\left(1 - \frac{1}{\mathcal{N}}\right)\alpha K$$

which gives

$$I_m = \frac{\eta_m B\beta_{hm}\frac{I_h}{N_h}\eta_A}{(\eta_m + \mu_m + c_m)(\mu_m + c_m)\left(\mu_m + c_m + B\beta_{hm}\frac{I_h}{N_h}\right)}\left(1 - \frac{1}{\mathcal{N}}\right)\alpha K. \tag{22}$$

Then, using $(16)_4$ with (22), we deduce

$$\left(\mu_m + c_m + B\beta_{hm}\frac{I_h}{N_h}\right)(\mu_h N_h + B\beta_{mh}I_m) =$$

$$\frac{\eta_m\nu_h\mu_h B^2\beta_{mh}\beta_{hm}\eta_A\left(1-\frac{1}{\mathcal{N}}\right)\alpha K}{(\mu_h + \nu_h)(\mu_h + \eta_h)(\eta_m + \mu_m + c_m)(\mu_m + c_m)},$$

or equivalently

$$\left(\mu_h N_h B\beta_{hm} + \frac{\eta_m B^2 \beta_{mh}\beta_{hm}\eta_A}{(\eta_m+\mu_m+c_m)(\mu_m+c_m)}\left(1-\frac{1}{\mathcal{N}}\right)\alpha K\right)\frac{I_h}{N_h} =$$

$$(\mu_m+c_m)\,\mu_h N_h\left(\mathcal{R}_0^2-1\right),$$

with $\mathcal{R}_0^2$ defined in (5).

Finally, we explicitely deduce the coordinates of the endemic equilibrium EE:

$$\begin{cases} I_h^* = \frac{(\mu_m+c_m)\mu_h\left(\mathcal{R}_0^2-1\right)}{\mu_h B\beta_{hm}+\frac{\eta_m B^2\beta_{mh}\beta_{hm}\eta_A}{(\eta_m+\mu_m+c_m)(\mu_m+c_m)}\left(1-\frac{1}{\mathcal{N}}\right)\alpha k}N_h, \\ E_h^* = \frac{\mu_h+\eta_h}{\nu_h}I_h^*, \\ S_h^* = N_h - \frac{(\mu_h+\nu_h)(\mu_h+\eta_h)}{\mu_h\nu_h}I_h^*, \\ R_h^* = \frac{\eta_h}{\mu_h}I_h^*. \end{cases}$$

and

$$\begin{cases} A_m^* = A_{m0} = \left(1-\frac{1}{\mathcal{N}}\right)\alpha K \\ S_m^* = \frac{\eta_A}{\mu_m+c_m+B\beta_{hm}\frac{I_h^*}{N_h}}\left(1-\frac{1}{\mathcal{N}}\right)\alpha K, \\ I_m^* = \frac{\eta_m B\beta_{hm}\frac{I_h^*}{N_h}\eta_A}{(\eta_m+\mu_m+c_m)(\mu_m+c_m)\left(\mu_m+c_m+B\beta_{hm}\frac{I_h^*}{N_h}\right)}\left(1-\frac{1}{\mathcal{N}}\right)\alpha K. \\ E_m^* = \frac{\mu_{moi}+c_m}{\eta_m}I_m^*. \end{cases}$$

We recover the results obtained in [13] (appendix A).

2. This is the tedious case. Here, we will consider $\mu_m \le \mu_E \le \mu_{moi}$ with $\mu_m \neq \mu_{moi}$. Using (18) in $(17)_1$, we have

$$(\eta_A+\mu_A+c_A)A_m = \mu_b(1-\frac{A_m}{\alpha K})\left(\frac{\eta_A}{\mu_m+c_m}A_m - I_m X\right),$$

with

$$X = \frac{\mu_{moi}-\mu_E}{\mu_E+c_m} + \frac{(\mu_E-\mu_m)(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_m(\mu_m+c_m)(\mu_E+c_m)}. \tag{23}$$

Then, we deduce

$$\begin{aligned} I_m &= \frac{1}{X}\frac{\eta_A+\mu_A+c_A}{\mu_b}\left(\mathcal{N}-\frac{\alpha K}{\alpha K-A_m}\right)A_m, \qquad (24)\\ &= \frac{1}{X}\frac{\eta_A+\mu_A+c_A}{\mu_b(\alpha K-A_m)}\mathcal{N}\left(\left(1-\frac{1}{\mathcal{N}}\right)\alpha K - A_m\right)A_m, \\ &= \frac{1}{X}\frac{\eta_A+\mu_A+c_A}{\mu_b(\alpha K-A_m)}\mathcal{N}\left(A_{m0}-A_m\right)A_m, \end{aligned}$$

Because $I_m \neq 0$, we necessarely are looking for A_m such that

$$0 < A_m < A_{m0}. \tag{25}$$

Multiplying $(16)_4$ by $B\beta_{hm}$ leads to

$$B\beta_{hm}\frac{I_h}{N_h} = \frac{\nu_h\mu_h B^2\beta_{hm}\beta_{mh}I_m}{(\mu_h+\nu_h)(\mu_h+\eta_h)(\mu_h N_h + B\beta_{mh}I_m)}. \tag{26}$$

Then using $(17)_4$, we deduce

$$\begin{aligned} I_m &= \frac{\eta_A\eta_m\nu_h\mu_h B^2\beta_{mh}\beta_{mh}}{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}\times \\ &\quad \frac{I_m A_m}{(\mu_m+c_m)(\mu_h+\nu_h)(\mu_h+\eta_h)(\mu_h N_h+B\beta_{mh}I_m)+\nu_h\mu_h B^2\beta_{mh}\beta_{mh}I_m}, \end{aligned}$$

which simplifies as follows ($I_m \neq 0$)

$$\begin{aligned} A_m &= \frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m\nu_h\mu_h B^2\beta_{mh}\beta_{mh}}\times \\ &\quad \left((\mu_m+c_m)(\mu_h+\nu_h)(\mu_h+\eta_h)(\mu_h N_h+B\beta_{mh}I_m)+\nu_h\mu_h B^2\beta_{mh}\beta_{mh}I_m\right) \end{aligned}$$

that is

$$\begin{aligned} A_m &= \frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m}I_m+\frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\nu_h\eta_A\eta_m\mu_h B^2\beta_{mh}\beta_{mh}}\times \\ &\quad (\mu_m+c_m)(\mu_h+\nu_h)(\mu_h+\eta_h)(\mu_h N_h+B\beta_{mh}I_m). \end{aligned}$$

Since $\mathcal{N}>1$, and using the fact that

$$\begin{aligned} \left(1-\tfrac{1}{\mathcal{N}}\right)\frac{\alpha k}{\mathcal{R}_0^2} &= \frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)(\mu_m+c_m)(\mu_h+\nu_h)(\mu_h+\eta_h)}{\nu_h\eta_A\eta_m B^2\beta_{mh}\beta_{mh}}, \\ &= \frac{A_{m0}}{N_h\mathcal{R}_0^2}, \end{aligned}$$

we can rewrite A_m in the following way

$$\begin{aligned} A_m &= \frac{A_{m0}}{\mu_h N_h}\frac{1}{\mathcal{R}_0^2}(\mu_h N_h+B\beta_{mh}I_m)+\frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m}I_m \\ &= \frac{A_{m0}}{\mathcal{R}_0^2}+\left(\frac{A_{m0}}{\mathcal{R}_0^2}\frac{B\beta_{mh}}{\mu_h N_h}+\frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m}\right)I_m. \end{aligned}$$

From the previous equality we deduce that $A_m \geq \frac{A_{m0}}{\mathcal{R}_0^2}$. Using (24), we replace I_m in the previous equality to get

$$\begin{aligned} A_m(\alpha K-A_m) &= \frac{A_{m0}}{\mathcal{R}_0^2}(\alpha K-A_m)+\frac{\eta_A}{\mu_m+c_m}\frac{1}{X}\times \\ &\quad \times\left(\frac{A_{m0}}{\mathcal{R}_0^2}\frac{B\beta_{mh}}{\mu_h N_h}+\frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m}\right)(A_{m0}-A_m)A_m, \end{aligned}$$

which leads to solve $P(A_m)=0$, with

$$P(A_m)=aA_m^2+bA_m+c, \tag{27}$$

where

$$c=\frac{1}{\mathcal{R}_0^2}\alpha K A_{m0}>0,$$

$$\begin{aligned} b &= \frac{\eta_A}{(\mu_m+c_m)X}\left(\frac{A_{m0}}{N_h\mu_h}\frac{B\beta_{mh}}{\mathcal{R}_0^2}+\frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m}\right)A_{m0} \\ &\quad -\left(\alpha K+\frac{1}{\mathcal{R}_0^2}A_{m0}\right), \end{aligned}$$

and

$$\begin{aligned} a &= 1-\frac{1}{X}\frac{\eta_A}{\mu_m+c_m}\left(\frac{A_{m0}}{\mathcal{R}_0^2}\frac{B\beta_{mh}}{\mu_h N_h}+\frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m}\right) \\ &\leq 1-\frac{1}{X}\frac{\eta_A}{\mu_m+c_m}\frac{(\mu_E+c_m+\eta_m)(\mu_{moi}+c_m)}{\eta_A\eta_m}. \end{aligned}$$

We will now show that $a < 0$. In particular we will find a lower bound for

$$\frac{1}{X}\frac{\eta_A}{\mu_m + c_m}\frac{(\mu_E + c_m + \eta_m)(\mu_{moi} + c_m)}{\eta_A \eta_m}.$$

In order to obtain this lower bound, we will consider the following function

$$\begin{aligned} X_{\mu_E}(x) &= \frac{\mu_{moi} - x}{x + c_m} + \frac{(x - \mu_m)(x + c_m + \eta_m)(\mu_{moi} + c_m)}{\eta_m(\mu_m + c_m)(x + c_m)} \\ &= \frac{1}{(\mu_m + c_m)\eta_m}\left(-(\mu_m + c_m)\eta_m + (\mu_{moi} + c_m)(x + \eta_m - \mu_m)\right), \end{aligned}$$

such that $X_{\mu_E}(\mu_E) = X$, defined in (23), page 342. For all $x \in [\mu_m, \mu_{moi}]$, we set

$$Y(x) = \frac{1}{X_{\mu_E}(x)}\frac{\eta_A}{\mu_m + c_m}\frac{(x + c_m + \eta_m)(\mu_{moi} + c_m)}{\eta_A \eta_m},$$

that can be simplified as follows

$$Y(x) = \frac{(x + c_m + \eta_m)(\mu_{moi} + c_m)}{(\mu_{moi} - \mu_m)\eta_m + (\mu_{moi} + c_m)(x - \mu_m)}.$$

$Y(x)$ is a smooth function for all x in $[\mu_m, \mu_{moi}]$, and thus

$$\begin{aligned} Y'(x) &= (\mu_{moi} + c_m)\left(\tfrac{1}{(\mu_{moi} - \mu_m)\eta_m + (\mu_{moi} + c_m)(x - \mu_m)}\right)^2 \times \\ &\quad \times \left((\mu_{moi} - \mu_m)\eta_m + (\mu_{moi} + c_m)(x - \mu_m)\right) - (\mu_{moi} + c_m)(x + c_m + \eta_m)\big). \end{aligned}$$

Thus to study the sign of $Y'(x)$, it suffices to study

$$\begin{aligned} & (\mu_{moi} - \mu_m)\eta_m + (\mu_{moi} + c_m)(x - \mu_m) - (\mu_{moi} + c_m)(x + c_m + \eta_m) \\ = \;& (\mu_{moi} - \mu_m)\eta_m - (\mu_{moi} + c_m)\mu_m - (\mu_{moi} + c_m)(c_m + \eta_m) \\ = \;& -\mu_m\eta_m - (\mu_{moi} + c_m)\mu_m - \mu_{moi}c_m - c_m(c_m + \eta_m) \\ < \;& 0, \end{aligned}$$

from which we deduce that $Y'(x) < 0$. Thus, we have

$$Y(\mu_{moi}) \leq Y(x) \leq Y(\mu_m), \qquad \forall x \in [\mu_m, \mu_{moi}].$$

In particular we have:

$$\begin{aligned} Y(\mu_E) &\geq \frac{(\mu_{moi} + c_m + \eta_m)(\mu_{moi} + c_m)}{(\mu_{moi} - \mu_m)\eta_m + (\mu_{moi} + c_m)(\mu_{moi} - \mu_m)} \\ &\geq \frac{\mu_{moi} + c_m}{\mu_{moi} - \mu_m} = 1 + \frac{\mu_m + c_m}{\mu_{moi} - \mu_m} \end{aligned}$$

which implies that $a < 1 - Y(\mu_E) < 0$.

Moreover, we have

$$\begin{aligned} b &= (1 - a)A_{m0} - \left(\alpha K + \frac{1}{\mathcal{R}_0^2}A_{m0}\right), \\ &= A_{m0}\left(1 - a - \frac{\mathcal{N}}{\mathcal{N} - 1} - \frac{1}{\mathcal{R}_0^2}\right), \\ &= -A_{m0}\left(\frac{1}{\mathcal{N} - 1} + a + \frac{1}{\mathcal{R}_0^2}\right). \end{aligned}$$

Finally, with $a < 0$, and $c > 0$, equation (27) has only one positive solution given by the following well known formula

$$A_m^* = \frac{-b - \sqrt{b^2 - 4ac}}{2a} > 0.$$

Because $a < 0$, we have $P(A_m) \geq 0$ if $A_m \in [0, A_m^*]$. Then, computing $P(A_{m0})$ leads to

$$P(A_{m0}) = aA_{m0}^2 + bA_{m0} + c = A_{m0}\left(\alpha K - A_{m0}\right)\left(\frac{1}{\mathcal{R}_0^2} - 1\right) < 0,$$

which implies that $A_m^* < A_{m0}$. Finally, using some of the previous formula, we deduce the coordinates of the endemic equilibrium EE.

Altogether, since $\mathcal{N} > 1$ and $\mathcal{R}_0^2 > 1$, an endemic equilibrium exists.

6.4. **Appendix D.** The two main assumptions to verify in Theorem 3.3 are D2 and D4. Thus we have to show that $\rho\left(Id + \phi A_1\left(X_S, 0\right)\right) < 1$ and $\rho\left(Id + \phi \overline{A}_2\left(X\right)\right) < 1$. We first show the following useful lemma

Lemma 6.1. *Let $A\left(x\right)$ be a stable Metzler matrix on a compact subset $\mathcal{K} \subset \mathbb{R}_+^n$, i.e. such that $\alpha(A(X)) < 0$ for all $X \in \mathcal{K}$. Let $\phi(\Delta t)$ be a time-step function such that $Id + \phi\left(\Delta t\right)\underline{A}$ is a non-negative matrix, i.e. $Id + \phi\left(\Delta t\right)\underline{A} \geq 0$, then we have*

$$\rho\left(Id + \phi\left(\Delta t\right)A\left(X\right)\right) = 1 + \phi\left(\Delta t\right))\,\alpha\left(A\left(X\right)\right) < 1, \text{ for all } X \in \mathcal{K}.$$

Proof. We have $Id + \phi\left(\Delta t\right)A\left(X\right) \geq 0$ for all $X \in \mathcal{K}$. Then, using Perron-Frobenius theory, we know that there exists r_X, a positive real, and a non negative right eigenvector v_X for all $X \in \mathcal{K}$, such that

$$\left(Id + \phi\left(\Delta t\right)A\left(x\right)\right)v_X = r_X v_X.$$

In particular $\rho\left(Id + \phi\left(\Delta t\right)A\left(X\right)\right) = r_X$. Moreover, we have

$$A\left(X\right)v_X = \left(\frac{r_X - 1}{\phi\left(\Delta t\right)}\right)v_X.$$

Thus, $\frac{r_X - 1}{\phi(\Delta t)}$ is an eigenvalue of $A\left(x\right)$. But $\frac{r_X - 1}{\phi(\Delta t)}$ is real and negative because $\alpha\left(A\left(X\right)\right) < 0$, which necesseraly implies that

$$0 < r_X < 1, \qquad \text{for all } x \in \mathcal{K}.$$

□

Previously, we have showed that $A_1(X_S, 0)$ is a stable Metzler Matrix, that is $\alpha(A(X_S, 0)) < 0$. Moreover we have choosed $\phi(\Delta t)$ in (14), such that $Id + \phi(\Delta t)A_1(X) > 0$, for all $X \in \mathcal{D}$, which implies that $Id + \phi(\Delta t)A_1(X_S, 0) > 0$, for all $(X_S, 0) \in \mathcal{D}$. Thus, from the previous lemma, we deduce that $\rho(Id + \phi(\Delta t)A_1(X)) < 1$ and thus $\rho(Id + \phi(\Delta t)A_1(X_S, 0)) < 1$, which implies D2.

Similarly, we have showed that $\overline{A}_2$ is a stable Metzler matrix if $\mathcal{R}_G < 1$. Thus, using the previous Lemma and the time step-function (14), imply that $\rho(Id + \phi(\Delta t)A_2(X)) < 1$ for all $X \in \mathcal{D}$, and thus $\rho(Id + \phi(\Delta t)\overline{A}_2) < 1$ for all $\Delta t > 0$.

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