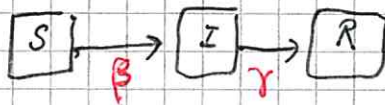


Modèle classique KERMACK-MCKENDRICK (1927)

$$\begin{cases} \frac{dS}{dt} = -\beta SI \\ \frac{dI}{dt} = \beta SI - \gamma I \\ \frac{dR}{dt} = \gamma I \end{cases}$$

ou SIR (Susceptibles, infectés, removed)

Modèle compartimental :



$S(t)$: susceptibles: # d'individus non encore infectés par la maladie au temps t

$I(t)$: infectés: # " infectés et capables d'infecter d'autres individus de la catégorie des susceptibles

$R(t)$: removed: # " retirés du compartiment de infectés soit parce qu'ils ont guéri soit parce qu'ils sont morts.

=> les guéris ici ne peuvent plus être infectés et ne peuvent plus être contagieux.

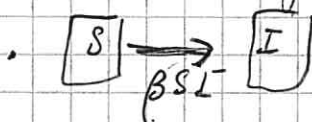
Population divisée en compartiments homogènes. Ici ^{la} population passe juste d'un compartiment à l'autre:

on a la conservation de la population totale:

$$N = S + I + R$$

$\frac{dN}{dt} = 0$ (souvent on élimine une équation mais ici c'est pratique de tout garder)

Modélisation des flux:



individus qui se font infecter par unité de temps (proportionnel à SI)

C'est à dire proportionnel au nombre de contacts entre S et I si la population est uniformément mélangée : "proportional mixing" ou loi d'action de masse par analogie avec la chimie.

$(A+B \rightarrow C)$ vitesse de réaction est proportionnelle # de choc produits entre A et B
" produit des concentrations A et B

✓ C'est une hypothèse forte mais non valide pour certaines maladies (ex: MST : autre modèle avec des sous-populations par exemple)

• $\boxed{I} \xrightarrow{\delta I} \boxed{R}$ δI : proportion constante de I passés en R à chaque unité de temps

Alors ici $\frac{1}{\delta}$: estimation du temps passé en I

si I dure n jours, population de I renouvelée en n jours

et donc chaque jour on enlève $\frac{I}{n}$ individus $\rightarrow \boxed{I} \rightarrow \boxed{I}$

1 jour δI part
 $\frac{1 \times I}{\delta} = \frac{I}{\delta}$ \times I tout entier part
toute la population est renouvelée.

• Adimensionnement

Rappel sur l'adimensionnement :

on considère une EDO du 1^{er} ordre à coef constants :

$$ax' + bx = c g(t)$$

1. identifier les variables indépendantes et les dépendantes
2. Remplacer chacune d'elle par une quantité normalisée
3. Diviser par le coefficient du terme de + grand ordre
4. essayer d'obtenir le max. de coef. égaux à 1

exemple: $ax' + bx = cg(t)$ variable indépendante: t
 dépendante: x

on pose: $x = \alpha X$ $t = \gamma \tau \Rightarrow \tau = \frac{t}{\gamma}$ $x(\tau(t))$
 on a alors $ax' + bx = cg(t)$ qui s'écrit:
 $x(t) = \alpha X(\tau)$ $\left| \begin{array}{l} \frac{dx}{dt} \\ \frac{d\tau}{dt} \end{array} \right.$

a. $\frac{dX(\tau)}{d\tau} + b \alpha X(\tau) = \frac{c}{\alpha \gamma} g(\gamma \tau)$

\Leftrightarrow a. $\frac{d}{d\tau} \alpha X(\tau) + b \alpha X(\tau) = c g(\gamma \tau)$

a. $\alpha \cdot \frac{1}{\gamma} \cdot X'(\tau) + b \alpha \cdot X(\tau) = c g(\gamma \tau) = c G(\tau)$

on divise par $\frac{\alpha \gamma}{\gamma}$:

$X'(\tau) + \frac{b \alpha}{a \gamma} X(\tau) = \frac{c \gamma}{a \alpha} G(\tau)$

on souhaite avoir $\frac{b \alpha}{a \gamma} = 1$ donc on choisit $\gamma = \frac{a}{b}$

et alors $\frac{c \gamma}{a \alpha} = \frac{c}{a \alpha} \cdot \frac{a}{b} = \frac{c}{\alpha b}$ et $\frac{c}{\alpha b} = 1 \Rightarrow \alpha = \frac{c}{b}$

on aura alors le problème adimensionné:

$X'(\tau) + X(\tau) = G(\tau)$ où $\gamma = \frac{a}{b}$ $\alpha = \frac{c}{b}$, $x(t) = \alpha X(\tau)$
 et $t = \gamma \tau$.

Soi, on a: $\left\{ \begin{array}{l} \frac{dS}{dt} = -\beta SI \\ \frac{dI}{dt} = \beta SI - \gamma I \\ \frac{dR}{dt} = \gamma I \end{array} \right.$

variables dépendantes: S, I, R
 indep. temps
 on a 2 paramètres: β et γ

La dynamique de \bar{I} est contrôlée par $\beta S \bar{I} - \gamma \bar{I}$

On va changer de variable:

$$S = S_* \bar{S} \quad I = I_* \bar{I} \quad R = R_* \bar{R} \quad \text{et } t = t_* \bar{t}$$

S_*, \dots, t_* : unités (ex: # d'individus par m^2 , jours, ...)

\bar{S}, \dots, \bar{t} : nombres sans dimension

Alors

$$\begin{cases} \frac{S_*}{t_*} \frac{d\bar{S}(\bar{t})}{d\bar{t}} = -\beta S_* I_* \bar{S} \cdot \bar{I} \\ \frac{I_*}{t_*} \frac{d\bar{I}(\bar{t})}{d\bar{t}} = \beta S_* \bar{S} \bar{I} - \gamma t_* \bar{I} \\ \frac{R_*}{t_*} \frac{d\bar{R}(\bar{t})}{d\bar{t}} = \gamma t_* \bar{I} \end{cases}$$

on obtient $\frac{d\bar{S}(\bar{t})}{d\bar{t}} = -\beta I_* t_* \bar{S} \bar{I}$

$$\frac{d\bar{I}(\bar{t})}{d\bar{t}} = \beta S_* t_* \bar{S} \bar{I} - \gamma t_* \bar{I}$$

$$\frac{d\bar{R}(\bar{t})}{d\bar{t}} = \gamma \frac{I_* t_*}{R_*} \bar{I}$$

on choisit d'utiliser le rap. de faire dépendre \bar{I} du rapport $\frac{\beta}{\gamma}$

on va poser $\gamma t_* = 1 \Rightarrow t_* = \frac{1}{\gamma}$

on choisit de poser $I_* = R_* = S_*$ on a alors:

$$\begin{cases} \frac{d\bar{S}}{d\bar{t}} = -\left(\frac{\beta}{\gamma} S_*\right) \bar{S} \bar{I} \\ \frac{d\bar{I}}{d\bar{t}} = \left(\frac{\beta S_*}{\gamma}\right) \bar{S} \bar{I} - \bar{I} \\ \frac{d\bar{R}}{d\bar{t}} = \bar{I} \end{cases}$$

on peut choisir S_* comme on veut

par exemple: $S_* = N$ ou $S_* = S(0)$

(c'est à peu près précis si la CI est $S(0) = N - \varepsilon$
 $\bar{I}(0) = \varepsilon$
 $R(0) = 0$

avec ε petit)

R_0 : est un effet seuil!

Preons $S_x = S(0)$ et posons $R_0 = \frac{\beta S(0)}{\gamma}$

$$\text{on a } \frac{d\bar{S}}{dt} = -R_0 \bar{S} \bar{I}$$

$$\text{on prend: } \bar{S}(0) = 1$$

$$\frac{d\bar{I}}{dt} = R_0 \bar{S} \bar{I} - \bar{I}$$

$\bar{I}(0)$ donné en général petit

$$\frac{d\bar{R}}{dt} = \bar{I}$$

$$\bar{R}(0) = 0$$

Alors jusqu'à $\frac{d\bar{I}}{dt} = (R_0 \bar{S} - 1) \bar{I}$ et $\bar{S}(0) = 1$

si ce n'est pas ressemblé à $R(t)$ est

• si $R_0 < 1$ \bar{I} décroît initialement

• si $R_0 > 1$ \bar{I} croît initialement \rightarrow épidémie

effet seuil: décrit par R_0 :

R_0 : taux de reproduction de l'infection dans une population à $S(0)$ susceptibles

(nombre d'infections secondaires causées par un seul infecté par une population initiale composée essentiellement d'individus susceptibles ($S(0) \approx N$))

R_0 se généralise à de nombreux autres modèles d'épidémiologie (nombreux compartiments, modèle stochastiques, variations annuelles des paramètres, ...). La question est toujours de calculer le R_0 puis de le contrôler pour le rendre < 1 .

Equilibres:

$$0 = -R_0 \bar{S} \bar{I}$$

$$0 = R_0 \bar{S} \bar{I} - \bar{I} \quad \Rightarrow \quad \bar{I} = 0 \quad \bar{S} \text{ et } \bar{R} \text{ quelconques}$$

$$0 = \bar{I}$$

Mais si on part de $\bar{S}(0)=1$, $\bar{I}(0)$ donné $\neq 0$ ($= I_0$) et $\bar{R}(0)=0$ on a:

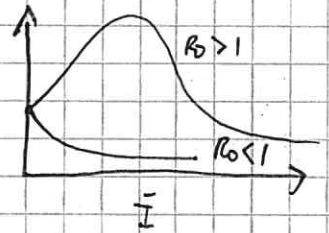
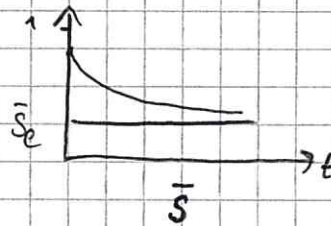
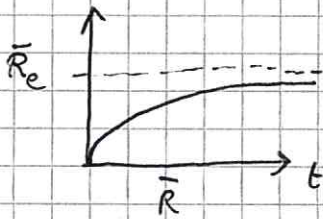
* conservation de la population, donc à l'équilibre $\bar{I}=0$ et \bar{S}_e et \bar{R}_e fixes
 $\bar{S}_e + \bar{R}_e = 1 + I_0$

lien entre les variables:

$$\frac{d\bar{S}}{d\bar{R}} = \frac{d\bar{S}}{dt} \cdot \frac{dt}{d\bar{R}} = -R_0 \bar{S} \quad \Rightarrow \quad \bar{S}(t) = e^{-R_0 \bar{R}(t)}$$

donc à l'équilibre $e^{-R_0 \bar{R}(t)} + \bar{R}(t) = 1 + I_0$

on a une seule solution $\bar{R}_e (> 0)$ si $I_0 \neq 0$.

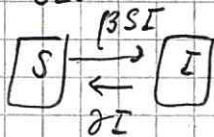


$\bar{I} > 0 \quad \forall t, \quad \bar{R} \nearrow, > 0, \quad \bar{S} \searrow$

\Rightarrow pas d'oscillations (comme pour la rougeole ou la varicelle)

\Rightarrow par voie des oscillations il faut "pouvoir remonter \bar{S} "

• Modèle SIS:



adimensionné

$$\frac{d\bar{S}}{dt} = -R_0 \bar{S} \bar{I} + \bar{I}$$

avec $\bar{S} + \bar{I} = N$

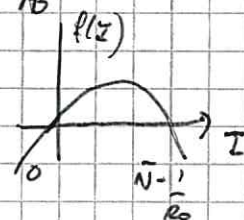
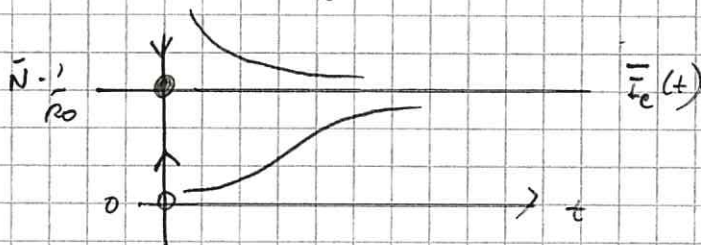
$$\frac{d\bar{I}}{dt} = R_0 \bar{S} \bar{I} - \bar{I}$$

on a une seule equation:

$$\frac{d\bar{I}}{dt} = R_0(\bar{N} - \bar{I})\bar{I} - \bar{I} = f(\bar{I})$$

$$\bar{N} > \frac{1}{R_0}$$

polynôme de d°2 racines: 0 et $\bar{N} - \frac{1}{R_0} > 0$ si $R_0 > \frac{1}{\bar{N}}$



≠ régulière donc trajectoires ne se croisent pas (Cauchy-Lipschitz)

→ trajectoires monotones

→ pas d'oscillations

• Modèle SIR avec dynamique vitale:

$$\begin{cases} \frac{dS}{dt} = \mu N - \beta SI - \mu S \\ \frac{dI}{dt} = \beta SI - \gamma I - \mu I \\ \frac{dR}{dt} = \gamma I - \mu R \end{cases}$$

Equilibre: $I = R = 0$ et $S = N$ ou, si $I \neq 0$ $S = \frac{\gamma + \mu}{\beta}$

$$I = \frac{\mu(N - S)}{\beta S}$$

$$R = \frac{\gamma I}{\mu}$$

on peut étudier la stabilité de cet équilibre (partir d'éliminer une équation (conservation de la population), linéariser, Jacobienne

Toujours stable mais pour R_0 assez grand, valeurs propres complexes (passe au avec R_0 partie réelle < 0 , oscillations amorties

Pas d'oscillations entretenues dans ce modèle simple mais avec forçage annuel très fort ou.

Control of the Transmission of Chikungunya Fever Epidemic Through the use of Adulticide

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Abstract: Problem statement: Another newly emerging disease, chikungunya fever, has appeared in various places such as the Island of Réunion, Thailand and other India. To control an epidemic of disease once it has been established, the use of adulticide is proposed. **Approach:** To simulate the effects of different control measurement, a mathematical model incorporating the specific features of this disease has been proposed. Using the standard methods for analyzing the dynamical stability of the system, the role of the efficacy of the adulticide on the basic reproduction number of the disease is studied. **Results and Conclusion:** It was found that below a particular value of the efficacy which depends on the values of the parameters used in the model, adulticide would not be effective at controlling the epidemic.

Keywords: Mathematical model, chikungunya fever, basic reproduction number, equilibrium, stability analysis, skin rash, transmission, dengue fever, *aedes aegypti* mosquito, symptoms, adulticide, equilibrium state

INTRODUCTION

Chikungunya fever is an arboviral disease caused by a member of the genus: *alphavirus* (family: Togaviridae), which was first isolated in 1953 in Tanzania (Pioloux *et al.*, 2007). The symptoms of this disease are a fever, skin rash and incapacitating arthralgia. In the major outbreak of this disease in 2005 on the island of Réunion, 244,000 out of a population of 775,000 inhabitants reported that they had experienced these symptoms (Moulay *et al.*, 2011). A different genotype (Asian strain) of this virus was found in India and Thailand in the early sixties.

The probable vector in the recent outbreak on the Réunion Island was the *Aedes albopictus* mosquito, while the probable vector in the outbreak in India was the *Aedes aegypti* mosquito. In the ongoing outbreak in Thailand, a new strain of the Chikungunya virus was isolated in both mosquito serotypes (Thavara *et al.*, 2009). Studies have shown that *Aedes albopictus* is more susceptible to the virus and therefore a more effective transmitter. The virus was found in both sexes of these two species of mosquitoes, indicating a possible role for transovarial transmission of the virus in the field populations of the mosquitoes.

The only defense against the appearance of an epidemic due to this virus is the control of the vector by use of insecticides. This can be done by the applications of larvicides to kill the mosquitoes in their larval state or of adulticides to kill them in their adult stage. Since the use of adulticides is more detrimental to the environment, The Ministry of Public Health in Thailand has launched national mosquito larva eradication program for the purpose of controlling both a Chikungunya and a dengue epidemic (Buathong, 2009). This approach is consistent with the recommendations of the 35th Session of the Subcommittee of the Executive Committee on Planning and Programming of PAHO (SPP35/7, 2001). They also pointed out that the use of adulticide be considered as a last resort strategy when the epidemic is established. While their recommendations were for Dengue fever, the policies also apply to the control of Chikungunya fever. Massad *et al.* (2008) recently studied the risk of Chikungunya fever in a Dengue epidemic area. They found that the basic reproduction number for Chikungunya fever was 64.4 % of that for Dengue fever. They assumed that both viruses were being transmitted by the same mosquito, *Aedes aegypti*. As we have pointed out, the Chikungunya

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virus is also transmitted by the *Aedes albopictus* mosquito which is a more effective transmitter of this virus than is the *Aedes aegypti* mosquito. This specie of mosquitoes is present in Thailand.

Mathematical models have become important tools in analyzing the spread and control of diseases using simulation approaches as in Adetunde (2009) ; Koriko and Yusuf, (2008) proposed mathematical models of Tuberculosis disease, determined the disease free and endemic equilibrium point and analyzed the stability.

In this study, we are interested in the role of applying adulticide on the temporal evolution of this disease and how the efficacy of the adulticide relates to the control of the spread. This can be done by using a mathematical model for the transmission of Chikungunya fever. Dumont, Chiroleu and Domerg (2008) used a SEIR (susceptible, exposed, infected, recovered) model for the human population and a LSEI (larvae-susceptible-exposed-infected) model for the mosquito population to describe the transmission of this disease on the Réunion Island. They found that a quick and focus interventions may be effective for controlling the diseases. Dumont and Chiroleu (2010) recently studies in more detail the vector control of this disease. They took into account the fact that the mean life of a mosquito infected by the Chikungunya virus is nearly half of that of an uninfected mosquito. Their preliminary results showed that the early use of massive spraying and mechanical control can stop the propagation of the Chikungunya disease.

There have been several reports on the development of resistance of the mosquitoes to several of the insecticides being employed in Thailand. Jirakanjanakit *et al.* (2007) found that *Aedes aegypti* had developed resistance to two commonly used insecticides, permethrin and deltamethrin. In another study, Jirakanjanakit *et al.* (2007) found that while temephos, a larvicide, was effective against the *Aedes aegypti* mosquitoes in mainly provinces in Thailand, its efficacy against the mosquitoes in two provinces ranged between 50.5-71.4%. Perich *et al.* (2000) found that the resting behavior of *Aedes aegypti* lowered the efficacy of adulticide, making a spraying program to be ineffectual.

We are interested in this study on whether there is an efficacy value below which an epidemic will not occur. We do this by performing a stability analysis based on the Routh-Hurwitz criteria (Marsden and McCracken, 1976) of a mathematical model for the transmission of Chikungunya fever which takes into account the application of an adulticide. We will determine the basic reproduction number for the disease

and see when it will be less than one. We present the model and its analysis, respectively. We follow this with the results of our numerical calculations. Finally we present our discussion and conclusions.

MATERIALS AND METHODS

Model formulation: Our model is based on the standard SIR model instead of the SEIR model since we are interested in the effects of applying adulticide on the transmission of Chikungunya disease and not on the effects of delay times. In our model, the human population is divided into the susceptible human (\bar{S}_h), infected human (\bar{I}_h) and recovered human (\bar{R}_h) compartments. The mosquito population is divided into the susceptible mosquito (\bar{S}_m) and infected mosquito (\bar{I}_m), the recovered mosquito does not exist, since an infected mosquito does not recover. The dynamics of the disease is depicted in the compartment diagram, Fig. 1,

Looking at Fig. 1, we see that the transmission dynamics of the Chikungunya fever are described by the following ordinary differential equations; (Note: the unbarred variables are the normalized variables, i.e., the human and mosquito population are divided by N_h and N_m , respectively: $N_h = \bar{S}_h + \bar{I}_h + \bar{R}_h$ and $N_m = \bar{S}_m + \bar{I}_m$):

$$\frac{dS_h}{dt} = \mu_h(1 - S_h) - b\beta_{mh} \frac{A}{\mu_m + p} \frac{I_m}{N_h} S_h \quad (1)$$

$$\frac{dI_h}{dt} = b\beta_{mh} \frac{A}{\mu_m + p} \frac{I_m}{N_h} S_h - (\gamma_h + \mu_h) I_h \quad (2)$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \mu_h R_h \quad (3)$$

$$\frac{dS_m}{dt} = A - b\beta_{hm} \frac{S_m}{N_h} I_h - \mu_m S_m - p S_m \quad (4)$$

$$\frac{dI_m}{dt} = b\beta_{hm} \frac{S_m}{N_h} I_h - (\mu_m + p) I_m \quad (5)$$

We assumed that the total human population, N_h , remains constant, so that the sum of the normalized human populations is one, i.e., $1 = S_h + I_h + R_h$ and that the total mosquito population also remains constant, leading to $A / (\mu_m + p) = S_m + I_m$, where S_m and I_m are the normalized mosquito populations.

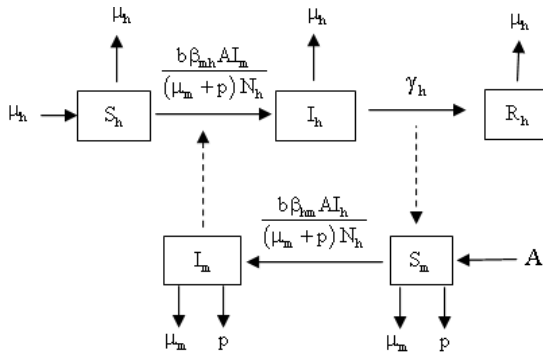


Fig. 1: Flow chart for the transmission of Chikungunya fever

μ_h is the birth (death) rate of human population, γ_h is the recovery rate of the infected human, A is the recruitment rate of the mosquito population, b is the biting rate of mosquito population, β_{hm} is the probability that the infected mosquito transmits the virus to susceptible human by one bite, β_{mh} is the probability that the infected human transmits the virus to susceptible mosquito and μ_m is the death rate of mosquito population. Most importantly, p is the efficacy of adulticide chemical in killing the mosquito.

Analysis of the model: The model will be analyzed to investigate the equilibrium points and its stability. The conditions that the total mosquito and human populations are constants reduce the number of dependent variables to three, which we pick to be S_h, I_h and I_m . We find the total mosquito population at equilibrium to be $N_m = A / (\mu_m + p)$. This last relation also means that the number of mosquitoes can be controlled by changing the efficacy of the adulticide or by altering the recruitment rate of the adult mosquitoes, i.e., by removing the sites in which the larvae can breed.

Equilibrium points: The equilibrium points which is obtained by setting the LHS of Eq. 1, 2 and 5 to zero, i.e.:

$$\frac{dS_h}{dt} = 0, \quad \frac{dI_h}{dt} = 0, \quad \frac{dI_m}{dt} = 0 \tag{6}$$

Doing this, we obtain:

$$S_h = \frac{\mu_h N_h (L + b\beta_{hm} I_h)}{QKI_h + \mu_h N_h (L + b\beta_{hm} I_h)}, \tag{7}$$

$$I_m = \frac{KI_h}{L + b\beta_{hm} I_h}$$

And two values of I_h :

$$I_h = 0 \text{ and } I_h^* = \frac{-Y + \sqrt{Y^2 - 4XZ}}{2X} \tag{8}$$

Where:

$$X = TQK + VQK + VT + V^2$$

$$Y = DQK + UQK + UT + 2UV + VD - VQKN_h$$

$$Z = UD + U^2 - UQKN_h$$

$$\text{with } Q = \frac{b\beta_{mh}}{N_h}, K = b\beta_{hm} (A / (\mu_m + p)), D = L\gamma_h, \tag{9}$$

$$U = L\mu_h, V = \mu_h b\beta_{hm}$$

The first value leads to a disease free equilibrium state while the second value leads to an endemic equilibrium state.

Disease free state (E_0): In the absence of any infected mosquitoes, the equilibrium state will be the disease free state:

$$E_0(S_h, I_h, I_m) = (1, 0, 0) \tag{10}$$

Endemic disease state (E_1): This occurs when the $I_h^* = \frac{-Y + \sqrt{Y^2 - 4XZ}}{2X}$ is positive. The values of the susceptible humans and infected mosquitoes at equilibrium will be:

$$S_h^* = \frac{\mu_h N_h (L + b\beta_{hm} I_h^*)}{QKI_h^* + \mu_h N_h (L + b\beta_{hm} I_h^*)}, I_m^* = \frac{KI_h^*}{L + b\beta_{hm} I_h^*} \tag{11}$$

Thus the equilibrium endemic state becomes:

$$E_1(S_h^*, I_h^*, I_m^*) = \left(\frac{\mu_h N_h (L + b\beta_{hm} I_h^*)}{QKI_h^* + \mu_h N_h (L + b\beta_{hm} I_h^*)}, I_h^*, \frac{KI_h^*}{L + b\beta_{hm} I_h^*} \right) \tag{12}$$

Local asymptotically stability of equilibrium state:

To determine local asymptotical stability of the equilibrium state, we first expand the solutions of Eq. 1, 2 and 5 about their equilibrium values, i.e., $\bar{X} = \bar{X}^* + \delta\bar{X}$ where \bar{X}^* is the equilibrium state given by either Eq. 10 or 12. Performing this expansion, we get:

$$\left. \frac{d\delta\bar{X}}{dt} \right|_{\bar{X}=\bar{X}^*} = \text{Jacobian } (J)_{\bar{X}=\bar{X}^*} \cdot \delta\bar{X} \tag{13}$$

Where, the Jacobian is given:

$$J(S_h^*, I_h^*, I_m^*) = \begin{bmatrix} -(b\beta_{mh} \frac{I_m^*}{N_h} + \mu_h) & 0 & -b\beta_{mh} \frac{S_h^*}{N_h} \\ b\beta_{mh} \frac{I_m^*}{N_h} & -(\gamma_h + \mu_h) & b\beta_{mh} \frac{S_h^*}{N_h} \\ 0 & b\beta_{hm} \frac{((A / (\mu_m + p)) - I_m^*)}{N_h} & -(b\beta_{hm} \frac{I_h^*}{N_h} + \mu_m + p) \end{bmatrix} \quad (14)$$

with the equilibrium values substituted in.

Assuming that $\delta \bar{X}(t) = \bar{X}_0 e^{\lambda t}$, the eigenvalues are obtained by solving:

$$\det(J_{\bar{X}=\bar{X}^*} - \lambda I) = 0 \quad (15)$$

Evaluating the determinant, we obtain what is known as the characteristic equation. Since we are looking for local asymptotically stable states, the eigenvalues should be negative and satisfy the Routh-Hurwitz criteria (Marsden and McCracken, 1976).

Local asymptotically stability of disease free state: Evaluating the Jacobian at the disease free state $E_0 = (1,0,0)$, we find that:

$$J = \begin{bmatrix} -\mu_h & 0 & -b\beta_{mh} \\ 0 & -(\gamma_h + \mu_h) & 0 \\ 0 & b\beta_{hm} \frac{(A / (\mu_m + p))}{N_h} & -(\mu_m + p) \end{bmatrix}_{E_0} \quad (16)$$

Substituting this Jacobian into Eq. 15, we arrive at the following characteristic equation:

$$(\mu_h + \lambda)(\lambda^2 + G\lambda + H) = 0 \quad (17)$$

Where:

$$G = p + \mu_m + \mu_h + \gamma_h, H = \gamma_h \mu_h + \gamma_h p + \mu_h \mu_m + \mu_h p - b^2 \beta_{hm} \beta_{mh} \frac{(A / (\mu_m + p))}{N_h} \quad (18)$$

Looking at Eq. 17, we see that one of the eigenvalues is $\lambda_1 = -\mu_h$. The other two are the solutions of $\lambda^2 + G\lambda + H = 0$. They will be negative when $G > 0$, $H > 0$ or when:

$$b^2 \beta_{hm} \beta_{mh} (A / (\mu_m + p)) < N_h (\mu_m + p)(\gamma_h + \mu_h) \quad (19)$$

The Routh-Hurwitz criteria for all the eigenvalues to be negative will be satisfied when $R_0 < 1$ where:

$$R_0 = \frac{b^2 \beta_{hm} \beta_{mh} (A / (\mu_m + p))}{N_h (\mu_m + p)(\gamma_h + \mu_h)} \quad (20)$$

Local asymptotically stability of endemic equilibrium state: Evaluating the Jacobian at the endemic equilibrium state:

$$E_1(S_h^*, I_h^*, I_m^*) = \left(\frac{\mu_h N_h (L + \beta_{hm} I_h^*)}{QKI_h^* + \mu_h N_h (L + \beta_{hm} I_h^*)}, I_h^*, \frac{KI_h^*}{L + b\beta_{hm} I_h^*} \right) \quad (21)$$

where, \bar{I}_h^* is the solution of $I_h^* = \frac{-Y + \sqrt{Y^2 - 4XZ}}{2X}$ where the definitions of X, Y and Z are given in Eq. 9, we get:

$$J = \begin{bmatrix} -(b\beta_{mh} \frac{I_m^*}{N_h} + \mu_h) & 0 & -b\beta_{mh} \frac{S_h^*}{N_h} \\ b\beta_{mh} \frac{I_m^*}{N_h} & -(\gamma_h + \mu_h) & b\beta_{mh} \frac{S_h^*}{N_h} \\ 0 & b\beta_{hm} \frac{(A / (\mu_m + p)) - I_m^*}{N_h} & -(b\beta_{hm} \frac{I_h^*}{N_h} + \mu_m + p) \end{bmatrix}_{E_1} \quad (22)$$

The characteristic equation obtained from $\det(J - \lambda I) = 0$ is:

$$\lambda^3 + \gamma \lambda^2 + \mu \lambda + \eta = 0 \quad (23a)$$

Where:

$$\gamma = w + k + q, \quad \mu = kw + qw + kq - vl, \quad \eta = kql + lmv - kvl \quad (23b)$$

With:

$$k = b\beta_{mh} \frac{I_m^*}{N_h} + \mu_h, \quad l = b\beta_{mh} \frac{S_h^*}{N_h}, \quad m = b\beta_{mh} \frac{I_m^*}{N_h}, \quad q = \gamma_h + \mu_h, \quad v = \frac{b\beta_{hm} ((A / (\mu_m + p)) - I_m^*)}{N_h} \quad (23c)$$

$$w = b\beta_{hm} \frac{I_h^*}{N_h} + \mu_m + p$$

The coefficients of the characteristic equation will be positive if the following Routh-Hurwitz criteria:

$$\gamma \mu > \eta \quad (24a)$$

Where:

$$\gamma \mu = kw^2 + qw^2 + 3kqw - wvl + k^2w + k^2q - kvl + q^2w + kq^2 - qvl \quad \text{and} \quad \eta = kql + lmv - kvl \quad (24b)$$

Is satisfied. For values meeting these criteria, E_1 will be locally asymptotically stable.

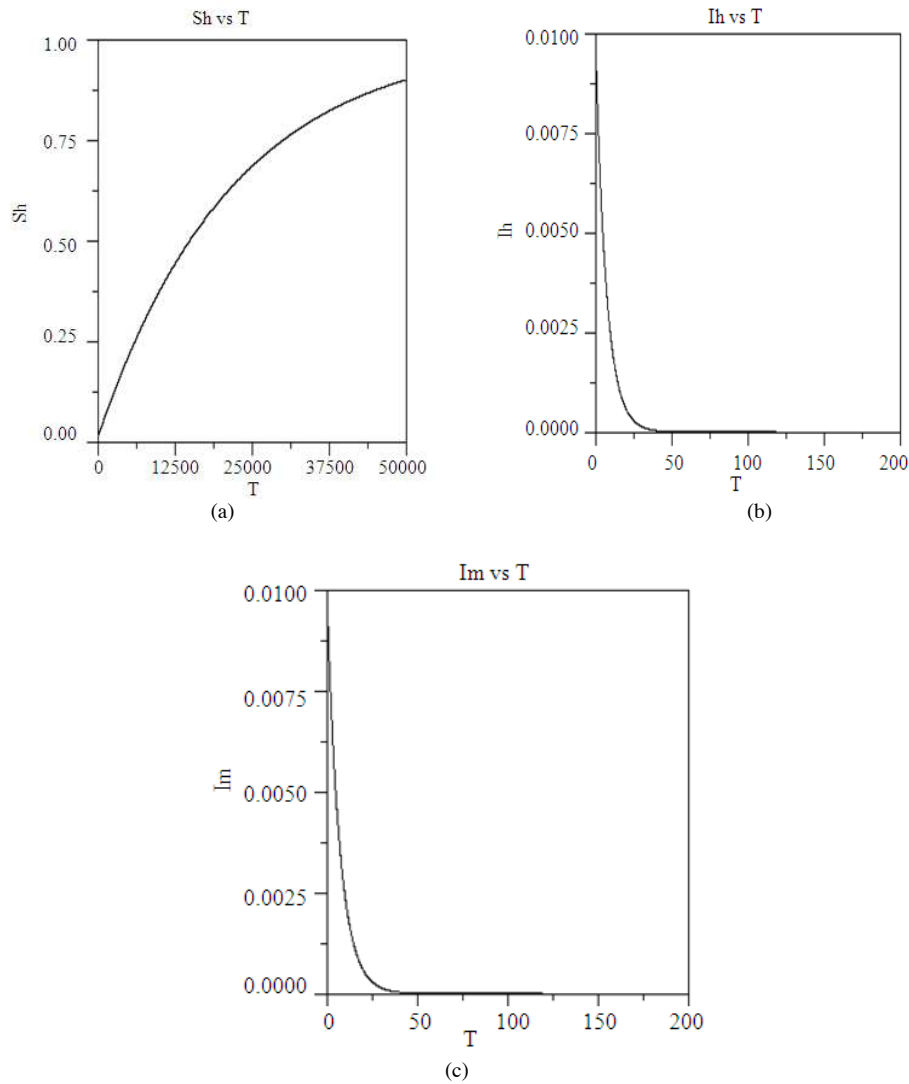


Fig. 2: Time series evolution of the population compartments for the case where the disease free state is the equilibrium state. (a) Susceptible human proportion (S_h). (b) Infected human proportion (I_h). (c) Infected mosquito proportion (I_m). The time evolutions of the three populations were obtained by solving Eq. 1, 2 and 5 using the following values taken from Table 1; $A = 5000$, $b = 1$, $\mu_m = 0.25$, $p = 1$, $\gamma_h = 0.1428$, $\mu_h = 0.0000457$, $\beta_{mh} = 0.5$, $\beta_{lm} = 0.7$, $N_h = 10,000$. These values lead to a basic reproduction number $R_0 = 0.784063 < 1$. As we see, the equilibrium state is the disease free state $E_0 = (1, 0, 0)$

RESULTS AND DISCUSSION

Stability of disease free state: For the numerical values of the parameters listed in Table 1, the calculated eigenvalues and basic reproduction numbers are:

$$\begin{aligned} \lambda_1 &= -0.0000457, \quad \lambda_2 = -1.14033, \\ \lambda_3 &= -0.00251 \quad \text{and} \quad R_0 = 0.784063 \end{aligned} \tag{25}$$

We have numerical solved Eq. 1, 2 and 5 using the values of the parameters listed in Table 1. Since these values leads to all of the eigenvalues to be negative and the basic reproduction number to be less than one, the equilibrium state will be the disease free state E_0 given by Eq. 10. Looking at Fig. 2, we see that this is true.

Stability of endemic state: Next we change the value of p to be equal to 0.1 and keep the other values of the parameters the same. With these values, we obtain:

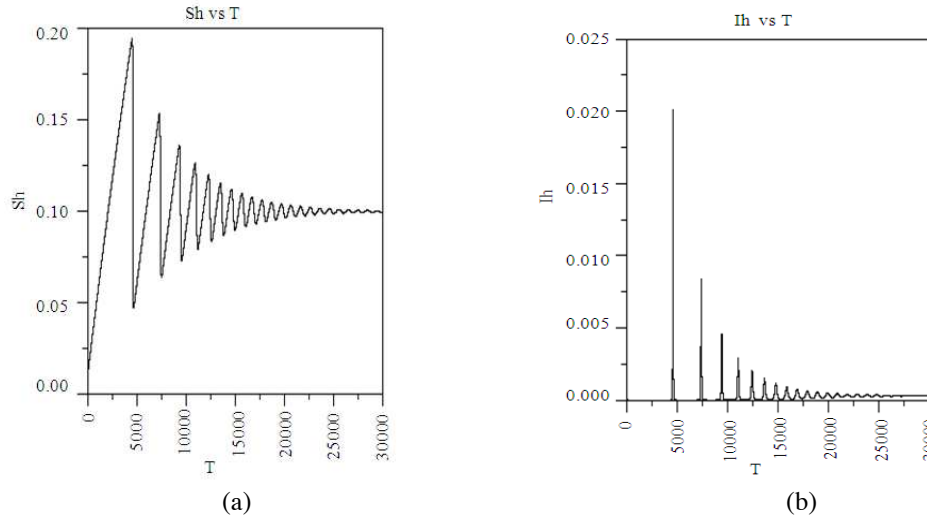


Fig. 3: Time series evolution of the population compartments for the case where the endemic state is the equilibrium state. (a) Susceptible human proportion (S_h). (b) Infected human proportion (I_h). The time evolutions of the two populations were obtained by solving Eq. 1, 2 and 5 using the same values used to obtain Fig. 2 except that the efficacy is now set to 0.1. Using $p = 0.1$ instead of $p = 1.0$, we get a basic reproduction number $R_0 = 10.0008 > 1$. The equilibrium state becomes the endemic state $E_1(0.100107, 0.000576, 0.00115)$

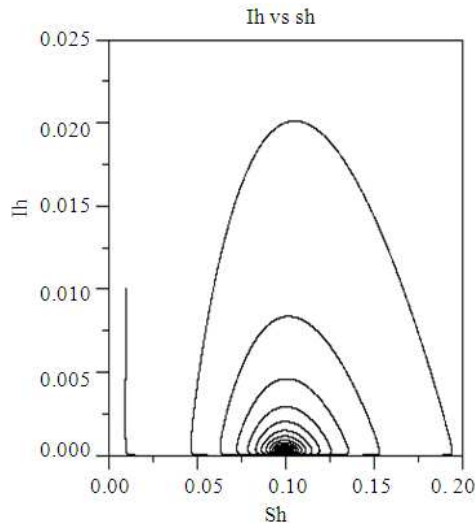


Fig. 4: Trajectory of the human population compartments in the S_h - I_h plane for the same set of parameter values used to obtain the time evolution behaviors shown in Fig. 3. As we see, the trajectory spirals into the endemic equilibrium state; $E_1(0.100107, 0.000576, 0.00115)$

$$\begin{aligned} \lambda_1 &= -0.000015, & \lambda_2 &= -0.436135 + 0.163625i, \\ \lambda_3 &= -0.436135 - 0.163625i \end{aligned} \quad (26)$$

These values will lead the basic reproduction number R_0 to be 10.0008. This along with the fact that the real

parts of the eigenvalues are all negative leads the equilibrium states to be the endemic state $E_1(0.100107, 0.000576, 0.00115)$ and that this state will be locally asymptotically stable. The fact the λ_2 and λ_3 are complex conjugates means that the temporal behavior of the populations will exhibit oscillatory behaviors.

Table 1: Parameter values leading to disease free state

Parameters	value	References
b	1.0000000 (per day)	Rodrigues <i>et al.</i> (2010)
γ_h	0.1428000 (per day)	
β_{hm}	0.7000000	Pongsumpan (2006)
β_{mh}	0.5000000	
μ_h	0.0000457 (per day)	Nishiura (2006)
N_h	10,000.0000000	
μ_m	0.2500000 (per day)	
A	5,000.0000000	
p	1.0000000	

This is indeed seen in Fig. 3 where the time series solutions for susceptible and infected human populations are shown. As we see, as $t \rightarrow \infty$, the two populations converge to the endemic population levels. In Fig. 4, we see the trajectory of the solutions in the S_h - I_h plane. There we see, the trajectory spiraling into the equilibrium endemic state.

Our results show that the use of adulticide to control a Chikungunya fever epidemic once it develops depends on the efficacy of the adulticide to kill the mosquitoes. We have look to see what the value of the efficacy is needed for the adulticide to be effective. For the values of the parameters used, we find that the basic reproduction number R_0 is 0.726 for an efficacy value $p = 0.9$ and is 1.111 for $p = 0.8$. The need for such a high value of the efficacy is caused by our choice of 0.7 and 0.5 for the values of β_{hm} and β_{mh} , respectively. Using lower values of these two parameters would lead the required efficacy of the adulticide to be effective to be lower.

CONCLUSION

The values of the parameters for the mosquitoes used in the previous section are for the *Aedes aegypti* mosquitoes. A genetic change at position 226 in the gene for the glycolprotein E1/E2 created a mutated Chikungunya virus strain which had an increased capability for replication in the *Aedes albopictus* mosquito (Tsetsarkin, 2009). This change in the vector for transmission of the virus has made this disease more of a treat to the public health since *Aedes albopictus* has developed a capability to adapt to non tropical regions (Moulay *et al.*, 2011), is aggressive day time biter (30-46 times per hour) (Cancrini, *et al.*, 2003), lives a long life (4-8 weeks) and has long flight radius (400-600 meters) (Pioloux *et al.*, 2007). These changes will change the numerical results but not the conclusion that control of the Chikungunya epidemics by means of spraying of adulticide must take into account the

changing efficacy of the adulticide and when to switch to a new adulticide.

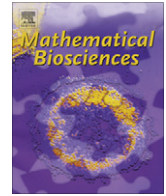
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The chikungunya disease: Modeling, vector and transmission global dynamics

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ABSTRACT

Models for the transmission of the chikungunya virus to human population are discussed. The chikungunya virus is an alpha arbovirus, first identified in 1953. It is transmitted by *Aedes* mosquitoes and is responsible for a little documented uncommon acute tropical disease. Models describing the mosquito population dynamics and the virus transmission to the human population are discussed. Global analysis of equilibria are given, which use on the one hand Lyapunov functions and on the other hand results of the theory of competitive systems and stability of periodic orbits.

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1. Introduction

An unprecedented chikungunya epidemic has appeared on the Reunion Island (775,000 inhabitants) with over 244,000 reported and 205 deaths (directly or indirectly linked) as of April 2006. *Aedes albopictus* [1], long present on the island, is the main vector of this disease. *Aedes aegypti* [2], which is also known to transmit dengue fever, is the other vector of chikungunya. After the Grande Comore Island epidemic, first cases were reported in the Reunion Island in March 2005. It was the first time that a chikungunya epidemic was described in this part of the world.

The Asian tiger mosquito or forest day mosquito (*Aedes albopictus*), from the mosquito family Culicidae, is characterized by its black and white striped legs, small black and white body. It is native of the tropical and subtropical areas of Southeast Asia. In the past couple of decades this specie has invaded many countries throughout the world, through the increasing transport of goods and international travels. It has recently appeared in Europe, like in France [3], in the USA and in Australia.

The chikungunya is an arthropod-borne viral disease (arbovirus). The name is derived from the Makonde word meaning “that which bends up” in reference to the stooped posture developed as a result of the arthritic symptoms of the disease. It was first described by Marion Robinson and Lumsden [4,5], following an outbreak in 1952 on the Makonde Plateau, in Tanzania [5].

Some arboviruses are able to cause emergent diseases and transmit the virus upon biting, allowing it to enter the bloodstream which

can cause viremia. The dynamics of arboviral diseases like dengue or chikungunya are influenced by many factors such as humans, the mosquito vector, the virus itself, as well as the environment which affects all the present mechanisms directly or indirectly.

Through the 20th century, mathematical models have been established as major tools for epidemiological models (see [6–8] and references therein), and in particular the study of vector-borne infections [9–12].

In [13,14], the authors study a SI-SIR model in which the total human population size is constant. Models with a variable human population are studied in [15,16]. In [15] the authors use a non classical contact rate among humans that depend on the total vector population size. Such models do not take into account the dynamics of the vector.

In [17,18], mathematical models describing the dynamics of vector-borne diseases taking into account the controlling mechanisms applied on the vector population are developed. In [17], the human population is supposed to be constant and the incidence rate among humans depends on the total vector population size. Moreover, only the local stability of equilibria was studied analytically.

This paper deals with two models involving differential equations for the mosquito population and virus transmission to the human population. Following [15], we consider a model which takes into account the dynamics of the vector with a non-constant population size and a contact rate that depends on the vector population size.

The local and global stability of equilibria are studied. This work can be seen as a complement to the study of [17,18]. The conclusion discusses the use of a contact rate among humans that depends on the vector population size.

This paper is organized as follows. In the second section we give the biological explanation of the problem and address the vector

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life cycle (embryonic, larvae, pupae and adult stages), the reproduction and oviposition habitat selection, and finally the transmission of the virus phenomenon.

The third section deals with the formulation of dynamical models, first of all for the population growth that is the *Aedes albopictus* mosquito, and secondly for the virus transmission to the human population. The first model uses a stage structure model; the second uses SI and SIR type models.

The fourth section is devoted to the mathematical analysis of both models, focusing on the boundedness and the positivity of the solutions, and on local or global stability of equilibria.

For the first system we use the Lyapunov theory to establish the global stability of the endemic equilibrium, while for the second we use the general theory of competitive systems and compound matrices. As usual in mathematical epidemiological studies, we also found two thresholds parameters that determine the global dynamical behavior.

2. Biological problem

2.1. Vector life cycle

The life of the vector, consists of four stages: embryonic stage (eggs), larvae stage, pupae stage and adult stage. The first three stages need water for their development while the last one needs only air. In this paper we will not distinguish the larvae stage and the pupae stage: these two stages are called the immature stage. The lifespan of each stage depends on several factors, such as temperature or the availability of food and water [19].

2.2. Oviposition habitat selection

Mosquitoes have developed various approaches to avoid predation. Many species breed in areas where predators are rare or absent. The oviposition habitat selection is made to make sure that the mosquito larvae can develop relatively unmolested. That is the case of the Asian tiger mosquito or *Aedes albopictus* mosquito which is a container-inhabiting species and which lays its eggs in any water-containing receptacle in urban, suburban, rural and forest areas. The primary immature habitats of this species are artificial containers [20,21].

These habitats are largely devoid of predators, thus offering a relatively secure refuge for larval development. Most female can lay their eggs not only on moist substrate but on dry substrate that is subject to flooding with rains or tides. They breed in small, often ephemeral, pools such as those in tree holes, bamboo pots and leaf axils. This strategy does have a negative side for mosquito: the development depends on the availability of water and they must be able to develop quickly before the water dries. Mosquitoes lay their eggs on the water or any moist surface, but they can also breed in natural habitats like vegetation or near rivers ...

2.3. The embryonic stage

The eggs need 48–72 hours to become mature [22]. They need water to hatch, but they are desiccation-resistant and cold-resistant and they have the capacity to cling to the inner side of any potential containers. Moreover, eggs are capable of winter diapause and mature eggs can wait until two years to hatch if the hydration conditions are not sufficient for the development of larvae [23,24].

2.4. The larvae and pupae stages

Depending on temperature and availability of food, *Aedes albopictus* can complete larval development (four stages) between five to

ten days; the pupae stage needs two days to develop [25]. An increase in larval density or a decrease in food (for example, a decrease in water due to evaporation) can cause more mortality and reduction in the number of adult subjects. Though limited food is the primary cause of death, parasites and predators may exert substantial influence on the population size. The amount of water in the containers also plays an important role in determining mosquito density. Although the overall population in containers appears greater, it is actually decreasing as resources decline and intra-specific competition increases [26,27], resulting in greater larval mortality and the production of small-sized adults. Moreover, it has been observed that the larvae of *Aedes albopictus* are cannibal, they are able to eat earlier-stage larva under certain conditions.

2.5. The adult stage

The exit of the pupae stage normally happens very early in the morning, perhaps in order to escape numerous predators whose main activity takes place during daytime [21,28]. Before any activity, male and female need to have a meal of sugar and water [29]. The flight range of adults is limited (from one to two hundred meters), they have not been observed to fly in strong winds [30,31]. Its major means of dispersal is through the transport of used and waste tires. The move of other water-holding containers could also play a role in expanding its range. The life expectancy for males is fifteen days whereas it is from two to four weeks for females [22] and can reach ten weeks under labs conditions.

2.6. Reproduction

Aedes albopictus is very aggressive during the daytime [32] with biting generally occurring during early morning and late afternoon [30]. Females require blood to produce their eggs. They feed on a number of hosts including human (indoors and outdoors), domestic and wild animals and birds. Their generalized feeding behavior contributes to their being potential vectors.

Females lay eggs one by one above the water level or on the sides of a variety of containers which serve as breeding habitat. They rely on rainfalls to raise water level in containers and inundate the eggs for hatching. Females lay from one hundred to three hundred eggs per oviposition and have from one to four ovipositions during their life.

2.7. Transmission of the virus

A vector is infected after biting an infected human. There is a delay (from seven to twelve days) or incubation period when mosquitoes are incurring the disease but still unable to transmit it. Recent research have shown, that a genetic mutation in the chikungunya virus identified in Réunion Island, has facilitated the transmission by *Aedes albopictus*. Indeed, the extrinsic incubation period was reduced to two days [33]. Mosquitoes remain infective until death. Vertical transmission in the vector has not yet been observed until today.

A human is infected after being bitten by an infected vector, after a delay of four to seven days (incubation period), the human is able to transmit the virus. This period, which can go on five to seven days, is the viraemia period. After this time, human recovers.

3. Vector population and virus transmission modeling

3.1. Formulation of a dynamical model for vector population growth

To describe the *Aedes albopictus* population dynamics we use a stage structured model, which consists of three main stages (see

Fig. 1: embryonic (E), larvae (L, which consists here of the larvae and pupae populations) and adult (A, which consists only of adults females). Even if eggs and immature stages are both aquatic, we dissociate them because these two populations respond differently to control measures. Indeed, eggs can cling and are desiccation-resistant and hence, drying the breeding sites does not kill eggs, but only larvae and pupae. Moreover, chemical interventions on the breeding sites has impact on the larvae population, but not on the eggs.

We assume that the number of laid eggs is proportional to the number of females.

The above hypotheses lead to the following equations.

$$\begin{cases} \frac{dE}{dt}(t) = bA(t) - sE(t) - dE(t), \\ \frac{dL}{dt}(t) = sE(t) - s_L L(t) - d_L L(t), \\ \frac{dA}{dt}(t) = s_L L(t) - d_m A(t). \end{cases} \quad (1)$$

Moreover, as we said in Sections 2.2 and 2.4, it has been observed that mosquitoes are able to detect the best breeding site for the eggs development. Indeed if there are too much eggs in the oviposition habitat or too few nutrients and water resources, then females laid less eggs or choose another site. It seems reasonable to express this biological phenomenon with a mathematical model which explicitly incorporates the idea of limited carrying capacity resources. This model should take into account the availability of nutrients and the occupation by eggs or larvae of the available breeder sites. That is why we assume that,

- per capita oviposition rate is given by,

$$b \left(1 - \frac{E(t)}{K_E} \right) A(t),$$

where K_E is the availability of nutrients and space, b represents the rate at which the population would grow if they were unencumbered by environmental degradation,

- the transition rate from class E to class L is s but when the availability of food is not sufficient for the class L, then the larvae can eat the young larvae to complete its development and we suppose that the death rate due to the lack of food is proportional to the young larvae sE and to the coefficient L/K_L that represent the availability of food for each larvae. At the end, the number of eggs that hatch and survive is given by,

$$s \left(1 - \frac{L(t)}{K_L} \right) E(t).$$

Then system (1) reads as follows,

$$\begin{cases} \frac{dE}{dt}(t) = b \left(1 - \frac{E(t)}{K_E} \right) A(t) - sE(t) - dE(t), \\ \frac{dL}{dt}(t) = s \left(1 - \frac{L(t)}{K_L} \right) E(t) - s_L L(t) - d_L L(t), \\ \frac{dA}{dt}(t) = s_L L(t) - d_m A(t). \end{cases} \quad (2)$$

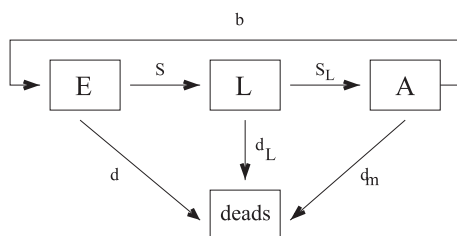


Fig. 1. A stage structured model for *Aedes albopictus* population dynamics. E states for eggs, L for larvae and pupae, A for female adult. s, s_L, b, d, d_L, d_m are nonnegative system parameters. In the diagram, b = eggs laying rate, s = E to L transfer rate, s_L = L to A transfer rates, d, d_L, d_m = mortality rates of eggs, larvae and adult population.

This system is mathematically well defined over the whole \mathbb{R}^3 . Nevertheless, the region of biological interest is Δ which is given by,

$$\Delta = \left\{ (E, L, A) \mid \begin{array}{l} 0 \leq E \leq K_E \\ 0 \leq L \leq K_L \\ 0 \leq A \leq \frac{s_L}{d_m} K_L \end{array} \right\}, \quad (3)$$

which its interior, denoted $int(\Delta)$, is given by

$$int(\Delta) = \left\{ (E, L, A) \mid \begin{array}{l} 0 < E < K_E \\ 0 < L < K_L \\ 0 < A < \frac{s_L}{d_m} K_L \end{array} \right\}. \quad (4)$$

We will see in Lemma 4.3 that Δ is a positive invariant set for system (2).

3.2. A compartmental model for the virus transmission to human population

Let us denote by N_H the human population size for which we assume an exponential growth. Then, its dynamics is described by,

$$\frac{dN_H}{dt}(t) = (b_H - d_H)N_H(t), \quad (5)$$

where b_H and d_H are, respectively, the human birth and natural death rates.

Let \bar{S}_H, \bar{I}_H and \bar{R}_H denote the total number of respectively susceptible, infective, and immune in the human population and \bar{S}_m, \bar{I}_m be the total number of susceptible and infective mosquitoes. The immune class in the vector population does not exist, since mosquitoes carry the infection throughout their life. The model is schematically represented in Fig. 2.

The effective contact rate β_H is the average number of contacts per day which would result in infection if the vector is infectious and, as in [15,34], we can assume that it is constant. The effective contact rate β_m is the average number of contacts per day that effectively transmit the infection to vectors. These hypotheses lead to the following equations,

$$\begin{cases} \frac{d\bar{S}_H}{dt}(t) = b_H(\bar{S}_H(t) + \bar{I}_H(t) + \bar{R}_H(t)) - \beta_H \frac{\bar{I}_m(t)}{\bar{A}(t)} \bar{S}_H(t) - d_H \bar{S}_H(t), \\ \frac{d\bar{I}_H}{dt}(t) = \beta_H \frac{\bar{I}_m(t)}{\bar{A}(t)} \bar{S}_H(t) - \gamma \bar{I}_H(t) - d_H \bar{I}_H(t), \\ \frac{d\bar{R}_H}{dt}(t) = \gamma \bar{I}_H(t) - d_H \bar{R}_H(t), \\ \frac{d\bar{S}_m}{dt}(t) = s_L L(t) - d_m \bar{S}_m(t) - \beta_m \frac{\bar{I}_H(t)}{N_H(t)} \bar{S}_m(t), \\ \frac{d\bar{I}_m}{dt}(t) = \beta_m \frac{\bar{I}_H(t)}{N_H(t)} \bar{S}_m(t) - d_m \bar{I}_m(t). \end{cases} \quad (6)$$

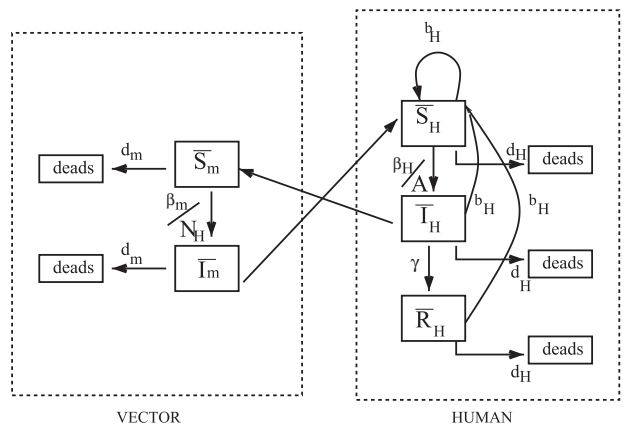


Fig. 2. A compartmental model for the chikungunya virus transmission with the nonnegative parameters: β_m = effective contact rate between susceptible vectors and humans, β_H = effective contact rate between susceptible humans and vectors, γ = recovery rate of infected humans, d_H = mortality rate of human population, d_m = mortality rate of vector population.

All parameters in this model are positive.

Introducing the proportions $S_H = \bar{S}_H/N_H, I_H = \bar{I}_H/N_H, R_H = \bar{R}_H/N_H, S_m = \bar{S}_m/A, I_m = \bar{I}_m/A$ in system (6) and by using relations $\bar{S}_H + \bar{I}_H + \bar{R}_H = N_H$ and $\bar{S}_m + \bar{I}_m = A$, the adult mosquito population is assumed to be described by the third equation of system (2), we obtain the following system that describes the dynamics of the proportion of individuals in each class, with the notation $u'(t) = \frac{du}{dt}(t)$,

$$\begin{cases} \begin{cases} E'(t) = bA(t)\left(1 - \frac{E(t)}{K_E}\right) - (s + d)E(t), \\ L'(t) = sE(t)\left(1 - \frac{L(t)}{K_L}\right) - (s_L + d_L)L(t), \\ A'(t) = s_L L(t) - d_m A(t), \end{cases} & (a) \\ \begin{cases} S'_H(t) = -(b_H + \beta_H I_m(t))S_H(t) + b_H, \\ I'_H(t) = \beta_H I_m(t)S_H(t) - (\gamma + b_H)I_H(t), \\ I'_m(t) = -\left(s_L \frac{L(t)}{A(t)} + \beta_m I_H(t)\right)I_m(t) + \beta_m I_H(t). \end{cases} & (b) \end{cases} \quad (7)$$

Remark 1. Obviously, this system has two different time scales, the one of mosquitoes of the order of weeks and the human lifespan of order of decades. Moreover, whether $b_H \neq d_H$ or $b_H = d_H$, when we consider the proportions, just above given, simple computations lead to the same system (7). Indeed, it suffices to note that $S'_H = (1/N_H^2)(\bar{S}_H N_H - \bar{S}_H N'_H), I'_H = (1/N_H^2)(\bar{I}_H N_H - \bar{I}_H N'_H)$ and $S_H + I_H + R_H = 1$, similarly $I'_m = (1/A^2)(\bar{I}_m A - \bar{I}_m A')$ and $S_m + I_m = 1$, where N'_H is given by (5) and $\bar{S}_H, \bar{I}_H, \bar{I}_m$ are given in system (6).

This system, as we will see in Section 5.2, is defined on the bounded subset of \mathbb{R}^6 , which is the region of biological interest, $\Delta \times \Omega$, where Δ is given by Eq. 3 and,

$$\Omega = \left\{ (S_H, I_H, I_m) \in \mathbb{R}_+^3 \mid \begin{matrix} 0 \leq S_H + I_H \leq 1 \\ 0 \leq I_m \leq 1 \end{matrix} \right\} \quad (8)$$

and which its interior, denoted $int(\Omega)$, is given by

$$int(\Omega) = \left\{ (S_H, I_H, I_m) \in \mathbb{R}_+^3 \mid \begin{matrix} 0 < S_H + I_H < 1 \\ 0 < I_m < 1 \end{matrix} \right\}. \quad (9)$$

Obviously, this model may be enhanced by taking into account the delay between the transfer to mosquitoes and the transmission to humans (from five to six days), see [35]. One can also use a SEI type model for the vector, see [12], although, if we consider a huge mosquito population, the number of mosquitoes in state E (exposed) can be neglected in comparison to the whole population.

4. Analysis of the population dynamics models

We investigate the asymptotic behavior of orbits starting in the non-negative cone,

$$\mathbb{R}_+^3 = \{(x, y, z) \in \mathbb{R}^3 \mid x \geq 0, y \geq 0, z \geq 0\}.$$

Let us also denote,

$$\mathbb{R}_+^{*3} = \{(x, y, z) \in \mathbb{R}^3 \mid x > 0, y > 0, z > 0\}.$$

Obviously, system (2) which is a C^∞ differential system, admits a unique maximal solution for any associated Cauchy problem. We shall use the following threshold parameter,

$$r = \left(\frac{b}{s+d}\right) \left(\frac{s}{s_L+d_L}\right) \left(\frac{s_L}{d_m}\right), \quad (10)$$

which arises in an obvious manner, when computing equilibria. It is easy to prove the following result.

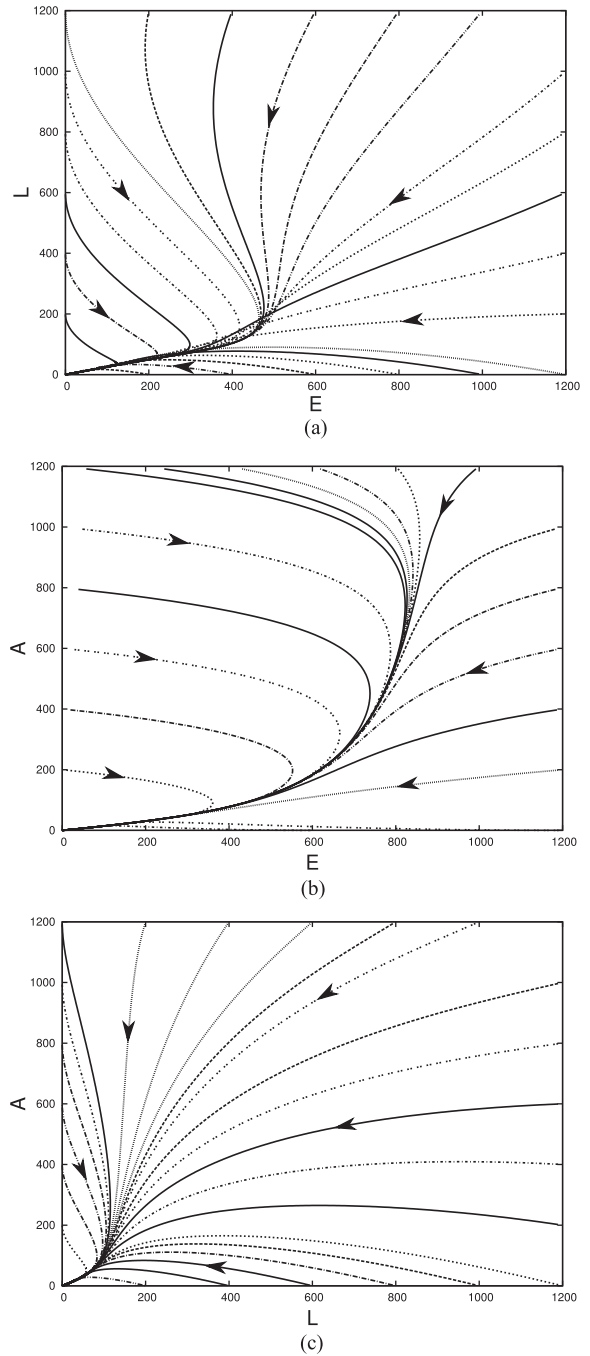


Fig. 3. Phase portraits of system (2) with parameters: $b = 5, s = 0.2, d = 0.6, K_E = 1000, s_L = 0.3, d_L = 0.6, K_L = 500, d_m = 0.7$. In this case $r = 0.595238$, then all trajectories tend to the mosquito-free equilibrium X_0^* .

Proposition 4.1. System (2) always has the mosquito-free equilibrium $X_0^* = (0, 0, 0)$.

- If $r \leq 1$, then system (2) has no other equilibrium.
- If $r > 1$, there is a unique endemic equilibrium,

$$X^* = \left(1 - \frac{1}{r}\right) \left(\frac{K_E}{\gamma_E}, \frac{K_L}{\gamma_L}, \frac{s_L}{d_m} \frac{K_L}{\gamma_L}\right) = (E^*, L^*, A^*),$$

where,

$$\gamma_E = 1 + \frac{(s+d)d_m K_E}{b s_L K_L} \quad \text{and} \quad \gamma_L = 1 + \frac{(s_L+d_L)K_L}{s K_E}.$$

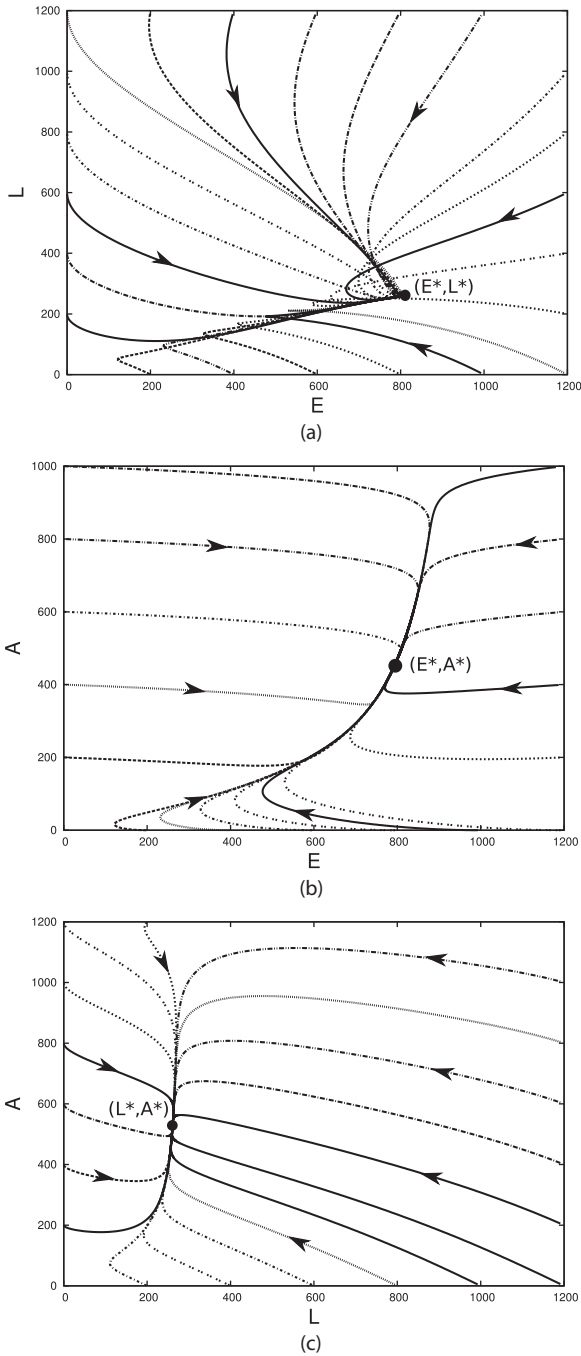


Fig. 4. Phase portraits of system (2) with parameters: $b = 6, s = 0.5, d = 0.2, K_E = 1000, s_L = 0.5, d_L = 0.25, K_L = 500, d_m = 0.25$. In this case $r = 11.428571$, then all trajectories tend to the endemic equilibrium X^* .

4.1. Non-negativity and boundedness of solutions

Lemma 4.2. Let $(t_0, X_0 = (E_0, L_0, A_0)) \in \mathbb{R}_+ \times \mathbb{R}_+^3$ and $([t_0, T], X = (E, L, A))(T \in]t_0, +\infty])$ be the maximal solution of the Cauchy problem associated to (2) with the initial condition (t_0, X_0) . Then,

$$\forall t \geq t_0, X(t) \in \mathbb{R}_+^3.$$

Proof. Let $(t_0, X_0 = (E_0, L_0, A_0)) \in \mathbb{R}_+ \times \mathbb{R}_+^3$ and $([t_0, T], X = (E, L, A))$ be the maximal solution of the Cauchy problem associated to (2) with the initial condition (t_0, X_0) . Let us assume that this solution becomes negative, i.e. $\tilde{t}_1 > t_0$ exists such that $X(\tilde{t}_1) \notin \mathbb{R}_+^3$. Let us define, $t_1 = \inf\{t, X(t) \notin \mathbb{R}_+^3\}$, i.e.

$$t_0 \leq t < t_1, X(t) \in \mathbb{R}_+^3$$

and $\varepsilon > 0$ exists such that

$$\forall t_1 < t \leq t_1 + \varepsilon, X(t) \notin \mathbb{R}_+^3. \tag{11}$$

Since $N_0^* = (0, 0, 0)$ is an equilibrium, the uniqueness of the solutions implies $X(t_1) \neq (0, 0, 0)$. For $t = t_1$, six cases are possible.

1. $X(t_1) = (0, L(t_1), A(t_1))$ with $(L(t_1), A(t_1)) \in (\mathbb{R}_+^*)^2$. Then, taking t_1 as an initial time, $E'(t_1) = bA(t_1) > 0$. Since,

$$\begin{aligned} E(t) &= E'(t_1)(t - t_1) + o_{t \rightarrow t_1}(t - t_1) \\ &= bA(t_1)(t - t_1) + o_{t \rightarrow t_1}(t - t_1), \end{aligned}$$

thus, $\tilde{\varepsilon} > 0$ exists such that, $\forall t_1 < t \leq t_1 + \tilde{\varepsilon}$ we have $E(t) > 0$. Besides $L(t_1)$ and $A(t_1)$ are positive for all $t \in [t_1, t_1 + \tilde{\varepsilon}]$, therefore $\forall t \in [t_1, t_1 + \min\{\tilde{\varepsilon}, \tilde{\varepsilon}\}]$,

$$X(t) \in \mathbb{R}_+^3,$$

which is a contradiction.

2. Let $X(t_1) = (0, 0, A(t_1))$ with $A(t_1) > 0$. We can show as above that $\tilde{\varepsilon} > 0$ exists such that $\forall t_1 < t \leq t_1 + \tilde{\varepsilon}, E(t) > 0$. Now from the second equation of (2), since $L(t_1) = 0, L'(t_1) = 0$ and $L''(t_1) = sE'(t_1) = sbA(t_1) > 0$, then

$$\begin{aligned} L(t) &= L''(t_1) \frac{(t - t_1)^2}{2} + o_{t \rightarrow t_1}((t - t_1)^2) \\ &= sbA(t_1) \frac{(t - t_1)^2}{2} + o_{t \rightarrow t_1}((t - t_1)^2), \end{aligned}$$

thus, $\tilde{\varepsilon} > 0$ exists such that $\forall t_1 < t \leq t_1 + \tilde{\varepsilon}$, we have $L(t) > 0$. Besides $A(t_1) > 0$, is positive for all $t \in [t_1, t_1 + \tilde{\varepsilon}]$, therefore $\forall t \in [t_1, t_1 + \min\{\tilde{\varepsilon}, \tilde{\varepsilon}\}]$

$$X(t) \in \mathbb{R}_+^3,$$

which is a contradiction.

Similar proof can easily be done for the other cases that are $X(t) = (E(t_1), 0, A(t_1))$ or $X(t) = (E(t_1), L(t_1), 0)$ or $X(t) = (E(t_1), 0, 0)$ or $X(t) = (0, L(t_1), 0)$. \square

Lemma 4.3. The set

$$\Delta = \left\{ \begin{array}{l} 0 \leq E \leq K_E \\ (E, L, A) \mid 0 \leq L \leq K_L \\ 0 \leq A \leq \frac{s_L}{d_m} K_L \end{array} \right\}$$

is an invariant region under the flow induced by (2).

Proof. Let $(t_0, X_0 = (E_0, L_0, A_0)) \in \mathbb{R}_+ \times \mathbb{R}_+^3$ and $([t_0, T], X = (E, L, A))$ be the maximal solution of the Cauchy problem associated to system (2) with the initial condition $(t_0, X_0), T \in]t_0, +\infty]$. Let $t_1 \in [t_0, T]$. We only have to show that,

1. if $E(t_1) \leq K_E$ then $\forall t_1 \leq t < T, E(t) \leq K_E$
2. if $L(t_1) \leq K_L$ then $\forall t_1 \leq t < T, L(t) \leq K_L$
3. if $A(t_1) \leq \frac{s_L}{d_m} K_L$ then $\forall t_1 \leq t < T, A(t) \leq \frac{s_L}{d_m} K_L$

since we have already shown that solutions are nonnegative, Lemma 4.2.

1. Assume that $\varepsilon_1 > 0$ exists such that $E(t_1 + \varepsilon_1) > K_E$. Let,

$$t_1^* = \inf\{t \geq t_1 \mid E(t) > K_E\}.$$

Since, $E(t_1^*) = K_E$, then,

$$E(t) = K_E + E'(t_1^*)(t - t_1^*) + \circ_{t \rightarrow t_1^*}(t - t_1^*).$$

Moreover, from the first equation of system (2), $E'(t_1^*) = -(s + d)K_E < 0$, then there exists $\tilde{\varepsilon} > 0$ such that $\forall t_1^* \leq t < t_1^* + \tilde{\varepsilon}$, $E(t) < K_E$ which is a contradiction. As a result, $\forall t \in [t_0, T]$, $E(t) \leq K_E$.
 2. Assume that $\varepsilon_1 > 0$ exists such that $L(t_1 + \varepsilon_1) > K_L$. Let,

$$t_1^* = \inf\{t \geq t_1 \mid L(t) > K_L\}.$$

Since $L(t_1^*) = K_L$, then,

$$L(t) = K_L + L'(t_1^*)(t - t_1^*) + \circ_{t \rightarrow t_1^*}(t - t_1^*).$$

Moreover from the second equation of system (2), $L'(t_1^*) = -(s_L + d_L)K_L < 0$, $\tilde{\varepsilon} > 0$ exists such that $\forall t_1^* \leq t < t_1^* + \tilde{\varepsilon}$, $L(t) < K_L$ which is a contradiction. As a result, $\forall t \in [t_0, T]$, $L(t) \leq K_L$.
 3. Assume that $\varepsilon_1 > 0$ exists such that $A(t_1 + \varepsilon_1) > \frac{s_L}{d_m}K_L$. Let,

$$t_1^* = \inf\{t \geq t_1 \mid A(t) > \frac{s_L}{d_m}K_L\}.$$

Since $A(t_1^*) = \frac{s_L}{d_m}K_L$, then,

- If $L(t_1^*) < K_L$, then, $A'(t_1^*) < 0$.

$$A(t) = \frac{s_L}{d_m}K_L + A'(t_1^*)(t - t_1^*) + \circ_{t \rightarrow t_1^*}(t - t_1^*)$$

with

$$A'(t_1^*) = s_L(L(t_1^*) - K_L).$$

- If $L(t_1^*) = K_L$ then, $A'(t_1^*) = 0$ and

$$A(t) = \frac{s_L}{d_m}K_L + A''(t_1^*)\frac{(t - t_1^*)^2}{2} + \circ_{t \rightarrow t_1^*}((t - t_1^*)^2)$$

with $A''(t_1^*) = s_L L'(t_1^*) = -s_L(s_L + d_L)K_L < 0$.

In both cases, there exists $\tilde{\varepsilon} > 0$ such that $\forall t_1^* < t \leq t_1^* + \tilde{\varepsilon}$, $A(t) < \frac{s_L}{d_m}K_L$ which is a contradiction. As a result $\forall t \in [t_0, T]$, $A(t) \leq \frac{s_L}{d_m}K_L$. To conclude, Δ is invariant under the flow induced by (2). \square

Proposition 4.4. All non-negative solutions (i.e. solutions initiating in \mathbb{R}_+^3) eventually enter the set Δ .

Proof. Let $(t_0, X_0 = (E_0, L_0, A_0)) \in \mathbb{R}_+ \times \mathbb{R}_+^3$ such that $(E_0, L_0, A_0) \notin \Delta$ (since Δ is invariant) and $[t_0, T], X = (E, L, A)$ be the maximal solution of the Cauchy problem associated to system (2) with the initial condition (t_0, X_0) .

We know that Δ is an invariant region (Lemma 4.3).

It is then sufficient to show that there exists $t \geq t_0$ such that $X(t) \in \Delta$.

- Assume that for all $t \in [t_0, +\infty[$, $E(t) > K_E$. Then, due to the first equation of system (2), for all $t \in [t_0, +\infty[$, $E'(t) < -(s + d)K_E$. Then, by comparison, $\forall t \in [t_0, +\infty[$, we have,

$$E(t) \leq E_0 - (s + d)K_E(t - t_0).$$

For $t_1 = t_0 + \frac{E_0 - K_E}{(s + d)K_E}$, we obtain $E(t) \leq K_E$ which is a contradiction. Therefore, for all $t > t_1$, $E(t) \leq K_E$.

- If $L(t_1) \leq K_L$, then the solution $L(t)$ belongs to Δ which is invariant. Otherwise, let assume on the contrary that for all $t \in [t_1, +\infty[$, t_1 given above, $L(t) > K_L$. Then $\forall t \in [t_1, +\infty[$, due to the second equation of system (2), $L'(t) < -(s_L + d_L)K_L$. Then, by comparison $\forall t \in [t_1, +\infty[$ we have,

$$L(t) \leq L(t_1) - (s_L + d_L)K_L(t - t_1).$$

For $t_2 = t_1 + \frac{L(t_1) - K_L}{(s_L + d_L)K_L}$, we obtain $L(t_2) \leq K_L$ which is a contradiction. Thus, there exists $t_2 > t_1$ such that $L(t_2) \leq K_L$.

$$L(t) \leq K_L.$$

- If $A(t_2) \leq \frac{s_L}{d_m}K_L$, the solution $A(t)$ is within Δ which is invariant. Otherwise, let assume on the contrary that for all $t \in [t_2, +\infty[$, $A(t) > \frac{s_L}{d_m}K_L$. Then, due to the third equation of system (2), $\forall t \in [t_2, +\infty[$,

$$A'(t) < s_L(L(t) - K_L) < 0.$$

Then, there exists $c > 0$ such that $A'(t) \leq -c$, since $L(t)$ is now bounded. By comparison, we have $\forall t \in [t_2, T]$,

$$A(t) \leq A(t_2) - c(t - t_2).$$

For $t_3 = t_2 + \frac{A(t_2) - \frac{s_L}{d_m}K_L}{c}$, we have $A(t) \leq \frac{s_L}{d_m}K_L$ which is a contradiction. To conclude, for $t \geq \max(t_1, t_2, t_3)$, $(E(t), L(t), A(t)) \in \Delta$. \square

4.2. Stability of the equilibria

Proposition 4.5. The mosquito-free equilibrium $X_0^* = (0, 0, 0)$ is locally asymptotically stable iff $r < 1$.

Proof. The local stability of the mosquito-free equilibrium X_0^* is given by the Jacobian matrix of the system (2) evaluated at this point, $DF(X_0^*)$,

$$DF(X_0^*) = \begin{pmatrix} -(s + d) & 0 & b \\ s & -(s_L + d_L) & 0 \\ 0 & s_L & -d_m \end{pmatrix}. \tag{12}$$

The characteristic equation of (12) is given by,

$$\lambda^3 + \alpha_1 \lambda^2 + \alpha_2 \lambda + \alpha_3,$$

where,

$$\begin{aligned} \alpha_1 &= (s + d) + (s_L + d_L) + d_m, \\ \alpha_2 &= (s + d)(s_L + d_L) + (s + d)d_m + (s_L + d_L)d_m, \\ \alpha_3 &= d_m(s + d)(s_L + d_L)(1 - r). \end{aligned}$$

We apply the Routh-Hurwitz criterion. Clearly $\alpha_1 > 0$, $\alpha_2 > 0$ and $D_1 = \alpha_1 \alpha_2 - \alpha_3 > 0$ since,

$$\begin{aligned} D_1 &= \alpha_1 \alpha_2 - \alpha_3 \\ &= ((s + d) + (s_L + d_L) + d_m)(s + d)((s_L + d_L) + d_m) \\ &\quad + d_m(s_L + d_L)(r(s + d) + (s_L + d_L) + d_m) > 0. \end{aligned}$$

If $r < 1$ then $\alpha_3 > 0$, thus using the Routh-Hurwitz criterion all eigenvalues of $DF(X_0^*)$ have negative real part, thus X_0^* is locally asymptotically stable for (2). If $r \geq 1$ then $\alpha_3 < 0$ and we show that $DF(X_0^*)$ has at least one eigenvalue with non-negative real part consequently X_0^* is not asymptotically stable. \square

Remark 2. Moreover, we can easily prove that X_0^* is globally asymptotically stable for $r \leq 1$ using quadratic Lyapunov function (the proof is similar to the one given below in Proposition 4.7 for X^* , see also Fig. 3).

Proposition 4.6. If $r > 1$, X^* is locally asymptotically stable.

Proof. The local stability of the endemic equilibrium X^* is given by the Jacobian matrix of the system (2) evaluated at this point,

$$DF(X^*) = \begin{pmatrix} -d_1 & 0 & d_2 \\ d_3 & -d_4 & 0 \\ 0 & d_5 & -d_6 \end{pmatrix} \tag{13}$$

with

$$d_1 = \frac{bs_L}{d_m \gamma_L} \frac{K_L}{K_E} \left(1 - \frac{1}{r}\right) + (s + d),$$

$$d_2 = (s + d) \frac{d_m \gamma_L K_E}{s_L \gamma_E K_L},$$

$$d_3 = \frac{(s_L + d_L) \gamma_E K_L}{\gamma_L K_E},$$

$$d_4 = \frac{sK_E}{\gamma_E K_L} \left(1 - \frac{1}{r}\right) + (s_L + d_L),$$

$$d_5 = s_L,$$

$$d_6 = d_m.$$

The characteristic equation of (12) is given by,

$$\chi_{X^*}(\lambda) = \lambda^3 + \alpha_1 \lambda^2 + \alpha_2 \lambda + \alpha_3,$$

where

$$\alpha_1 = d_1 + d_4 + d_6,$$

$$\alpha_2 = d_1 d_4 + d_1 d_6 + d_6 d_4,$$

$$\alpha_3 = d_1 d_4 d_6 - d_2 d_3 d_5$$

$$= d_m \left(1 - \frac{1}{r}\right) \left(\frac{bs_L}{d_m \gamma_L \gamma_E} \left(1 - \frac{1}{r}\right) + (s + d) \frac{sK_E}{\gamma_E K_L} + (s_L + d_L) \frac{bs_L}{d_m \gamma_L} \frac{K_L}{K_E}\right).$$

If $r > 1$, then $\alpha_1 > 0, \alpha_2 > 0$ and $\alpha_3 > 0$ and,

$$D_1 = \alpha_1 \alpha_2 - \alpha_3$$

$$= \alpha_1 \times \left(\frac{bs_L}{d_m \gamma_L} \frac{K_L}{K_E} \left(1 - \frac{1}{r}\right) + (s + d)\right) \times \left(\frac{sK_E}{\gamma_E K_L} \left(1 - \frac{1}{r}\right) + (s_L + d_L) + d_m\right) + d_m \left(\frac{sK_E}{\gamma_E K_L} \left(1 - \frac{1}{r}\right)\right) \left(\frac{sK_E}{\gamma_E K_L} \left(1 - \frac{1}{r}\right) + (s_L + d_L) + d_m\right) + d_m (s_L + d_L) \left(\frac{sK_E}{\gamma_E K_L} \left(1 - \frac{1}{r}\right) + (s + d) + (s_L + d_L) + d_m\right) > 0.$$

Then, thanks to the Routh-Hurwitz criterion all eigenvalues of $D_F(X^*)$ have negative real part. Consequently X^* is locally asymptotically stable (see also Fig. 4). \square

Proposition 4.7. *If $r > 1$ the endemic equilibrium X^* is globally asymptotically stable in $\text{int}(\Delta)$ (Δ is given by Lemma 4.3).*

Proof. Assume $r > 1$. Let $X^* (E^*, L^*, A^*) = (x^*, y^*, z^*)$. To prove the global stability of X^* , we use the Lyapunov function $V_1 : \mathbb{R}^3 \rightarrow \mathbb{R}$ defined by,

$$V_1(x, y, z) = \frac{1}{2} \left(a_1 (x - x^*)^2 + a_2 (y - y^*)^2 + a_3 (z - z^*)^2 \right),$$

where $a = (a_1, a_2, a_3)^T \in (\mathbb{R}_+^*)^3$ is a positive constant vector. Note that since $r > 1$, then x^*, y^* and z^* are positive. We have,

$$V_1(X^*) = 0 \quad \text{and} \quad \forall (x, y, z) \in \mathbb{R}_3 \setminus \{X^*\}, V_1(x, y, z) > 0.$$

Hence, V_1 is well defined. The orbital derivative, that is the derivative of V_1 along solutions of system (2) is,

$$\begin{aligned} \dot{V}_1(x, y, z) &= a_1(x - x^*) \left(bz \left(1 - \frac{x}{K_E}\right) - (s + d)x \right) \\ &\quad + a_2(y - y^*) \left(sx \left(1 - \frac{y}{K_L}\right) - (s_L + d_L)y \right) \\ &\quad + a_3(z - z^*) (s_L y - d_m z). \end{aligned} \tag{14}$$

Let $\tilde{x} = x - x^*, \tilde{y} = y - y^*, \tilde{z} = z - z^*$ and $\tilde{X} = (\tilde{x}, \tilde{y}, \tilde{z})^T$.

Then

$$\dot{V}_1(x, y, z) = \tilde{X}^T \begin{pmatrix} -a_1(s + d) & 0 & a_1 b \left(1 - \frac{x^*}{K_E}\right) \\ a_2 s \left(1 - \frac{y^*}{K_L}\right) & -a_2(s_L + d_L) & 0 \\ 0 & a_3 s_L & -a_3 d_m \end{pmatrix} \tilde{X} - \frac{a_1 b}{K_E} \tilde{x}^2 z - \frac{a_2 s}{K_L} \tilde{y}^2 x.$$

Let $A_1 = -D + R_1$ with,

$$D = \begin{pmatrix} a_1(s + d) & 0 & 0 \\ 0 & a_2(s_L + d_L) & 0 \\ 0 & 0 & a_3 d_m \end{pmatrix}$$

and

$$R_1 = \begin{pmatrix} 0 & 0 & a_1 b \left(1 - \frac{x^*}{K_E}\right) \\ a_2 s \left(1 - \frac{y^*}{K_L}\right) & 0 & 0 \\ 0 & a_3 s_L & 0 \end{pmatrix}.$$

Let us denote by $\langle \cdot, \cdot \rangle$ the scalar product in \mathbb{R}^3 . Then the orbital derivative reads as,

$$\dot{V}_1(x, y, z) = \langle A_1 \tilde{X}, \tilde{X} \rangle - \frac{a_1 b}{K_E} \tilde{x}^2 z - \frac{a_2 s}{K_L} \tilde{y}^2 x.$$

The symmetric matrix S_1 defined by,

$$S_1 = -D + \frac{1}{2}(R_1^T + R_1)$$

is given using simple algebraic computations by

$$S_1 = \begin{pmatrix} -a_1(s + d) & \frac{a_2}{2}(s_L + d_L) \frac{y^*}{x^*} & \frac{a_1}{2}(s + d) \frac{x^*}{z^*} \\ \frac{a_2}{2}(s_L + d_L) \frac{y^*}{x^*} & -a_2(s_L + d_L) & \frac{a_3 s_L}{2} \\ \frac{a_1}{2}(s + d) \frac{x^*}{z^*} & \frac{a_3 s_L}{2} & -a_3 d_m \end{pmatrix}.$$

Therefore, we have,

$$\langle A_1 \tilde{X}, \tilde{X} \rangle = \langle S_1 \tilde{X}, \tilde{X} \rangle.$$

The characteristic polynomial of S_1 is,

$$\chi_{S_1}(\lambda) = \lambda^3 + \alpha_1 \lambda^2 + \alpha_2 \lambda + \alpha_3,$$

where,

$$\alpha_1 = a_1(s + d) + a_2(s_L + d_L) + a_3 d_m,$$

$$\begin{aligned} \alpha_2 &= \frac{1}{4} a_1(s + d) \beta_1 + \frac{1}{4} a_2(s_L + d_L) \beta_2 + \frac{1}{4} a_3 \beta_3 + \frac{3}{4} (a_1 a_3 d_m (s + d) \\ &\quad + a_1 a_2 (s + d)(s_L + d_L) + a_2 a_3 d_m (s_L + d_L)) \end{aligned}$$

with

$$\beta_1 = \left(a_3 d_m - a_1(s + d) \left(\frac{x^*}{z^*}\right)^2 \right),$$

$$\beta_2 = \left(a_1(s + d) - a_2(s_L + d_L) \left(\frac{y^*}{x^*}\right)^2 \right),$$

$$\beta_3 = (a_2 d_m (s_L + d_L) - a_3 s_L^2)$$

and

$$\alpha_3 = \frac{1}{4} (a_1 a_2 (s + d)(s_L + d_L) \beta_1 + a_2 a_3 d_m (s_L + d_L) \beta_2 + a_1 a_3 (s + d) \beta_3).$$

Let us choose $a_1, a_2,$ and a_3 satisfying,

$$a_1 = \frac{1}{s+d} \left(\frac{y^*}{x^*}\right)^2 > 0,$$

$$a_2 = \frac{s+d}{s_L+d_L} \left(\frac{x^*}{y^*}\right)^2 a_1,$$

$$a_3 = \frac{d_m(s+d)}{s_L^2} \left(\frac{x^*}{y^*}\right)^2 a_1 = a_1 \frac{s+d}{d_m} \left(\frac{x^*}{z^*}\right)^2$$

with such a choice, one can easily verify that $\beta_1 = \beta_2 = \beta_3 = 0$. Thus $\alpha_1 > 0, \alpha_2 > 0$ and $\alpha_3 = 0$, therefore the characteristic polynomial reads as,

$$\chi_{S_1}(\lambda) = \lambda(\lambda^2 + \alpha_1\lambda + \alpha_2).$$

Then,

$$S_1 = \begin{pmatrix} -\left(\frac{y^*}{x^*}\right)^2 & \frac{y^*}{2x^*} & \frac{d_m y^*}{2s_L x^*} \\ \frac{y^*}{2x^*} & -1 & \frac{d_m}{2s_L} \\ \frac{d_m y^*}{2s_L x^*} & \frac{d_m}{2s_L} & -\frac{d_m^2}{s_L^2} \end{pmatrix}$$

since S_1 has one zero eigenvalue and two negatives eigenvalues. The matrix S_1 satisfies $\forall \tilde{X} \in \mathbb{R}_+^3,$

$$\langle S_1 \tilde{X}, \tilde{X} \rangle \leq 0.$$

Note that if $\tilde{X} \notin \text{Ker}(S_1)$ then $\langle S_1 \tilde{X}, \tilde{X} \rangle < 0$.

Then $\forall (x, y, z) \in \Delta \setminus \{X^*\},$

$$\tilde{X} \notin \text{Ker}(S_1) \Rightarrow \dot{V}_1(x, y, z) = \langle A_1 \tilde{X}, \tilde{X} \rangle - \left(\frac{a_1 b}{K_E} \tilde{x}^2 z + \frac{a_2 s}{K_L} \tilde{y}^2 x \right) \leq \langle A_1 \tilde{X}, \tilde{X} \rangle < 0.$$

If $\tilde{X} \in \text{Ker}(S_1)$, it is sufficient to verify that

$$\left(\frac{a_1 b}{K_E} \tilde{x}^2 z + \frac{a_2 s}{K_L} \tilde{y}^2 x \right) > 0.$$

Note that

$$\left(\frac{a_1 b}{K_E} \tilde{x}^2 z + \frac{a_2 s}{K_L} \tilde{y}^2 x \right) = 0 \iff \begin{cases} x = 0 \text{ and } z = 0 \\ \text{or } x = x^* \text{ and } y = y^* \\ \text{or } z = 0 \text{ and } y = y^* \end{cases}$$

$$\iff \begin{cases} \tilde{x} = -x^* \text{ and } \tilde{z} = -z^* \\ \text{or } \tilde{x} = 0 \text{ and } \tilde{y} = 0 \\ \text{or } \tilde{z} = -z^* \text{ and } \tilde{y} = 0. \end{cases}$$

Let

$$a_1 = \frac{(s_L+d_L)^2}{s+d} \left(\frac{y^*}{x^*}\right)^2,$$

$$a_2 = s_L + d_L,$$

$$a_3 = \left(\frac{s_L+d_L}{s_L}\right)^2 d_m,$$

we have

$$S_1 = (s_L + d_L)^2 \begin{pmatrix} -\left(\frac{y^*}{x^*}\right)^2 & \frac{y^*}{2x^*} & \frac{d_m y^*}{2s_L x^*} \\ \frac{y^*}{2x^*} & -1 & \frac{d_m}{2s_L} \\ \frac{d_m y^*}{2s_L x^*} & \frac{d_m}{2s_L} & -\frac{d_m^2}{s_L^2} \end{pmatrix}$$

and then

$$\text{Ker}(S_1) = \left\{ z \begin{pmatrix} \frac{x^*}{z^*} \\ \frac{y^*}{z^*} \\ 1 \end{pmatrix}, z \in \mathbb{R} \right\}.$$

Finally, we easily see that

$$\left\{ (x, y, z) \in \mathbb{R}^3 \middle/ \begin{matrix} (\tilde{x}, \tilde{y}, \tilde{z}) \in \text{Ker}(S_1) \\ \text{and } \left(\frac{a_1 b}{K_E} \tilde{x}^2 z + \frac{a_2 s}{K_L} \tilde{y}^2 x \right) = 0 \end{matrix} \right\} = \{X_0^*, X^*\}.$$

Consequently $\forall (x, y, z) \in \Delta \setminus \{X^*\},$

$$\dot{V}_1(x, y, z) < 0,$$

i.e. V_1 is a strict Lyapunov function and X^* is globally asymptotically stable in Δ . \square

5. Dynamics analysis of the virus transmission model

This section addresses the existence and global stability of equilibrium points of (7) by showing the persistence of the system and using the theory of competitive systems. We will focus on the case $r > 1, r$ given by (10) which is the condition of survival of all populations as we studied in the previous section.

For this aim, we shall use the following reproduction number [7,8], which is defined as the average number of secondary infections produced by an infected individual in a completely susceptible population

$$R_0 = \frac{\beta_m \beta_H}{d_m(\gamma + b_H)} = \frac{\beta_m \beta_H}{s_L \frac{L^*}{A^*} (\gamma + b_H)}, \tag{15}$$

which arises by computing the steady state.

5.1. Existence of equilibria

Proposition 5.1. *We assume that $r > 1$. System (7) always has the disease free equilibrium $N_0^* = (E^*, L^*, A^*, 1, 0, 0)$. Moreover, if $R_0 > 1$, it has an unique endemic equilibrium with disease $N^* = (E^*, L^*, A^*, S_H^*, I_H^*, I_m^*)$ defined on $\Delta \times \Omega$, the last are done by (3) and (8), where*

$$S_H^* = \frac{b_H}{\beta_H + b_H} + \frac{\beta_H}{(\beta_H + b_H)R_0},$$

$$I_H^* = \frac{d_m b_H}{\beta_m(\beta_H + b_H)}(R_0 - 1), \tag{16}$$

$$I_m^* = \frac{b_H}{\beta_H + b_H R_0}(R_0 - 1)$$

and (E^*, L^*, A^*) is the endemic equilibrium of the independent system (2) given by Proposition 4.1.

Proof. Obviously, as $R_0 > 1$, both equilibria are non-negative. Besides, one can easily see that $(1, 0, 0)$ is an equilibrium of the sub-system of (7) given by the three last equations, then it is clear that N_0^* is an equilibrium of (7), belonging to $\Delta \times \Omega$.

It is also easy to check that N^* is an equilibrium of (7), thus we only have to show that (S_H^*, I_H^*, I_m^*) belongs to Ω , since we know that (E^*, L^*, A^*) is in Δ .

Since $R_0 > 1$, then,

$$I_m^* = \frac{R_0 - 1}{R_0 + \frac{\beta_H}{b_H}} \leq 1$$

and

$$I_H^* = \frac{R_0 - 1}{R_0} \frac{1}{\left(1 + \frac{\gamma}{b_H}\right)\left(1 + \frac{b_H}{\beta_H}\right)} \leq 1.$$

Moreover,

$$S_H^* + I_H^* = \frac{b_H}{\beta_H + b_H} + \frac{\beta_H}{(\beta_H + b_H)R_0} + \frac{R_0 - 1}{R_0} \frac{1}{\left(1 + \frac{\gamma}{b_H}\right)\left(1 + \frac{b_H}{\beta_H}\right)}$$

$$= \frac{1}{\beta_H + b_H} \left(b_H \left(1 + \frac{\beta_H}{b_H + \gamma}\right) + \frac{\beta_H}{R_0} \left(1 - \frac{b_H}{b_H + \gamma}\right) \right),$$

which is less than 1, since $R_0 > 1$ and hence,

$$b_H + \frac{\gamma}{R_0} < b_H + \gamma \iff \frac{b_H}{b_H + \gamma} + \frac{1}{R_0} \left(1 - \frac{b_H}{b_H + \gamma}\right) < 1$$

$$\iff \frac{b_H \beta_H}{b_H + \gamma} + \frac{\beta_H}{R_0} \left(1 - \frac{b_H}{b_H + \gamma}\right) < \beta_H$$

$$\iff b_H \left(1 + \frac{\beta_H}{b_H + \gamma}\right) + \frac{\beta_H}{R_0} \left(1 - \frac{b_H}{b_H + \gamma}\right) < \beta_H + b_H$$

$$\iff \frac{1}{\beta_H + b_H} \left(b_H \left(1 + \frac{\beta_H}{b_H + \gamma}\right) + \frac{\beta_H}{R_0} \left(1 - \frac{b_H}{b_H + \gamma}\right) \right) < 1. \quad \square$$

Proposition 5.2. *The equilibrium $N_0^* = (E^*, L^*, A^*, 1, 0, 0)$ is globally asymptotically stable in Ω iff $R_0 \leq 1$.*

Proof. Similar to proof of Proposition 4.7, using the Lyapunov function $V_1 : \mathbb{R}^6 \rightarrow \mathbb{R}$ defined by,

$$V_1(x_1, x_2, x_3, x_4, x_5, x_6) = \frac{1}{2} (a_1(x - E^*)^2 + a_2(y - L^*)^2 + a_3(z - A^*)^2)$$

$$+ \frac{1}{2} (a_4(x_4 - 1)^2 + a_5x_5^2 + a_6x_6^2),$$

where,

$$a_1 = \frac{(s_L + d_L)^2}{s + d} \left(\frac{L^*}{E^*}\right)^2, \quad a_2 = s_L + d_L,$$

$$a_3 = \left(\frac{s_L + d_L}{s_L}\right)^2 d_m, \quad a_4 = \frac{b_H}{(\gamma + b_H)},$$

$$a_5 = \frac{\beta_H^2}{d_m(\gamma + b_H)}, \quad a_6 = R_0^2. \quad \square$$

System (7) is the coupling of the two subsystems (7a) and (7b), for which the coupling term is the function $s_L \frac{L(t)}{A(t)} I_m(t)$, that is system (7a) drives system (7b). Therefore, since the previous section was devoted to the study of the subsystem (7a) corresponding to the population dynamics we only have to analyze the subsystem (7b),

$$\begin{cases} S_H'(t) = -(b_H + \beta_H I_m(t))S_H(t) + b_H, \\ I_H'(t) = \beta_H I_m(t)S_H(t) - (\gamma + b_H)I_H(t), \\ I_m'(t) = -\left(s_L \frac{L(t)}{A(t)} + \beta_m I_H(t)\right)I_m(t) + \beta_m I_H(t). \end{cases}$$

5.2. Global stability of the endemic equilibrium with disease

First of all, for the reader convenience, let us recall some useful preliminaries, see [36] and [37] in which a similar analysis has been done.

Definition 5.3. Consider the following systems,

$$x' = f(t, x), \tag{17}$$

$$y' = g(y), \tag{18}$$

where f and g are continuous and locally Lipschitz in $x \in \mathbb{R}^n$, thus the solutions exist for all positive time. System (17) is called asymptotically autonomous with limit system (18) if $f(t, x) \rightarrow g(x)$ as $t \rightarrow \infty$ uniformly for $x \in \mathbb{R}^n$.

Lemma 5.4 [36]. *Let e be a locally asymptotically stable equilibrium of (18) and ω be the ω -limit set of a forward bounded solution $x(t)$ of (17). If ω contains a point y_0 such that the solution of (18), with $y(0) = y_0$ converges to e as $t \rightarrow \infty$, then $\omega = e$, i.e., $x(t) \rightarrow e$ as $t \rightarrow \infty$.*

Corollary 1 [36]. *If the solutions of system (17) are bounded and the equilibrium e of the limit system (18) is globally asymptotically stable, then every solution $x(t)$ of the system (17) satisfies $x(t) \rightarrow e$ as $t \rightarrow \infty$.*

Let us apply this result to our subsystem (7b).

Since $X^* = (E^*, L^*, A^*)$, the endemic equilibrium of subsystem (7a), is globally asymptotically stable for $r > 1$ (Proposition 4.7), then $\frac{L(t)}{A(t)} \rightarrow \frac{L^*}{A^*}$ as $t \rightarrow +\infty$ uniformly. Therefore, thanks to the results above, system (7b) is a three-dimensional asymptotically autonomous differential system with limit system,

$$\begin{cases} S_H'(t) = -(b_H + \beta_H I_m(t))S_H(t) + b_H, \\ I_H'(t) = \beta_H I_m(t)S_H(t) - (\gamma + b_H)I_H(t), \\ I_m'(t) = -\left(s_L \frac{L^*}{A^*} + \beta_m I_H(t)\right)I_m(t) + \beta_m I_H(t). \end{cases} \tag{19}$$

The equilibrium of which are $\mathcal{L}_0^* = (1, 0, 0)$ and $\mathcal{L}^* = (S_H^*, I_H^*, I_m^*)$ if $R_0 > 1$.

First of all, note that the region of biological interest Ω given by (8) is positively invariant under the flow induced by (19), as the vector field on the boundary does not point to the outside of Ω which is obvious (similar proof is done for Lemma 4.3).

Theorem 5.5. *If $R_0 > 1$, the endemic equilibrium with disease \mathcal{L}^* of system (19) is globally asymptotically stable in $\text{int}(\Omega)$.*

To prove this theorem we shall use some preliminary results about competitive systems, see [38–40] and stability of periodic orbits, which we recall here for the reader convenience.

Let $D \subset \mathbb{R}^n$ be an open set, and $x \rightarrow f(x) \in \mathbb{R}^n$ be a C^1 function defined in D . We consider the autonomous system in \mathbb{R}^n given by,

$$x' = f(x). \tag{20}$$

System (20) is *competitive* in D , if, for some diagonal matrix $H = \text{diag}(\varepsilon_1, \dots, \varepsilon_n)$, where ε_i , ($i = 1, \dots, n$), is either 1 or -1 , the matrix $H(Df(x))H$ has non-positive off-diagonal elements for $x \in D$, where $Df(x)$ is the Jacobian matrix of (20), see [39,40]. It is shown in [39] that, if D is convex, the flow of such a system preserves, for $t < 0$, the partial order in \mathbb{R}^n defined by the orthant

$$K = \{(x_1, \dots, x_n) \in \mathbb{R}^n : \varepsilon_i x_i \geq 0\}.$$

Looking at the Jacobian matrix of system (19) and choosing the matrix H such as

$$H = \begin{pmatrix} -1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & -1 \end{pmatrix},$$

we can see that system (19) is competitive in Ω , with respect to the partial order defined by the orthant

$$K = \{(S_H, I_H, I_m) \in \mathbb{R}^3 : S_H \leq 0, I_H \geq 0, I_m \leq 0\}.$$

We recall additional definitions that we will use later [41] and also [38,13,15]. Suppose that (20) has a periodic solution $x = p(t)$ with minimal period $\omega > 0$ and orbit $\gamma = \{p(t) : 0 \leq t \leq \omega\}$. This orbit is *orbitally stable* iff, for each $\varepsilon > 0$, there exists a $\delta > 0$ such that any solution $x(t)$, for which the distance of $x(0)$ from γ is less than δ , remains at a distance less than ε from γ , for all $t \geq 0$. It is *asymptotically orbitally stable*, if the distance of $x(t)$ from γ also tends to zero as t goes to infinity. This orbit γ is *asymptotically orbitally stable with asymptotic phase* if it is asymptotically orbitally stable and there is $b > 0$ such that, any solution $x(t)$, for which the distance of $x(0)$ from γ is less than b , satisfies $\|x(t) - p(t - \tau)\| \rightarrow 0$ as $t \rightarrow +\infty$ for some τ which may depend on $x(0)$ [41].

System (20) is persistent in the sense described in [42], i.e. iff each solution $x(t)$ starting in $int(\Omega)$, has the property that $\liminf_{t \rightarrow +\infty} x(t)$ is at a positive distance from the boundary of Ω .

Definition 5.6. We say that system (20) has the *property of stability of periodic orbits*, iff the orbit of any periodic solution $\gamma(t)$, if it exists, is asymptotically orbitally stable.

The following theorem is the main tool to prove the global stability of the endemic equilibrium with disease.

Theorem 5.7 ([13,41]). Assume that $n = 3$, D convex and bounded. Suppose that (20) is competitive, persistent and has the property of stability of periodic orbits. If x_0 is the only equilibrium in $int(D)$, and if it is locally asymptotically stable, then it is globally asymptotically stable in $int(D)$.

Now, let us go back and apply those results to the global asymptotic stability study of (S_H^*, I_H^*, I_m^*) . The proof of this theorem is similar to the one in [38]. In order to prove the persistence of system (19), we shall prove the following proposition.

Proposition 5.8. On the boundary of Ω , system (19) has only one ω – limit point which is the equilibrium L_0^* . Moreover for $R_0 > 1$, L_0^* cannot be the ω -limit of any orbit in $int(\Omega)$.

Proof. The vector field is transversal to the boundary of Ω , except in the S_H -axis which is invariant with respect to (19). On the S_H -axis we have

$$S_H' = b_H(1 - S_H).$$

which implies that $S_H(t) \rightarrow 1$ as $t \rightarrow \infty$. Therefore, L_0^* is the only ω – limit point on the boundary of Ω .

To prove the second part of the proposition, we consider the functional

$$V = I_m + d_m \frac{1 + R_0}{2} \frac{1}{\beta_H} I_H, \tag{21}$$

the derivative of which along solutions is given by,

$$\begin{aligned} \dot{V} &= I_m' + d_m \left(\frac{1 + R_0}{2} \right) \frac{1}{\beta_H} I_H' \\ &= -s_L \frac{L^*}{A^*} I_m + \beta_m(1 - I_m)I_H \\ &\quad + d_m \left(\frac{1 + R_0}{2} \right) \frac{1}{\beta_H} [\beta_H I_m(t)S_H(t) - (\gamma + b_H)I_H(t)] \\ &= -d_m I_m + \beta_m(1 - I_m)I_H + d_m \left(\frac{1 + R_0}{2} \right) I_m S_H \\ &\quad - d_m \left(\frac{1 + R_0}{2} \right) \frac{(\gamma + b_H)}{\beta_H} I_H \\ &= \left[\beta_m(1 - I_m) - d_m \frac{1 + R_0}{2} \frac{(\gamma + b_H)}{\beta_H} \right] I_H + \left[d_m \frac{1 + R_0}{2} S_H - d_m \right] I_m \\ &= \left[(1 - I_m) - \left(\frac{1 + R_0}{2} \right) \frac{d_m(\gamma + b_H)}{\beta_m \beta_H} \right] \beta_m I_H \\ &\quad + \left[\left(\frac{1 + R_0}{2} \right) S_H - 1 \right] d_m I_m \\ &= \left[(1 - I_m) - \left(\frac{1 + R_0}{2} \right) \frac{1}{R_0} \right] \beta_m I_H + \left[\left(\frac{1 + R_0}{2} \right) S_H - 1 \right] d_m I_m \\ &= \left[(1 - I_m) - \frac{1}{2} \left(\frac{1}{R_0} + 1 \right) \right] \beta_m I_H \\ &\quad + \left[S_H - \left(\frac{2}{1 + R_0} \right) \right] d_m \left(\frac{1 + R_0}{2} \right) I_m. \end{aligned}$$

Since $R_0 > 1$, then $\frac{1}{2}(1/R_0 + 1) < 1$ and $2/(1 + R_0) < 1$. Therefore, there exists a neighborhood U of L_0^* such that for $(S_H, I_H, I_m) \in U \cup int(\Omega)$ the expression inside of the brackets are positives. In this neighborhood, we have $\dot{V} > 0$ unless $I_H = I_m = 0$. Moreover, the level sets of V are the planes

$$I_m + d_m \left(\frac{1 + R_0}{2} \right) \frac{1}{\beta_H} I_H = c,$$

which go away from the S_H -axis as c increases. Since V increases along the orbits starting in $U \cup int(\Omega)$, we conclude that they go away from L_0^* .

This proves the proposition, and therefore, the persistence of system, (19) when $R_0 > 1$. \square

Theorem 5.9. The trajectory of any nonconstant periodic solution to (19), if it exists, is asymptotically orbitally stable with asymptotic phase.

To prove this we used the following results.

Theorem 5.10 [43]. A sufficient condition for a periodic orbit $\gamma = \{p(t): 0 \leq t \leq \omega\}$ of (20) to be asymptotically orbitally stable with asymptotic phase is that the linear non-autonomous system,

$$y'(t) = \frac{\partial f^{[2]}}{\partial x}(p(t))y(t) \text{ is asymptotically stable.} \tag{22}$$

Eq. (22) is called the *second compound equation* of (20) and $\partial f^{[2]}/\partial x$ is the *second compound matrix* [38,43] of the Jacobian matrix $\partial f^{[2]}/\partial x$ of f . Generally speaking, for a $n \times n$ matrix A and an integer $1 \leq k \leq n$, the k th additive compound matrix of A is denoted by $A^{[k]}$. This is a $N \times N$ matrix, $N = \binom{n}{k}$, defined by

$$A^{[k]} = D_+(I + hA)^{(k)}|_{h=0},$$

where $B^{(k)}$ is the k th exterior power of a $n \times n$ matrix B and D_+ denotes the right-hand derivative. For example, if $n = 3$ with the notations,

$$A = \begin{pmatrix} a_{1,1} & a_{1,2} & a_{1,3} \\ a_{2,1} & a_{2,2} & a_{2,3} \\ a_{3,1} & a_{3,2} & a_{3,3} \end{pmatrix}.$$

We have,

$$A^{[1]} = A,$$

$$A^{[2]} = \begin{pmatrix} a_{1,1} + a_{2,2} & a_{2,3} & -a_{1,3} \\ a_{3,2} & a_{1,1} + a_{3,3} & a_{1,2} \\ -a_{3,1} & a_{2,1} & a_{2,2} + a_{3,3} \end{pmatrix},$$

$$A^{[3]} = tr(A).$$

Proof. of Theorem 5.10 The Jacobian matrix of (19) is given by

$$DF = \begin{pmatrix} -(b_H + \beta_H I_m) & 0 & -\beta_H S_H \\ \beta_H I_m & -(\gamma + b_H) & \beta_H S_H \\ 0 & \beta_m(1 - I_m) & -(s_L \frac{L^*}{A^*} + \beta_m I_H) \end{pmatrix}.$$

For the solution $\gamma(t)$, (22) becomes

$$\begin{cases} X' = -(2b_H + \beta_H I_m + \gamma)X + \beta_H S_H Y + \beta_H S_H Z, \\ Y' = \beta_m(1 - I_m)X - (b_H + \beta_H I_m + s_L \frac{L^*}{A^*} + \beta_m I_H)Y, \\ Z' = \beta_H I_m Y - (s_L \frac{L^*}{A^*} + \beta_m I_H + \gamma + b_H)Z. \end{cases} \tag{23}$$

In order to prove that (23) is asymptotically stable, we consider the following Lyapunov function, where $\|\cdot\|$ is the norm in \mathbb{R}^3 by

$$\|(X, Y, Z)\| = \sup\{|X|, |Y| + |Z|\}$$

with

$$V(t) = V(X(t), Y(t), Z(t); S_H(t), I_H(t), I_m(t)) = \left\| \begin{pmatrix} 1 & 0 & 0 \\ 0 & \frac{I_H(t)}{I_m(t)} & 0 \\ 0 & 0 & \frac{I_H(t)}{I_m(t)} \end{pmatrix} \begin{pmatrix} X \\ Y \\ Z \end{pmatrix} \right\| = \sup \left(|X|, \frac{I_H}{I_m} (|Y| + |Z|) \right).$$

Suppose that the solution $p(t) = (S_H(t), I_H(t), I_m(t))$ is periodic of minimal period ω . Then Proposition 5.8 implies that the orbit γ of $p(t)$ remains at a positive distance of the boundary of Ω . Therefore

$$I_H(t) \geq \varepsilon \text{ and } I_m(t) \geq \varepsilon \text{ with } 0 \leq \varepsilon \leq 1.$$

Hence, the function V is well defined along $p(t)$ and there exists a constant $c > 0$ such that,

$$V(X, Y, Z; S_H, I_H, I_m) \geq c(|X, Y, Z|) \tag{24}$$

for all $(X, Y, Z) \in \mathbb{R}^3$ and $(S_H, I_H, I_m) \in \gamma$.

The right-hand derivative of $V(t)$ exists and its calculation is described in [44] and [45]. In fact direct computation yields,

$$D_+|X(t)| \leq -(2b_H + \beta_H I_m + \gamma)|X(t)| + \beta_H S_H (|Y(t)| + |Z(t)|) \leq -(2b_H + \beta_H I_m + \gamma)|X(t)| + \beta_H S_H \frac{I_m}{I_H} \left(\frac{I_H}{I_m} (|Y(t)| + |Z(t)|) \right)$$

and

$$D_+|Y(t)| \leq \beta_m(1 - I_m)|X(t)| - \left(b_H + \beta_H I_m + s_L \frac{L^*}{A^*} + \beta_m I_H \right) |Y(t)|, \tag{25}$$

$$D_+|Z(t)| \leq \beta_H I_m |Y(t)| - \left(s_L \frac{L^*}{A^*} + \beta_m I_H + \gamma + b_H \right) |Z(t)|. \tag{26}$$

Thus,

$$D_+ \left[\frac{I_H}{I_m} (|Y(t)| + |Z(t)|) \right] = \left(\frac{I'_H}{I_H} - \frac{I'_m}{I_m} \right) \frac{I_H}{I_m} (|Y(t)| + |Z(t)|) + \frac{I_H}{I_m} D_+ (|Y(t)| + |Z(t)|) \leq \left(\frac{I'_H}{I_H} - \frac{I'_m}{I_m} \right) \frac{I_H}{I_m} (|Y(t)| + |Z(t)|) + \frac{I_H}{I_m} \left[\beta_m(1 - I_m)|X(t)| - (b_H + s_L \frac{L^*}{A^*} + \beta_m I_H) (|Y(t)| + |Z(t)|) \right] \leq \left(\frac{I'_H}{I_H} - \frac{I'_m}{I_m} - b_H - s_L \frac{L^*}{A^*} - \beta_m I_H \right) (|Y(t)| + |Z(t)|) \frac{I_H}{I_m} + \frac{I_H}{I_m} \beta_m(1 - I_m)|X(t)|.$$

Then we can obtain

$$D_+V(t) \leq \sup\{g_1(t), g_2(t)\}V(t), \tag{27}$$

where

$$g_1(t) = -(2b_H + \beta_H I_m + \gamma) + \beta_H S_H(t) \frac{I_m(t)}{I_H(t)},$$

$$g_2(t) = \frac{I_H}{I_m} \beta_m(1 - I_m) + \frac{I'_H}{I_H} - \frac{I'_m}{I_m} - b_H - s_L \frac{L^*}{A^*} - \beta_m I_H.$$

Rewriting the last two equations of (19) as:

$$\frac{I'_H}{I_H} + (\gamma + b_H) = \beta_H \frac{I_m}{I_H} S_H,$$

$$\frac{I'_m}{I_m} + s_L \frac{L^*}{A^*} = \beta_m \frac{I_H}{I_m} (1 - I_m),$$

then

$$g_1(t) = -(2b_H + \beta_H I_m + \gamma) + \frac{I'_H}{I_H} + (\gamma + b_H) = \frac{I'_H}{I_H} - (b_H + \beta_H I_m),$$

$$g_2(t) = \frac{I_H}{I_m} \beta_m(1 - I_m) + \frac{I'_H}{I_H} - \frac{I'_m}{I_m} - b_H - \beta_m \frac{I_H}{I_m} (1 - I_m) - \beta_m I_H = \frac{I'_H}{I_H} - b_H - \beta_m I_H,$$

we obtain

$$\sup\{g_1(t), g_2(t)\} = \sup \left\{ \frac{I'_H}{I_H} - (b_H + \beta_H I_m), \frac{I'_H}{I_H} - b_H - \beta_m I_H \right\} \leq -b_H + \frac{I'_H}{I_H}$$

and thus, from Eq. (27) and Gronwall's inequality, we obtain

$$V(t) \leq V(0)I_H(t)e^{-b_H t} \leq V(0)e^{-b_H t},$$

since $0 < I_H < 1$ in $int(\Omega)$, which implies that $V(t) \rightarrow 0$ as $t \rightarrow \infty$. By (24), it turns out that

$$(X(t), Y(t), Z(t)) \rightarrow 0 \text{ as } t \rightarrow \infty.$$

Therefore, system (23) is asymptotically stable and Theorem 5.9 holds. □

Theorem 5.11. Consider system (19). If $R_0 > 1$, then $\Omega - \{(S_H, 0, 0); 0 \leq S_H \leq 1\}$ is an asymptotic stability region for the endemic equilibrium with disease \mathcal{L}^* . Moreover all trajectories starting in the $S_H -$ axis approach the disease-free equilibrium \mathcal{L}_0^* .

Proof. The first part of the theorem follows from the transversality of the vector field of (19) on $\Omega - \{(S_H, 0, 0); 0 \leq S_H \leq 1\}$ and theorem (5.5). The second part is proved by Proposition 5.8. □

The graphs shown, Fig. 5(a)-(b)-Fig. 6(a)-(b), were obtained after the numerical integration of system (7). In the numerical simulations b_H happen to be very small with respect to the other parameters, since the average expected life in humans is about 60 years, whereas the length of the infected period is a few days and the vector life expectancy is about 4–10 weeks.

Theorem 5.12. Assume $R_0 > 1$ an $b_H \ll 1$, then the solutions of system (19) oscillate to the endemic equilibrium with disease.

Proof. The existence of oscillations around the equilibrium \mathcal{L}^* depends on whether the characteristic equation, defined by the Jacobian matrix (5.2),

$$P(\lambda) = \lambda^3 + A\lambda^2 + B\lambda + C,$$

where

$$A = (b_H + \beta_H I_m^*) + (\gamma + b_H) + (d_m + \beta_m I_H^*),$$

$$B = (b_H + \beta_H I_m^*)(\gamma + b_H) + (b_H + \beta_H I_m^*)(d_m + \beta_m I_H^*) + (\gamma + b_H)(d_m + \beta_m I_H^*) - \beta_H S_H^* \beta_m (1 - I_m^*) = (b_H + \beta_H I_m^*)(\gamma + b_H) + (b_H + \beta_H I_m^*)(d_m + \beta_m I_H^*) + (\gamma + b_H)\beta_m I_H^*,$$

$$C = (b_H + \beta_H I_m^*)(\gamma + b_H)(d_m + \beta_m I_H^*) + \beta_H S_H^* \beta_m I_m^* \beta_m (1 - I_m^*) - (b_H + \beta_H I_m^*)\beta_H S_H^* \beta_m (1 - I_m^*) = (\gamma + b_H)((b_H + \beta_H I_m^*)\beta_m I_H^* + \beta_H d_m I_m^*).$$

has eigenvalues with imaginary part different from zero. Recall that a polynomial of degree three has eigenvalues with imaginary part different from zero if the discriminant

$$\Delta = \frac{1}{4}q^2 + \frac{1}{27}p^3 \tag{28}$$

is bigger than zero, where

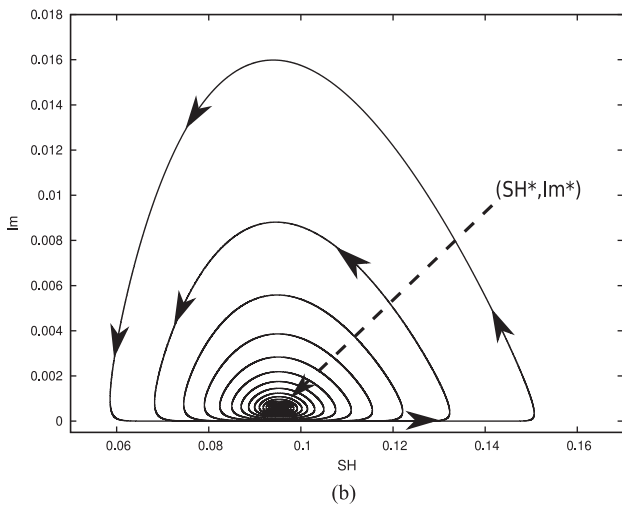
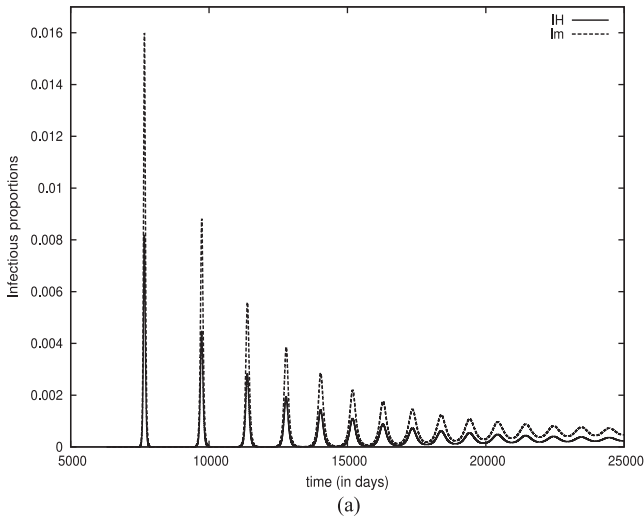


Fig. 5. Numerical solutions of model (7) (b). The graphs (a) and (b) show the proportion of infective humans and infective vectors versus time and the phase portrait in the (S_H, I_m) plan. The parameters in the simulation are: $d_m = 0.25$, $b_H = 0.0000457$, $\beta_M = 0.5$, $\beta_H = 0.75$, $\gamma_H = 0.1428$ and then $R_0 = 10.500841$.

$$q = \frac{2}{27}A^3 - \frac{AB}{3} + C, \quad p = B - \frac{A^2}{3}.$$

We substitute I_H^* , I_m^* and R_0 in the coefficients A, B and C and expand them in Taylor series around $b_H = 0$. After some computations we obtain the following approximations,

$$A = \gamma + d_m + \left(1 + \frac{\beta_m \beta_H}{d_m \gamma} + \frac{\beta_m}{\gamma} - \frac{d_m}{\beta_H}\right) b_H + \mathcal{O}(b_H^2),$$

$$B = \left((\gamma + d_m) \frac{\beta_m \beta_H}{d_m \gamma} + \beta_m - \frac{d_m \gamma}{\beta_H}\right) b_H + \mathcal{O}(b_H^2),$$

$$C = (\beta_H \beta_m - d_m \gamma) b_H + \mathcal{O}(b_H^2).$$

On the other hand, in terms of the coefficients A, B and C in Eq. (28), and collecting terms $\mathcal{O}(b_H^2)$, we get,

$$\Delta = \frac{1}{27}(\gamma + d_m)^3 (\beta_H \beta_m - \gamma d_m) b_H + \mathcal{O}(b_H^2).$$

The term $\beta_H \beta_m - \gamma d_m$ is positive since $R_0 > 1$, therefore

$$\lim_{b_H \rightarrow 0} \frac{\Delta}{b_H} > 0,$$

which implies that for b_H sufficiently small and positive, $\Delta > 0$. This proves the theorem (this result is similar to that one given in [13]). \square

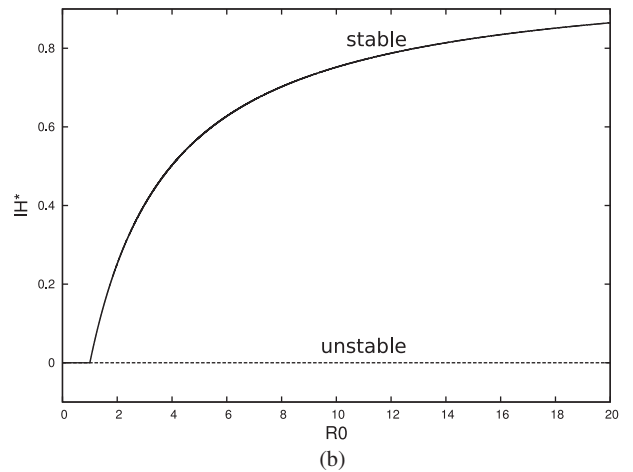
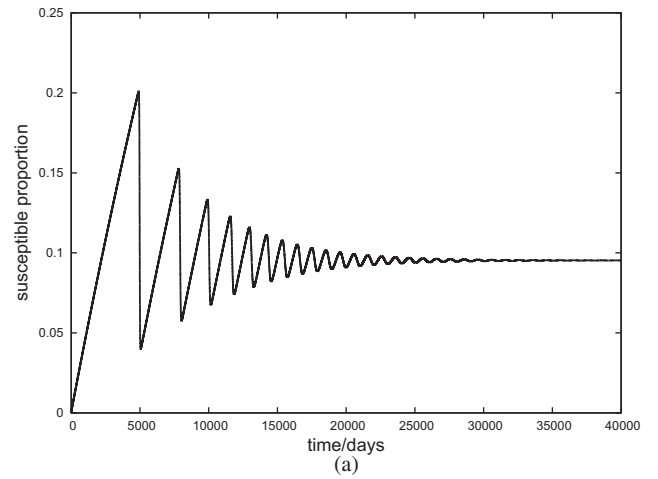


Fig. 6. (a) proportion of susceptible humans versus time (in days). (b) bifurcation diagram for equilibria of model (19) with respect to R_0 . For $R_0 > 1$ we plot the proportion of infective humans I_H^* given in Eq. (16), and we fix the parameters $b_H = 0.0000457$, $\beta_M = 0.9$, $\beta_H = 0.9$, $\gamma_H = 0.1428$, $d_m = 0.25$.

Next, we analyze the asymptotic behavior of the total population $N_H(t)$, and the total number of individuals in the epidemiological classes \bar{S}_H, \bar{I}_H and \bar{R}_H . For this we introduce the following parameters

$$R = \frac{\beta_H \beta_m}{d_m (\gamma + d_H)}$$

and

$$R_1 = R \cdot S_H^* (1 - I_m^*) = \begin{cases} R, & \text{if } R_0 \leq 1, \\ \frac{\gamma + b_H}{\gamma + d_H}, & \text{if } R_0 > 1. \end{cases}$$

First we study the dynamics of solutions whose initial conditions are outside the subspace $\bar{I}_H = \bar{I}_m = 0$. For $R_0 \neq 1$ we have the following results.

Proposition 5.13. For $b_H > d_H$, $(\bar{S}_H(t), \bar{I}_H(t), \bar{R}_H(t))$ tend, as $t \rightarrow \infty$, to $(\infty, 0, 0)$ if $R < 1$ and to (∞, ∞, ∞) if $(R_0 \leq 1$ and $R > 1)$ or $(R_0 > 1)$.

Proof. Since $I_m^* \rightarrow 0$ and $s_L \frac{1}{A} \rightarrow d_m$ as $t \rightarrow \infty$, in the limit, the proportion of infectious mosquitoes is related to the proportion of infected humans as

$$I_m = \frac{\beta_m}{d_m} I_H (1 - I_m),$$

thus, the limit form of the equation for $\bar{I}_H(t)$ is given in system (6) by

$$\bar{I}_H = \left(\frac{\beta_m \beta_H}{d_m} S_H (1 - I_m) - (\gamma + d_H) \right) \bar{I}_H = (\gamma + d_H) (R_1 - 1) \bar{I}_H,$$

which implies that $\bar{I}_H(t)$ declines exponentially if $R_1 < 1$, and grows exponentially if $R_1 > 1$. Moreover,

$$R_1 < 1 \iff R < 1$$

and

$$R_1 > 1 \iff (R_0 \leq 1 \text{ and } R > 1) \text{ or } (R_0 > 1).$$

The solution $\bar{R}_H(t)$ is given by

$$\bar{R}_H(t) = \bar{R}_{H_0}(t) e^{-d_H t} + e^{-d_H t} \gamma \int_0^t \bar{I}_H(s) e^{d_H s} ds.$$

From the exponential nature of $\bar{I}_H(t)$, it follows that $\bar{R}_H(t)$ declines exponentially if $R < 1$, and grows exponentially if $R_1 > 1$. \square

6. Conclusion

We have proposed models to describe the vector (*Aedes albopictus* mosquito) population dynamics and the chikungunya virus transmission to human population.

First of all, we have proposed model (2) to describe the vector population dynamics which takes into account auto-regulation phenomena of eggs and larvae stages. We have shown that this model is well defined. For this model we found that,

$$r = \left(\frac{b}{s+d} \right) \left(\frac{s}{s_L+d_L} \right) \left(\frac{s_L}{d_m} \right)$$

is the threshold condition for the existence of the endemic state, where $\left(\frac{b}{s+d} \right)$, $\left(\frac{s}{s_L+d_L} \right)$ and $\left(\frac{s_L}{d_m} \right)$ are respectively eggs, larvae and adults growth rates. For $r > 1$, we proved, using a Lyapunov functional, that the endemic equilibrium is globally asymptotically stable.

Moreover, following [15], we have proposed model (7) to describe the virus transmission to the human population. This is a model with variable human population and the contact rate among humans depends on the vector population.

In the case $r > 1$ (the biological interesting case) we found the following threshold parameters:

$$R_0 = \frac{\beta_m \beta_H}{d_m (\gamma + b_H)},$$

$$R = \frac{\beta_m \beta_H}{d_m (\gamma + d_H)}$$

and

$$R_1 = \begin{cases} R, & \text{if } R_0 \leq 1, \\ \frac{\gamma + b_H}{\gamma + d_H}, & \text{if } R_0 > 1. \end{cases}$$

On the one hand, parameter R_0 is the threshold condition for the existence of endemic proportions of infected humans and infected mosquitoes. On the other hand, the basic reproduction number R_1 controls the asymptotic behavior of the number of infected humans.

For $b_H = d_H$, we have $R_0 = R$ and hence, $(\bar{S}_H(t), \bar{I}_H(t), \bar{R}_H(t))$ tend, as $t \rightarrow +\infty$, to $(N_H(0), 0, 0)$ if $R < 1$ and to $N_H \cdot (S_H^*, I_H^*, R_H^*)$ if $R > 1$, and this work complete [17] (global stability of the disease-free equilibrium and the endemic equilibrium with disease).

For $b_H > d_H$, $(\bar{S}_H(t), \bar{I}_H(t), \bar{R}_H(t))$ tend, as $t \rightarrow +\infty$, to $(+\infty, 0, 0)$ if $R < 1$ and to (∞, ∞, ∞) if $R_1 > 1$.

Before concluding about the possible actions to take to eradicate the disease, we formulate some remarks about proposed models.

- The infective proportion I_H and the total number of infective humans \bar{I}_H may have different behaviors. Thus, I_H may tend to zero and \bar{I}_H would grow exponentially (case $R_0 < 1 < R$).
- For proposed models, the dynamics of the vector does not depend directly on parameters K_E and K_L . We have already pointed out that drying the breeding sites, and then reducing the carrying capacity K_L , has an impact on the parameters d_L and s . However, the size of the vector population depends on the carrying capacity, but the threshold parameter r does not and the proportion $\frac{b}{A}$ (whose expression is reduced to d_m) does not either. Otherwise, it would be the same for threshold parameters R_0 and R_1 .
- The use of the non classical incidence rate among humans leads to some simplifications on the threshold parameter R_0 (we obtain $\frac{A^*}{A}$ instead of $\frac{A^*}{N_H}$). That is another reason of its non-dependence on r, K_L and K_E .
- Our proposed models include models considering classical incidence rate with a constant human population. More precisely, for $b_H = d_H$, the model with a classical incidence rate among human population $\left(\frac{\beta_H \bar{S}_H \bar{I}_m}{N_H} \right)$ leads to the system (7) where β_H have to be replaced by $\beta_H \frac{A(t)}{N_H}$. As $A(t)$ tends to A^* for $t \rightarrow +\infty$, exactly the same calculations can be made (by substituting β_H by $\beta_H \frac{A^*}{N_H}$) and we obtain the following threshold parameter

$$R_0 = \frac{\beta_m \beta_H}{d_m (\gamma + b_H)} \frac{A^*}{N_H} (= R) \\ = \frac{\beta_m \beta_H}{d_m (\gamma + b_H)} \frac{1}{N_h} \left(1 - \frac{1}{r} \right) \frac{s K_E s_L K_L}{d_m (s K_E + (s_L + d_L) K_L)},$$

which controls the global stability of equilibria. The same approach can be applied to show the global stability of the endemic equilibrium with disease for models in [18] if we consider no influence of the disease on the death rate for vector population.

Following these models and the previous remarks, the eradication of the disease can be achieved if the mosquito population is eradicated or if parameter R is lowered below unity.

Threshold parameter r may provide conditions in order to control the proliferation of the mosquito population. Indeed, even if there is no chikungunya epidemic, we need to be vigilant since in less than 20 years *Aedes albopictus* has developed capabilities to adapt to non tropical regions. That is why several measures have been applied in Europe in order to control the mosquito proliferation. One of the possible interventions to reduce the impact of the epidemic would be to reduce the number of mosquitoes. In this aim we have to focus on some parameters that human intervention can easily control. For instance chemical intervention can reduce the threshold parameter r : chemical alduticide increases the mortality rate of mosquitoes d_m and chemical larvicide increases the death rate of the larvae d_L . Nevertheless, such intervention has fatal consequences, in particular on the environment. Moreover, the vector can develop a resistance to some insecticides that reduce the impact of chemical interventions. That is why, other method of control must be considered. For instance, the reduction of the number of breeding sites, by drying them, has a double impact. First, it reduces the transfer rate s between the eggs compartment and the immature stage: if there is no water, eggs cannot hatch. Second, it increases the death rate d_L of the immature stage: water is necessary for the development of the immature stage. Note that drying the breeding sites has little impact on d , the death rate of eggs, because they are resistant to desiccation. Another example is the introduction of sterile male mosquitoes in the population (see [46]) that has an incidence on the egg-laying. These interventions allow reducing the birth rate b and then the threshold r , and thus control the mosquitoes proliferation.

In case of an epidemic, we have to reduce the parameter R . Clearly, chemical adulticide can be used to increase the death rate d_m of the vector with its bad consequences on the environment. Moreover, all efforts made by the human population, like the use of mosquito nets or repulsive against mosquitoes bites, wearing appropriate clothes, or isolating infected patients in hospitals, will reduce the contact rates β_h and β_m without the disadvantages of the chemical adulticide. All these efforts and interventions can be formulated in terms of an optimal control problem [47].

However, if we want to eradicate the disease just by controlling the vector population, models with non-classical incidence rate lead necessary to eradicate the vector population while models with a classical incidence rate require only to reduce it. In the case of a classical incidence rate, all measures cited previously (drying the breeding sites, larvicide) impact on K_E , K_L , s , d_L and hence R .

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