

MODELING OF MOSQUITOES WITH DOMINANT OR RECESSIVE TRANSGENES AND ALLEE EFFECTS

JIA LI

Department of Mathematical Sciences
University of Alabama in Huntsville
Huntsville, AL 35899, USA

In Honor of Professor Horst R. Thieme's 60th Birthday

ABSTRACT. To study the impact of releasing transgenic mosquitoes on malaria transmission, we formulate discrete-time models for interacting wild and transgenic mosquitoes populations, based on systems of difference equations. We start with models including all homozygous and heterozygous mosquitoes. We then consider either dominant or recessive transgenes to reduce the 3-dimensional model systems to 2-dimensional systems. We include density-dependent vital rates and incorporate Allee effects in the functional mating rates. Dynamics of these models are explored by investigating the existence and stability of boundary and positive fixed points. Numerical simulations are provided and brief discussions are given.

1. Introduction. Mosquito-borne diseases, such as malaria, transmitted between humans by blood-feeding mosquitoes, have been big concerns for the public health in the United States and in the world. Each year 350-500 million cases of malaria occur worldwide, and over one million people die, most of them young children in sub-Saharan Africa. There were 109 countries that were endemic for malaria in 2008, 45 within the WHO African region. There were 1,337 cases of malaria, including 8 deaths, reported for 2002 in the United States, even though malaria has been eradicated in this country since the early 1950's. Malaria is by far the world's most important tropical parasitic disease. It kills more people than any other infectious disease except tuberculosis [25, 31, 26].

The transmission of malaria is not directly from a human to a human, but through infected mosquitoes. It is due to infection by one of 4 *Plasmodium* species. The infection in humans begins when sporozoites are injected into the blood of a human host by an infected female mosquito of the genus *Anopheles*. The sporozoites migrate to the liver where they enter liver cells and develop schizonts, which give rise, via asexual reproduction, to the form of the merozoites that invade the blood cells. In the blood, some merozoites differentiate into sexual erythrocytic stages (gametocytes), and the gametocytes are ingested by a mosquito when it ingests human blood. Within the mosquito the gametocytes develop into microgametes and macrogametes (the male and female gametes) that fuse to form a zygote. This

2000 *Mathematics Subject Classification.* 39A11, 39A99, 92D25, 92D40.

Key words and phrases. malaria transmission, discrete-time population model, transgenic mosquito, stability, period-doubling bifurcation.

This research was supported partially by U.S. National Science Foundation grant DMS-0412386. The author thanks an anonymous referee for valuable comments and suggestions.

becomes a motile ookinete form which bores through the gut wall of the vector and forms an oocyst from which large numbers of sporozoites are released. These sporozoites then invade the salivary glands of the mosquito from which they are injected into a human host when the vector feeds. Such a life cycle of the *Plasmodium* species causes the transmission of malaria between infected humans and mosquitoes [30, 2, 10].

No vaccines are available for malaria and other mosquito-borne diseases. An effective way to prevent them is to control mosquitoes, which has been one of the major intensive efforts in many years. Massive spraying of insecticides or eliminating breeding sites has greatly limited malaria in some areas. However, the number of malaria cases still continues to climb.

The development of genetically altered or transgenic mosquitoes, that are resistant to malaria infection, may provide a new and effective weapon against malaria. The new techniques use a peptide, termed SM1 that binds to mosquitoes' gut and salivary glands, to inject to or feed mosquitoes. The peptide blocks the receptor, and stops the parasite from getting a hold on the epithelium of mosquitoes so that it inhibits parasite invasion [3, 5, 7]. A transgenic mosquito that produces this peptide in the gut or salivary glands then becomes inhospitable to the parasite [14, 16, 24].

While these developments are promising and exciting, many questions have to be answered before the techniques can be implemented and transgenic mosquitoes can be deployed in the field [12]. Such questions include the determination of gene or genotype distributions of mosquitoes in the future generations after transgenic mosquitoes are released, in particular, as density-dependent fitnesses are taken into account [29].

To gain insight into such a complex process, we formulated simple discrete-time mathematical models for interacting wild and transgenic mosquito populations based on systems of difference or differential equations in [20, 22]. We assumed, in those studies, that the transgene was dominant such that mosquitoes with either one or two copies of the transgene were malaria resistant. We divided mosquitoes into two groups, the malaria resistant and malaria unresistant groups. We included the mixed heterozygous mosquitoes with only one copy of the transgene and the pure homozygous mosquitoes with two copies of the transgene in the malaria resistant group. We then assumed that the offspring produced by matings between malaria resistant mosquitoes are all malaria resistant.

Mosquitoes, nevertheless, are diploid. Each individual mosquito carries two copies of genes. Homozygously wild mosquitoes have two copies of the wild gene, denoted by WW , and homozygously transgenic mosquitoes have two copies of the transgene, denoted by AA . After the releasing of homozygously transgenic mosquitoes into homozygously wild mosquito population, the two types of mosquitoes are mixed up. After their matings, three different types of mosquitoes are produced. In addition to those with either WW or AA , there are heterozygous mosquitoes with one wild gene and one transgenic gene, denoted by WA . Moreover, the matings between heterozygous mosquitoes with genes WA can produce offspring with WW , WA , and AA . Furthermore the heterozygous mosquitoes can be either malaria resistant or unresistant, depending on whether the transgene is dominant or recessive, which will significantly distinguish model structures. To further investigate the impact of releasing transgenic mosquitoes, these possibilities need to be more specifically considered.

Because our focus is still on the impact of transgenic mosquitoes on the malaria transmission, to simplify the model structure and hence the mathematical investigation, we formulate discrete-time models, again by dividing the mosquito population into two groups, the malaria resistant or unresistant individuals. We put the heterozygous mosquitoes into either the malaria resistant or unresistant group, depending on the dominance of the genes.

Furthermore, we consider two kinds of different mating rates. We first assume the mating rates are constant, and then assume mating rates are of the Holling-II functional form to incorporate the Allee effects, considering the situation where the mating rates are low, when the mosquito population size is small due to possible mating difficulty, and are increased to approximately constants as the mosquito population size becomes large. We focus on the genetic distributions in future generations and the asymptotic dynamics of the model systems, and hence we determine the existence of all possible fixed points, including the boundary fixed points and positive fixed points, and investigate the stability of those fixed points. We provide numerical examples to verify our analytic results and to demonstrate the complex dynamics of the models. We also give brief discussions on the biological implications of our findings.

2. General model formulation. We let w_n , h_n , and g_n be the numbers of homozygously wild, heterozygous, and homozygously transgenic mosquitoes at generation n , respectively. The dynamics of the interactive mosquitoes are described by the following system

$$\begin{aligned} w_{n+1} &= F_{11}(w_n, h_n, P_n)s_{11}(P_n)w_n + F_{12}(h_n, P_n)s_{12}(P_n)h_n, \\ h_{n+1} &= F_{21}(w_n, h_n, g_n, P_n)s_{21}(P_n)h_n + F_{22}(g_n, P_n)s_{22}(P_n)w_n \\ &\quad + F_{23}(w_n, P_n)s_{23}(P_n)g_n, \\ g_{n+1} &= F_{31}(h_n, P_n)s_{32}(P_n)h_n + F_{32}(h_n, g_n, P_n)s_{31}(P_n)g_n, \end{aligned} \tag{2.1}$$

where F_{ij} , $i, j = 1, 2, 3$, are birth functions which are nonnegative for $(w_n, h_n, g_n) \geq (0, 0, 0)$ and zero for $(w_n, h_n, g_n) = (0, 0, 0)$; $s_{ij} \geq 0$, $i, j = 1, 2, 3$, are survival functions; and $P_n = w_n + h_n + g_n$, $n \geq 0$, is the total population size of generation n [21].

We focus on the impact of the transgenes on malaria transmission. If the transgene is dominant; that is, the mosquitoes with either one or two copies of the transgene are malaria resistant, we let the number of the wild mosquitoes, at generation n , be x_n , include all heterozygous and homozygously transgenic mosquitoes as one group, and denote the number of these mosquitoes, at generation n , by y_n , as shown in Figure 1.

The model dynamics for the dominant transgene is determined by

$$\begin{aligned} x_{n+1} &= (f_1(x_n, y_n)x_n + g(y_n)y_n)s_1(x_n, y_n), \\ y_{n+1} &= f_2(x_n, y_n)y_n s_2(x_n, y_n). \end{aligned} \tag{2.2}$$

If the transgene is recessive; that is, the mosquitoes with only one copy of the transgene are malaria unresistant, we include the heterozygous and the homozygously wild mosquitoes in one group, denoted by x_n , at generation n , and denote the group of the homozygously transgenic mosquitoes, with two copies of the transgene, by y_n , as shown in Figure 2.

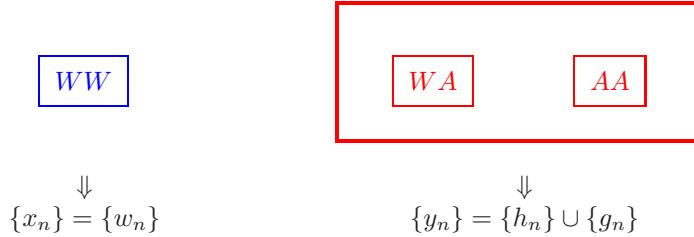


FIGURE 1. In the case of dominant transgenes, we include all mosquitoes with two copies of the wild gene in group x_n , and include all mosquitoes with one or two copies of the transgene in group y_n .

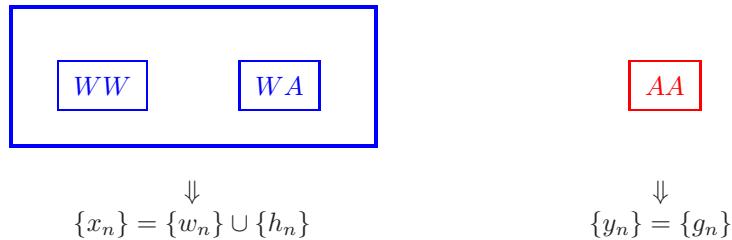


FIGURE 2. In the case of recessive transgenes, we include all wild mosquitoes and mosquitoes with only one copy of the transgene in group x_n , and all mosquitoes with two copies of the transgene in group y_n .

The model dynamics for the recessive transgene is determined by

$$\begin{aligned} x_{n+1} &= F_1(x_n, y_n) x_n s_1(x_n, y_n), \\ y_{n+1} &= (G(x_n)x_n + F_2(x_n, y_n)y_n) s_2(x_n, y_n). \end{aligned} \tag{2.3}$$

Following the line of the homogeneous population models in [20, 22], we assume harmonic means for the matings in the birth functions [4, 18], such that the fraction of matings with wild or transgenic mosquitoes is x_n/N_n or y_n/N_n , respectively, where $N_n = x_n + y_n$. We let $C(P_n)$, be the numbers of matings per mosquito per generation, where we assume that the transgenes do not change mosquitoes' mating behavior [16, 28, 20, 19].

We use the Ricker-type nonlinearity [8]

$$s_i = e^{-d_i - k_i(x_n + y_n)},$$

where d_i are the intrinsic (density-independent) death rates, and k_i are the carrying capacity parameters, for the survival probability for all mosquitoes. We further assume that the transgene does not impose a fitness load to the mosquitoes; that is, the transgenes do not affect mosquitoes' longevity and egg productions [16, 28, 20, 19], such that $d_i := d$ and $k_i := k$. Then the dynamics of the interacting mosquitoes for the dominant transgene are described by the system

$$\begin{aligned} x_{n+1} &= c(N_n) \frac{a_1 x_n^2 + a_2 x_n y_n + a_3 y_n^2}{x_n + y_n} e^{-d - k(x_n + y_n)}, \\ y_{n+1} &= c(N_n) \frac{(b_1 x_n + b_2 y_n) y_n}{x_n + y_n} e^{-d - k(x_n + y_n)}, \end{aligned} \tag{D}$$

for $x_n \geq 0$, $y_n \geq 0$, and $(x_n, y_n) \neq (0, 0)$, for all $n \geq 1$, where a_1 , a_2 , and a_3 are the numbers of wild offspring produced by a mating between two wild, a wild and a transgenic, and two transgenic mosquitos; b_1 and b_2 are the numbers of transgenic offspring produced through a mating between a wild and a transgenic, and two transgenic mosquitoes, respectively.

Similarly, the dynamics of the interacting mosquitoes for the recessive transgene are described by the system

$$\begin{aligned} x_{n+1} &= c(N_n) \frac{(\alpha_1 x_n + \alpha_2 y_n) x_n}{x_n + y_n} e^{-d-k(x_n+y_n)}, \\ y_{n+1} &= c(N_n) \frac{\beta_1 x_n^2 + \beta_2 x_n y_n + \beta_3 y_n^2}{x_n + y_n} e^{-d-k(x_n+y_n)}, \end{aligned} \quad (\text{R})$$

for $x_n \geq 0$, $y_n \geq 0$, and $(x_n, y_n) \neq (0, 0)$, for all $n \geq 1$, where α_i and β_j have similar meanings.

3. Constant mating rate. The mating rate $C(N_n)$ is density-dependent, in general. However, contacts for anophelines are usually associated with swarming in relative open areas in Africa [6], and with sufficiently large population sizes, mosquitoes can easily find their mating partners. Then we assume the matings are saturated so that the mating rate is constant, denoted by $c(N_n) := c$, for all N_n . We merge ce^{-d} into the coefficients and use the same a_i , $i = 1, 2, 3$, b_i , $i = 1, 2$, α_i , $i = 1, 2$, β_i , $i = 1, 2, 3$, for the parameters without confusion. Then the model equations with the dominant transgene become

$$\begin{aligned} x_{n+1} &= \frac{a_1 x_n^2 + a_2 x_n y_n + a_3 y_n^2}{x_n + y_n} e^{-k(x_n+y_n)}, \\ y_{n+1} &= \frac{(b_1 x_n + b_2 y_n) y_n}{x_n + y_n} e^{-k(x_n+y_n)}, \end{aligned} \quad (\text{D1})$$

for $x_n \geq 0$, $y_n \geq 0$, and $(x_n, y_n) \neq (0, 0)$, for all $n \geq 1$, and those for the recessive transgene become

$$\begin{aligned} x_{n+1} &= \frac{(\alpha_1 x_n + \alpha_2 y_n) x_n}{x_n + y_n} e^{-k(x_n+y_n)}, \\ y_{n+1} &= \frac{\beta_1 x_n^2 + \beta_2 x_n y_n + \beta_3 y_n^2}{x_n + y_n} e^{-k(x_n+y_n)}, \end{aligned} \quad (\text{R1})$$

for $x_n \geq 0$, $y_n \geq 0$, and $(x_n, y_n) \neq (0, 0)$, for all $n \geq 1$.

For system (D1), the equation for the wild mosquitoes is

$$x_{n+1} = a_1 x_n e^{-kx_n}, \quad (3.1)$$

in the absence of interaction. The trivial solution, $x_n \equiv 0$, of (3.1) is unstable if $a_1 > 1$.

Similarly, for system (R1), the trivial solution, $y_n \equiv 0$, of the equation for the transgenic mosquitoes in the absence of interaction is unstable if $\beta_3 > 1$. Because the main goal of this study is to investigate the gene distributions of the mosquitoes in future generations, we assume hereafter

$$a_1 > 1, \quad (3.2)$$

and

$$\beta_3 > 1, \quad (3.3)$$

respectively, so that the solutions of systems (D1) and (R1) do not approach the origin with any nonzero initial values.

3.1. Boundary fixed points. For system (D1), a boundary fixed point satisfies the equations

$$(x+y)x = (a_1x^2 + a_2xy + a_3y^2) e^{-k(x+y)}, \quad (\text{F1})$$

$$(x+y)y = (b_1x + b_2y) ye^{-k(x+y)}. \quad (\text{F2})$$

It follows from (F2) that if $x = 0$, then $y = 0$. Hence there exists no boundary fixed point with $x = 0$ and $y > 0$.

Setting $y = 0$ in (F1), and then solving (3.1) for a positive solution x , we obtain a unique boundary fixed of system (D1)

$$E_1 := \left(\frac{\ln a_1}{k}, 0 \right). \quad (3.5)$$

Similarly, we obtain a unique boundary fixed of system (R1)

$$E_2 := \left(0, \frac{\ln \beta_3}{k} \right). \quad (3.6)$$

Therefore, the boundary fixed point E_1 , or E_2 , exists if and only if condition (3.2), or condition (3.3), is satisfied.

We now investigate the stability of the two boundary fixed points. Linearizing system (D1) about the boundary fixed E_1 yields the Jacobian matrix

$$J(E_1) = \begin{bmatrix} -1 - kx + 2a_1e^{-kx} & \cdot \\ 0 & b_1e^{-kx} \end{bmatrix} = \begin{bmatrix} 1 - \ln a_1 & \cdot \\ 0 & \frac{b_1}{a_1} \end{bmatrix}.$$

Then E_1 is locally asymptotically stable if $|1 - \ln a_1| < 1$ and $b_1 < a_1$ [11, 13, 17, 27]. The investigation for E_2 is similar. These results are summarized as follows.

Theorem 3.1. *Boundary fixed point E_1 exists, given in (3.5), and is locally asymptotically stable if*

$$\max\{1, b_1\} < a_1 < e^2. \quad (3.7)$$

Boundary fixed point E_1 exists but is unstable if

$$\text{either } 1 < a_1 < b_1, \quad \text{or } a_1 > e^2. \quad (3.8)$$

Similarly, boundary fixed point E_2 exists, given in (3.6), and is locally asymptotically stable if

$$\max\{1, \alpha_2\} < \beta_3 < e^2. \quad (3.9)$$

Boundary fixed point E_2 exists but is unstable if

$$\text{either } 1 < \beta_3 < \alpha_2, \quad \text{or } \beta_3 > e^2. \quad (3.10)$$

Note that a_1 is the total death-adjusted number of wild offspring with no transgenes produced per wild mosquito, per unit of time, through all homogeneous matings, that is, the matings with wild mosquitoes, and b_1 is total death-adjusted number of transgenic offspring with one or two copies of the transgenes, per mosquito, per unit of time, through all heterogeneous matings between the two types of mosquitoes. Then the transgenic mosquitoes with one or two copies of transgenes can survive if $b_1 > a_1$ which means the total death-adjusted number of offspring with one or two copies of the transgenes through heterogeneous matings exceeding the total death-adjusted number of offspring with no transgenes produced per wild

mosquito. The transgenic mosquitoes with one or two copies of transgenes may also survive if $a_1 > e^2$ which implies that there are too many wild offspring and they cause oscillations with each component positive in the mosquito populations.

We also note that the homozygously transgenic and heterozygous mosquitoes can be wiped out all together in the case of the dominant transgene because they are bunched up as one group, whereas wild mosquitoes with no transgenes cannot be wiped out because as long as the heterozygous mosquitoes exist, they produce wild offspring, in addition to the wild offspring produced by the wild mosquitoes.

3.2. Positive fixed points. Systems (D1) and (R1) may have fixed points in which the two components are both positive. We focus on the investigation of the existence and stability of positive fixed points for system (D1) as follows.

To this end, we first let $p_n = x_n/y_n$ for $n \geq 0$, and $x_0 > 0$, $y_0 > 0$. It follows from equations (D1) that p_n satisfies

$$p_{n+1} = \frac{a_1 p_n^2 + a_2 p_n + a_3}{b_1 p_n + b_2} := F(p_n). \quad (3.11)$$

Solving for nonzero fixed points of (3.11), we have

$$p = \frac{b_2 - a_2 \pm \sqrt{(a_2 - b_2)^2 - 4a_3(a_1 - b_1)}}{2(a_1 - b_1)} \quad (3.12)$$

if $a_1 \neq b_1$, and it then follows that there exists a positive fixed point only if

$$4a_3(a_1 - b_1) \leq (a_2 - b_2)^2. \quad (3.13)$$

Suppose that condition (3.13) is satisfied. Then there exists a unique positive fixed point if $4a_3(a_1 - b_1) = (a_2 - b_2)^2$ and $a_2 < b_2$, and there exist two positive fixed points, $p^{\{1\}} < p^{\{2\}}$, given in (3.12), if $a_2 < b_2$ and $0 < 4a_3(a_1 - b_1) < (a_2 - b_2)^2$.

We next study the local stability of the fixed points of (3.11). We first establish the following lemma.

Lemma 3.2. *Consider function $v = H(u)$, $u > 0$, satisfying $H(u) > 0$, for all $u \geq 0$, and $\lim_{u \rightarrow +\infty} H(u) = +\infty$. Assume that there exist only two points $0 < u_1 < u_2$, such that $H(u_i) = u_i$, for $i = 1, 2$. Then $H'(u_2) > 1$.*

The proof of Lemma 3.2 follows directly from the fact that if we define $G(u) = H(u) - u$, then $G(0) > 0$, $G(u_i) = 0$, and

$$G'(u_1) < 0, \quad G'(u_2) > 0,$$

which implies

$$H'(u_2) > 1.$$

Applying Lemma 3.2 to the fixed points of (3.11), we have $F'(p^{\{2\}}) > 1$, and hence fixed point $p^{\{2\}}$ is unstable. The eigenvalue of the linearization of (3.11) about $p^{\{1\}}$ is given by $-1 + \frac{2a_1 p^{\{1\}} + a_2 + b_2}{b_1 p^{\{1\}} + b_2}$. Then fixed point $p^{\{1\}}$ is locally asymptotically stable if

$$\frac{2a_1 p^{\{1\}} + a_2 + b_2}{b_1 p^{\{1\}} + b_2} < 2.$$

We summarize the results for the fixed points of (3.11) below.

Theorem 3.3. Equation (3.11) has no positive fixed point if $(a_2 - b_2)^2 < 4a_3(a_1 - b_1)$, or $a_1 > b_1$ and $a_2 \geq b_2$, a unique positive fixed point

$$p^* := \frac{b_2 - a_2}{2(a_1 - b_1)}, \quad (3.14)$$

if $(a_2 - b_2)^2 = 4a_3(a_1 - b_1) > 0$ and $a_2 < b_2$, and two positive fixed points

$$\begin{aligned} p_*^{\{1\}} &:= \frac{b_2 - a_2 - \sqrt{(a_2 - b_2)^2 + 4a_3(b_1 - a_1)}}{2(a_1 - b_1)}, \\ p_*^{\{2\}} &:= \frac{b_2 - a_2 + \sqrt{(a_2 - b_2)^2 + 4a_3(b_1 - a_1)}}{2(a_1 - b_1)}, \end{aligned} \quad (3.15)$$

if $a_2 < b_2$ and $0 < 4a_3(a_1 - b_1) < (a_2 - b_2)^2$.

Furthermore, $p_*^{\{2\}}$ is always unstable, and $p_*^{\{1\}}$ is locally asymptotically stable if

$$\frac{2a_1p_*^{\{1\}} + a_2 + b_2}{b_1p_*^{\{1\}} + b_2} < 2. \quad (3.16)$$

We now turn our investigation to the positive fixed points of the following equivalent system of (D1):

$$p_{n+1} = \frac{a_1p_n^2 + a_2p_n + a_3}{b_1p_n + b_2}, \quad (3.17a)$$

$$y_{n+1} = \frac{(b_1p_n + b_2)y_n}{p_n + 1} e^{-k(p_n+1)y_n}. \quad (3.17b)$$

Let p be a positive fixed point of (3.11). Substituting $x = py$ into (F2) and solving for y , we obtain

$$y = \frac{1}{k(1+p)} \ln \frac{b_1p + b_2}{1+p}. \quad (3.18)$$

Then $y > 0$ if and only if

$$\frac{b_1p + b_2}{1+p} > 1.$$

The study for system (R1) is similar where we define $q_n = y_n/x_n$ and consider the equation

$$q_{n+1} = \frac{\beta_1q_n^2 + \beta_2q_n + \beta_3}{\alpha_1q_n + \alpha_2}. \quad (3.19)$$

The details are skipped. In summary, we have the following existence results.

Theorem 3.4. System (D1) has

a) no positive fixed point if $a_1 > b_1$ and $a_2 > b_2$,

$$(a_2 - b_2)^2 < 4a_3(a_1 - b_1), \quad (3.20)$$

or

$$(b_1 - 1)p \leq 1 - b_2, \quad (3.21)$$

for any p given in (3.14) or (3.15);

b) a unique positive fixed point $E_1^* := (x^*, y^*)$ with

$$x^* = \frac{p^*}{k(1+p^*)} \ln \frac{b_1p^* + b_2}{1+p^*}, \quad y^* = \frac{1}{k(1+p^*)} \ln \frac{b_1p^* + b_2}{1+p^*},$$

where p^* is given in (3.14), if $a_2 < b_2$, $4a_3(a_1 - b_1) = (a_2 - b_2)^2$, and

$$(b_1 - 1)p^* > 1 - b_2; \quad (3.22)$$

c) two positive fixed points $E_*^{\{i\}} := (x_*^{\{i\}}, y_*^{\{i\}})$, with

$$x_*^{\{i\}} = \frac{p_*^{\{i\}}}{k(1 + p_*^{\{i\}})} \ln \frac{b_1 p_*^{\{i\}} + b_2}{1 + p_*^{\{i\}}}, \quad y_*^{\{i\}} = \frac{1}{k(1 + p_*^{\{i\}})} \ln \frac{b_1 p_*^{\{i\}} + b_2}{1 + p_*^{\{i\}}},$$

$i = 1, 2$, where $p_*^{\{i\}}$ are given in (3.15), if

$$a_2 < b_2 \quad \text{and} \quad 0 < 4a_3(a_1 - b_1) < (a_2 - b_2)^2, \quad (3.23)$$

in addition to (3.22) being satisfied for both $p_*^{\{i\}}$.

Similarly, we define

$$q^* := \frac{\alpha_1 - \beta_2}{2(\beta_3 - \alpha_2)}, \quad (3.24)$$

and

$$\begin{aligned} q_*^{\{1\}} &= \frac{\alpha_1 - \beta_2 - \sqrt{(\beta_2 - \alpha_1)^2 + 4\beta_1(\alpha_2 - \beta_3)}}{2(\beta_3 - \alpha_2)}, \\ q_*^{\{2\}} &= \frac{\alpha_1 - \beta_2 + \sqrt{(\beta_2 - \alpha_1)^2 + 4\beta_1(\alpha_2 - \beta_3)}}{2(\beta_3 - \alpha_2)}, \end{aligned} \quad (3.25)$$

respectively. Then system (R1) has

$\alpha)$ no positive fixed point if $\beta_2 > \alpha_1$ and $\beta_3 > \alpha_2$,

$$(\beta_2 - \alpha_1)^2 < 4\beta_1(\beta_3 - \alpha_2), \quad (3.26)$$

or

$$(\alpha_2 - 1)q \leq 1 - \alpha_1, \quad (3.27)$$

for any q given in (3.24) or (3.25);

$\beta)$ a unique positive fixed point $E_2^* := (x^*, y^*)$ with

$$x^* = \frac{1}{k(1 + q^*)} \ln \frac{\alpha_1 + \alpha_2 q^*}{1 + q^*}, \quad y^* = \frac{q^*}{k(1 + q^*)} \ln \frac{\alpha_1 + \alpha_2 q^*}{1 + q^*},$$

where q^* is given in (3.24), if $\beta_2 < \alpha_1$, $4\beta_1(\beta_2 - \alpha_1) = (\beta_2 - \alpha_1)^2$, and

$$(\alpha_2 - 1)q^* > 1 - \alpha_1; \quad (3.28)$$

$\gamma)$ two positive fixed points $E_2^{\{i\}} := (x_*^{\{i\}}, y_*^{\{i\}})$, with

$$x_*^{\{i\}} = \frac{1}{k(1 + q_*^{\{i\}})} \ln \frac{\alpha_1 + \alpha_2 q_*^{\{i\}}}{1 + q_*^{\{i\}}}, \quad y_*^{\{i\}} = \frac{q_*^{\{i\}}}{k(1 + q_*^{\{i\}})} \ln \frac{\alpha_1 + \alpha_2 q_*^{\{i\}}}{1 + q_*^{\{i\}}},$$

$i = 1, 2$, where $q_*^{\{i\}}$ are given in (3.25), if

$$\beta_2 < \alpha_1 \quad \text{and} \quad 0 < 4\beta_1(\beta_2 - \alpha_1) < (\beta_2 - \alpha_1)^2, \quad (3.29)$$

in addition to (3.28) being satisfied for both $q_*^{\{i\}}$.

We next investigate the local stability of the positive fixed points for system (D1).

Notice that equation (3.17a) is uncoupled with equation (3.17b). Then we only need to study the linearization of (3.17b) which has the following eigenvalue

$$1 - k(1 + p)y = 1 - \ln \frac{b_1 p + b_2}{1 + p}, \quad (3.30)$$

at a positive fixed point, (p, y) , of system (3.17), and the eigenvalue is inside the unit circle if

$$\frac{b_1 p + b_2}{1 + p} < e^2. \quad (3.31)$$

In summary, we have the following stability results.

Theorem 3.5. *The positive fixed points of system (D1) with $p_*^{\{2\}}$ and system (R1) with $q_*^{\{2\}}$ are unstable. The positive fixed point of system (D1) with $p_*^{\{1\}}$ is locally asymptotically stable if conditions (3.16) and (3.31) are satisfied, and the positive fixed point of system (R1) with $q_*^{\{1\}}$ is locally asymptotically stable if the conditions*

$$\frac{2\beta_3 q_*^{\{1\}} + \alpha_1 + \beta_2}{\alpha_2 q_*^{\{1\}} + \alpha_1} < 2 \quad (3.32)$$

and

$$\frac{\alpha_2 q_*^{\{1\}} + \alpha_1}{1 + q_*^{\{1\}}} < e^2 \quad (3.33)$$

are both satisfied.

3.3. Numerical examples. We now provide numerical examples to demonstrate the dynamics of system (D1).

Example 1. In this example, we choose the parameters

$$a_1 = 2, \quad a_2 = 3, \quad a_3 = 5, \quad b_1 = 1, \quad b_2 = 2, \quad k = 0.2,$$

such that condition (3.7) is satisfied and hence the boundary fixed point $E_1 = (3.4657, 0)$ exists and is locally asymptotically stable. Condition (3.20) is also satisfied, and hence, there exist no positive fixed points. As we choose different initial values, all of the solutions eventually approach E_1 which seems globally asymptotically stable even though we have not proved it. The numerical simulations are shown in Figure 3.

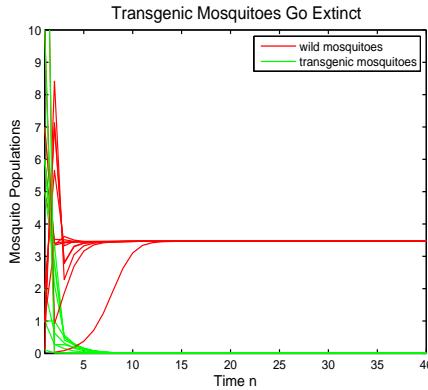


FIGURE 3. We use parameters $k = 0.2$, $a_1 = 2$, $a_2 = 3$, $a_3 = 5$, $b_1 = 1$, and $b_2 = 2$. With this parameter setting, the fixed point E_1 is locally asymptotically stable, and there exist no positive fixed points. It seems that all solutions approach E_1 .

Example 2. With the set of parameters,

$$a_1 = 8, \quad a_2 = 2, \quad a_3 = 2, \quad b_1 = 7.5, \quad b_2 = 5, \quad k = 0.2,$$

condition (3.8) is satisfied such that the boundary fixed point E_1 becomes unstable. Conditions (3.15), (3.16), (3.22), (3.23), and (3.31) are all satisfied. There exist two positive fixed points $E_*^{(1)} = (3.9096, 5.1177)$, with $p_*^{(1)} = 0.7639$, and $E_*^{(2)} = (8.2284, 1.5715)$, with $p_*^{(2)} = 5.2360$. $E_*^{(1)}$ is locally asymptotically stable and $E_*^{(2)}$ is unstable. The numerical simulations are shown on the left in Figure 4.

Notice that the stability of E_* that we have shown is only local. With different initial values, solutions can approach this positive fixed point or other stable sets, such as a synchronous 2-cycle shown on the right in Figure 4.

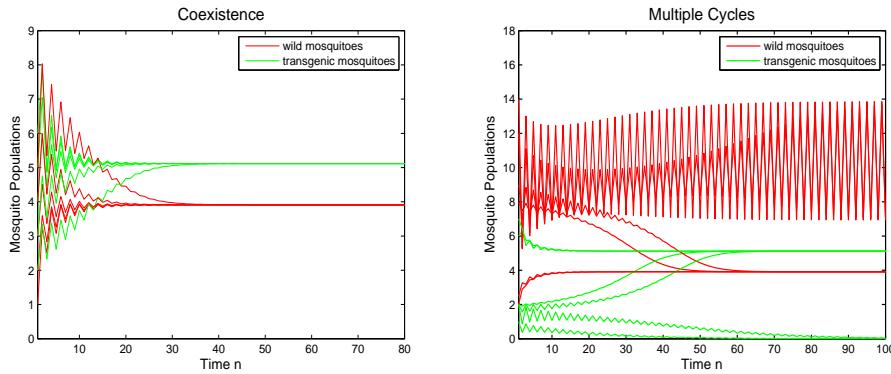


FIGURE 4. We use parameters $k = 0.2$, $a_1 = 8$, $a_2 = 2$, $a_3 = 2$, $b_1 = 7.5$, and $b_2 = 5$. Then boundary fixed point E_1 does not exist, fixed point $E_*^{(2)} = (8.2284, 1.5715)$ exists but is unstable, and fixed point $E_*^{(1)} = (3.9096, 5.1177)$ exists and is locally asymptotically stable, as shown in the left figure. However, the stability is only local. With different initial values, it seems that some of other solutions approach a synchronous cycle where $x \rightarrow 0$ eventually, as shown in the right figure.

Example 3. In this example, we use the following set of parameters:

$$a_1 = 2, \quad a_2 = 3, \quad a_3 = 5, \quad b_1 = 1, \quad b_2 = 9.7, \quad k = 0.2.$$

Conditions (3.7), (3.15), (3.16), (3.22), (3.23), and (3.31) are all satisfied. Hence, boundary fixed point E_1 and two positive fixed points $E_*^{(i)}$ all exist. The fixed points E_1 and $E_*^{(1)} = (4.0078, 4.6847)$, with $p_*^{(1)} = 0.8555$, are locally asymptotically stable, and the positive fixed point $E_*^{(2)} = (3.5021, 0.5992)$, with $p_*^{(2)} = 5.8445$, is unstable. The numerical simulations given in Figure 5 show the local stability of fixed points E_1 and $E_*^{(1)}$. Solutions with different initial values approach either E_1 or $E_*^{(1)}$.

Example 4. The dynamics of systems (D1) and (R1) are complex. While we have only shown the existence and stability of the boundary and positive fixed points, other cycles and even chaos can appear. We demonstrate such dynamics in this example by fixing the parameters

$$a_1 = 2, \quad a_2 = 3, \quad a_3 = 5, \quad b_1 = 1, \quad k = 0.2,$$

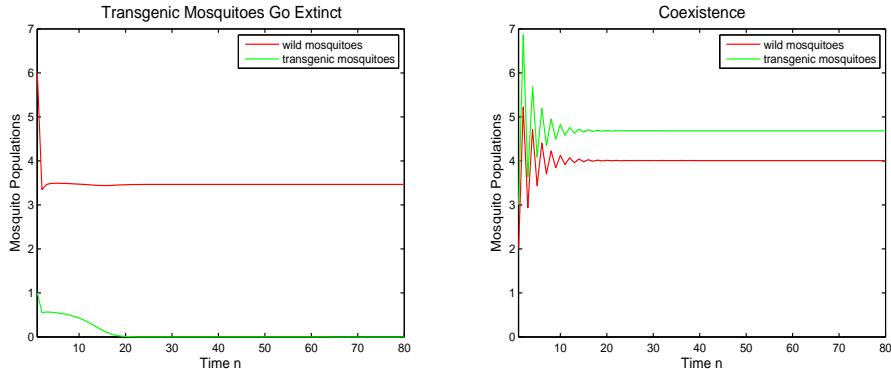


FIGURE 5. We use parameters $k = 0.2$, $a_1 = 2$, $a_2 = 3$, $a_3 = 5$, $b_1 = 1$, and $b_2 = 9.7$. With this parameter setting, fixed points E_1 and $E_*^{(1)}$ are both locally asymptotically stable. The dynamics of the system are determined by initial values. As $x_0 = 6$ and $y_0 = 1$, the trajectories approach boundary fixed point E_1 where the y -component is zero, as shown in the left figure. This implies the transgenic mosquitoes will be wiped out. However, if initially $x_0 = 3$ and $y_0 = 4$, the trajectories approach the positive fixed point, as shown in the right figure. Then the wild and transgenic mosquitoes coexist.

and initial value $(x_0, y_0) = (12, 1)$, but varying parameter b_2 . As b_2 changes from 10, 16, to 19, sequentially, a 2-cycle, a 4-cycle, and then an 8-cycle appear. When $b_2 = 25$, chaotic behavior occurs. See Figure 6.

4. Holling-II type mating rate – Allee effects. The mating rate $C(N_n)$ plays an important role in the population interactions. We have studied the case where C is constant in Section 3. In a real situation, in particular, as the cost of engineering transgenic mosquitoes is taken into account, the population of transgenic mosquitoes is relatively small. Then there exists possible mating difficulty such that the birth rate is approximately proportional to the total mosquitoes population, N_n , in this case. On the other hand, as the population size increases to a certain level, the number of matings can be saturated. Then, the mating rate is approximately constant. Such a phenomenon has been observed in many circumstances and is called an Allee effect [1, 9].

To incorporate the Allee effect into the population interactions, we use a rectangular hyperbola, or a Holling-II type functional form, for the mating function such that $C(N_n) = c_0 N_n / (q + N_n)$, where c_0 is the maximum mating rate and q is the half-saturation constant for the two types of mosquitoes [9, 15].

In the case where the transgenes are dominant, system (D) has the following form:

$$\begin{cases} x_{n+1} = c_0 \frac{a_1 x_n^2 + a_2 x_n y_n + a_3 y_n^2}{q + x_n + y_n} e^{-k(x_n + y_n)}, \\ y_{n+1} = c_0 \frac{(b_1 x_n + b_2 y_n) y_n}{q + x_n + y_n} e^{-k(x_n + y_n)}. \end{cases}$$

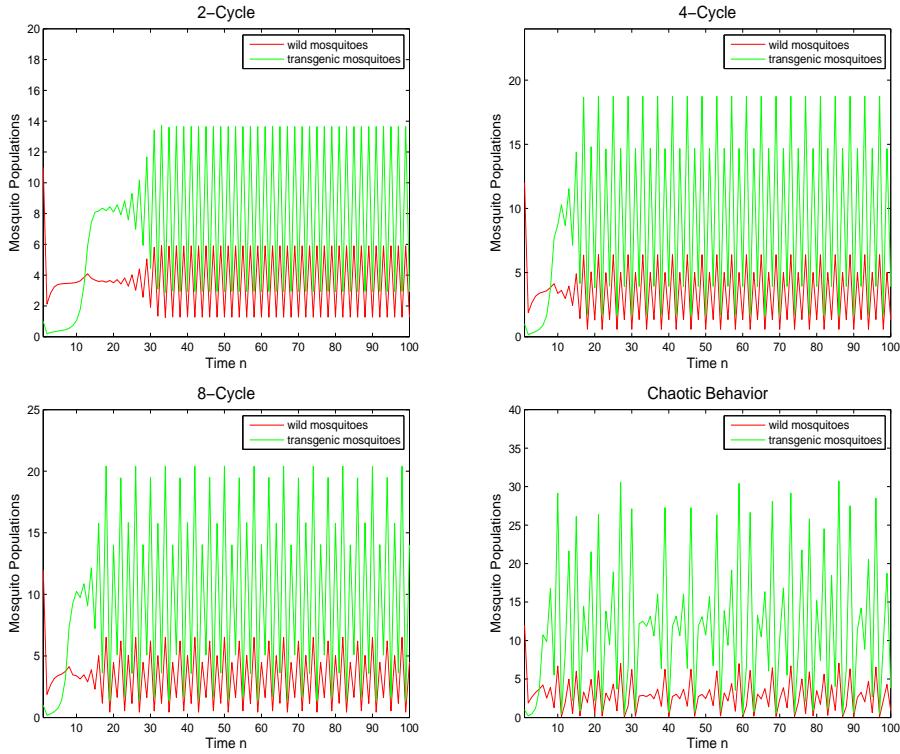


FIGURE 6. We use the same set of parameters as in Figure 5, but vary b_2 . We also fix initial value $x_0 = 12$ and $y_0 = 1$. As $b_2 = 10, 16$, and 19 , there appear 2-, 4-, and 8-cycles, as shown in the upper left, upper right, and lower left figures, respectively. When $b_2 = 25$, chaotic behavior occurs as shown in the lower right figure.

Normalizing the system but keep the same notations, without confusion, we obtain the following system:

$$\begin{cases} x_{n+1} = \frac{a_1 x_n^2 + a_2 x_n y_n + a_3 y_n^2}{1 + x_n + y_n} e^{-k(x_n + y_n)}, \\ y_{n+1} = \frac{(b_1 x_n + b_2 y_n) y_n}{1 + x_n + y_n} e^{-k(x_n + y_n)}. \end{cases} \quad (\text{D2})$$

Similarly, the normalized system for the recessive transgenes has the following form:

$$\begin{cases} x_{n+1} = \frac{(\alpha_1 x_n + \alpha_2 y_n) x_n}{1 + x_n + y_n} e^{-k(x_n + y_n)}, \\ y_{n+1} = \frac{\beta_1 x_n^2 + \beta_2 x_n y_n + \beta_3 y_n^2}{1 + x_n + y_n} e^{-k(x_n + y_n)}. \end{cases} \quad (\text{R2})$$

4.1. Boundary fixed points. We focus on the investigation for system (D2). The study for system (R2) is similar.

It is clear that there exist no boundary fixed points with $x = 0$ and $y > 0$, for system (D2). We then seek boundary fixed points with $x > 0$ and $y = 0$, denoted

again by $E_1 = (x, 0)$, where x satisfies

$$\frac{a_1 x}{1+x} = e^{kx}. \quad (4.1)$$

Similarly as in [23], defining function

$$H(x) := kx + \ln(1+x) - \ln x - \ln a_1,$$

we have $H''(x) > 0$, and $H'(x_c) = 0$ for the unique positive real number

$$x_c := \frac{\sqrt{k^2 + 4k} - k}{2k}.$$

Then, whether there exists a positive solution to equation (4.1) depending on if $H(x_c)$ is equal to zero. Hence we have the following existence results for boundary fixed points.

Theorem 4.1. *Define*

$$P_1(k) := \frac{\sqrt{k^2 + 4k} + k + 2}{2} e^{\frac{\sqrt{k^2 + 4k} - k}{2}}.$$

Then, system (D2) has no boundary fixed points with $x = 0$ and $y > 0$. It has no, a unique, or two boundary fixed points, with $y = 0$ and $x > 0$, if, $P_1(k) > a_1$, $P_1(k) = a_1$, or $P_1(k) < a_1$, respectively.

System (R2) has no boundary fixed points with $x > 0$ and $y = 0$. It has no, a unique, or two boundary fixed points, with $x = 0$ and $y > 0$, if $P_1(k) > \beta_3$, $P_1(k) = \beta_3$, or $P_1(k) < \beta_3$, respectively.

The linear stability analysis for the boundary fixed points can be performed similarly as that in [23]. We briefly illustrate it for system (D2) as follows.

The eigenvalues of the Jacobian of system (D2), at a boundary fixed point, $E_1 = (x, 0)$, are $\lambda_1 = \frac{2+x}{1+x} - kx$ and $\lambda_2 = b_1/a_1$.

It then follows from (4.1) that $-1 < \lambda_1 < 1$ if and only if

$$0 < \frac{kx(1+x) - 1}{1+x} < 2. \quad (4.2)$$

Suppose there are two boundary fixed points $E_1^{\{i\}} := (x^{\{i\}}, 0)$, $i = 1, 2$. Then it follows from $x^{\{1\}} < x_c < x^{\{2\}}$ and

$$H' \left(x^{\{1\}} \right) < 0 = H' \left(x_c \right) < H' \left(x^{\{2\}} \right)$$

that

$$\frac{kx^{\{1\}}(1+x^{\{1\}}) - 1}{1+x^{\{1\}}} = x^{\{1\}} H' \left(x^{\{1\}} \right) < 0.$$

Hence, $E_1^{\{1\}}$ is unstable.

It follows from (4.2) that the fixed point $E_1^{\{2\}}$ is locally asymptotically stable if, in addition to $b_1 < a_1$,

$$k \left(x^{\{2\}} \right)^2 + (k-2)x^{\{2\}} - 3 < 0. \quad (4.3)$$

Define

$$s_{\pm} := \frac{2 - k \pm \sqrt{k^2 + 8k + 4}}{2k}.$$

Then (4.3) is satisfied if and only if

$$s_- < x^{\{2\}} < s_+.$$

Notice that $s_- < 0$ and H is an increasing function for $x > x^{\{2\}}$. Then if $H(x^{\{2\}}) < H(s_+)$, $x^{\{2\}} < s_+$. Hence (4.3) is satisfied if

$$a_1 < e^{ks_+} \frac{1+s_+}{s_+}. \quad (4.4)$$

In the case where there is only one boundary fixed point. It can be proved, similarly as in [23], that it is unstable.

Substituting s_+ into (4.4), we arrive at the following stability results.

Theorem 4.2. Define

$$\begin{aligned} P_2(k) &:= \frac{2+k+\sqrt{k^2+8k+4}}{2-k+\sqrt{k^2+8k+4}} e^{\frac{2-k+\sqrt{k^2+8k+4}}{2}} \\ &= \frac{(k+2)\sqrt{k^2+8k+4}+k^2+6k+4}{\sqrt{k^2+8k+4}+2k} e^{\frac{2-k+\sqrt{k^2+8k+4}}{2}}. \end{aligned}$$

If there exists a unique boundary fixed point for system (D2) or (R2), the boundary fixed point is unstable. If there are two boundary fixed points for (D2) or (R2), the one with a smaller x component, $E_1^{\{1\}} = (x^{\{1\}}, 0)$ for system (D2), or the one with smaller y component, $E_2^{\{1\}} = (0, y^{\{1\}})$ for system (R2), is unstable, and the boundary fixed point with a larger x or y component, $E_1^{\{2\}} = (x^{\{2\}}, 0)$ or $E_2^{\{2\}} = (0, y^{\{2\}})$, is locally asymptotically stable, if $b_1 < a_1 < P_2(k)$, or $\alpha_2 < \beta_3 < P_2(k)$. Fixed point $E_1^{\{2\}}$ is unstable if $a_1 < b_1$, or $P_2(k) < a_1$; $E_2^{\{2\}}$ is unstable if $\beta_3 < \alpha_2$, or $P_2(k) < \beta_3$.

4.2. Positive fixed points. We next study the existence and stability of positive fixed points for systems (D2) and (R2) but only show the details for system (D2).

Consider the following equivalent system for (D2):

$$p_{n+1} = \frac{a_1 p_n^2 + a_2 p_n + a_3}{b_1 p_n + b_2}, \quad (4.5a)$$

$$y_{n+1} = \frac{(b_1 p_n + b_2) y_n^2}{1 + (1 + p_n) y_n} e^{-k(p_n+1)y_n}. \quad (4.5b)$$

The analysis for (4.5a) is same as that in Section 3. Then let p be a positive fixed point of (4.5a) and substitute it into the equation

$$\frac{(b_1 p + b_2) y}{1 + (1 + p) y} e^{-k(p+1)y} = 1. \quad (4.6)$$

Define a function

$$H(y) = k(1+p)y + \ln(1 + (1 + p)y) - \ln((b_1 p + b_2) y),$$

for $y > 0$. The positive solutions of (4.6) correspond to the positive solutions of $H(y) = 0$.

It is easy to check that

$$H'(y) = \frac{k(1+p)y(1 + (1 + p)y) - 1}{y(1 + (1 + p)y)},$$

$$H''(y) = -\frac{2(1+p)y+1}{y^2(1+(1+p)y)^2} > 0,$$

equation $H'(y) = 0$ has a unique positive root

$$\bar{y} = \frac{\sqrt{k^2 + 4k} - k}{2k(1+p)},$$

and

$$H(\bar{y}) = \ln \frac{(1+p)(\sqrt{k^2 + 4k} + k)}{(b_1p + b_2)(\sqrt{k^2 + 4k} - k)} + \frac{1}{2}(\sqrt{k^2 + 4k} - k) = \ln \left(\frac{1+p}{b_1p + b_2} P_1(k) \right).$$

Then it follows from $\lim_{y \rightarrow 0^+} H(y) = +\infty$ and $\lim_{y \rightarrow +\infty} H(y) = +\infty$ that equation $H(y) = 0$ can have no, one, or two positive solutions, depending on whether $\frac{1+p}{b_1p + b_2} P_1(k)$ is greater than, equal to, or less than one.

In summary, we have the following existence results.

Theorem 4.3. *System (4.5) has*

- a) *no positive fixed points if $a_1 > b_1$ and $a_2 > b_2$, $(a_2 - b_2)^2 < 4a_3(a_1 - b_1)$, or $(1+p)P_1(k) > b_1p + b_2$ for a given positive solution p in (3.14) or (3.15);*
- b) *a unique positive fixed point if $a_2 < b_2$, $(a_2 - b_2)^2 = 4a_3(a_1 - b_1) > 0$, and $(1+p)P_1(k) = b_1p + b_2$ satisfied with p given by (3.14);*
- c) *two positive fixed points if $a_1 < b_1$, $(a_2 - b_2)^2 = 4a_3(a_1 - b_1) > 0$, and $(1+p)P_1(k) < b_1p + b_2$ satisfied with p given in (3.14);*
- d) *four positive fixed points if $a_2 < b_2$, $(a_2 - b_2)^2 > 4a_3(a_1 - b_1) > 0$, and $(1+p)P_1(k) < b_1p + b_2$ satisfied with both $p^{\{1\}}$ and $p^{\{2\}}$ given in (3.15).*

The investigation of the local stability of the positive fixed points can also be performed similarly as in Section 3. That is, we only need to consider the linearization of (4.5b) at the positive fixed point $(p_*^{\{1\}}, y_*)$. For convenience we write $p_* = p_*^{\{1\}}$. Then the linearization has a real eigenvalue

$$\lambda = 2 - k(1+p_*)y_* - \frac{(1+p_*)y_*}{1+(1+p_*)y_*} = 1 - k(1+p_*)y_* + \frac{1}{1+(1+p_*)y_*}.$$

We consider $\lambda = \lambda(y)$ as a function of y . Then it follows from $\frac{d\lambda}{dy} < 0$ that $\lambda(y)$ is a decreasing function and hence

$$\lambda(y_*^{\{1\}}) > \lambda(\bar{y}) > \lambda(y_*^{\{2\}}).$$

Simple calculation shows $\lambda(\bar{y}) = 1$. Hence fixed point with $y_*^{\{1\}}$ is unstable, and $\lambda(y_*^{\{2\}}) < 1$. To obtain stability conditions for the positive fixed point with component $y_*^{\{2\}}$, we need $\lambda(y_*^{\{2\}}) > -1$. Define the function

$$G(y) := k(1+p)^2y^2 + (k-2)(1+p)y - 3. \quad (4.7)$$

Then $\lambda(y) = -1$ if and only if $G(y) = 0$.

Equation $G(y) = 0$ has a unique positive solution

$$\tilde{y} = \frac{2 - k + \sqrt{(k-2)^2 + 12k}}{2k(1+p)} = \frac{2 - k + \sqrt{k^2 + 8k + 4}}{2k(1+p)}.$$

Then, again since $\lambda(y)$ is a decreasing function, if $y_*^{\{2\}} < \tilde{y}$, $\lambda(y_*^{\{2\}}) > -1$, and if $y_*^{\{2\}} > \tilde{y}$, $\lambda(y_*^{\{2\}}) < -1$.

Moreover, note that $H(y)$ is increasing for $y > \bar{y}$, and that $\tilde{y} > \bar{y}$. Then it follows from $H(y_*^{\{2\}}) = 0$ that if $H(\tilde{y}) > 0$, $y_*^{\{2\}} < \tilde{y}$, and if $H(\tilde{y}) < 0$, $\tilde{y} < y_*^{\{2\}}$.

It is easy to check that

$$\begin{aligned} H(\tilde{y}) &= \frac{\sqrt{k^2 + 8k + 4} + 2 - k}{2} + \ln \frac{(1 + p)(\sqrt{k^2 + 8k + 4} + 2 + k)}{(b_1 p + b_2)(\sqrt{k^2 + 8k + 4} + 2 - k)} \\ &= \ln P_2(k) - \ln \frac{b_1 p + b_2}{1 + p}. \end{aligned}$$

Then $H(\tilde{y}) > 0$ is equivalent to

$$\frac{b_1 p + b_2}{1 + p} < P_2(k). \quad (4.8)$$

Hence $\lambda(y_*^{\{2\}}) > -1$, if condition (4.8) is satisfied. Note that if there exists only one or two positive fixed points, they are all associated with the unique p^* . Hence they are unstable. The stability results for all of the positive fixed points can be summarized as follows.

Theorem 4.4. *If system (D2) or (R2) has a unique or two positive fixed points, they are all unstable. If system (D2), or (R2), has four positive fixed points, those associated with $p_*^{\{2\}}$, $q_*^{\{2\}}$, $p_*^{\{1\}}$ and $y_*^{\{1\}}$ for system (D2), or $q_*^{\{1\}}$ and $x_*^{\{1\}}$ for system (R2), are all unstable. The positive fixed point of system (D2) with $p_*^{\{1\}}$ and $y_*^{\{2\}}$ is locally asymptotically stable if conditions (3.16) and (4.8), where $p = p_*^{\{1\}}$, are satisfied, and the positive fixed point of system (R1) with $q_*^{\{1\}}$ and $x_*^{\{2\}}$ is locally asymptotically stable if*

$$\frac{\alpha_2 q_*^{\{1\}} + \alpha_1}{1 + q_*^{\{1\}}} < P_2(k), \quad (4.9)$$

in addition to condition (3.32) being satisfied.

4.3. Numerical examples. The dynamics of systems (D2) and (R2) seem more complex than those of system (D1) and (R1). The origin is a trivial solution for the systems and is always locally asymptotically stable. This is due to the fact of mating difficulty if the mosquito population size is small. While there possibly exist more than one boundary or positive fixed points, only one could be locally stable. Nevertheless, other cycles can early appear. We provide numerical examples to demonstrate the dynamics of system (D2) as follows.

Example 5. With the following parameters

$$a_1 = 8, \quad a_2 = 3, \quad a_3 = 5, \quad b_1 = 1.1, \quad b_2 = 9.7, \quad k = 0.2,$$

we have

$$P_1(k) = 2.2296, \quad P_2(k) = 8.8368.$$

Since $(a_2 - b_2)^2 < 4a_3(a_1 - b_1)$, there exists no positive fixed points. It follows from $P_1(k) < a_1$ and $b_1 < a_1 < P_2(k)$ that there exist two boundary boundary fixed points

$$E_1^{\{1\}} = (0.1478, 0), \quad E_1^{\{2\}} = (9.9168, 0),$$

where $E_1^{\{1\}}$ is unstable, and $E_1^{\{2\}}$ is asymptotically stable, as shown in Figure 7.

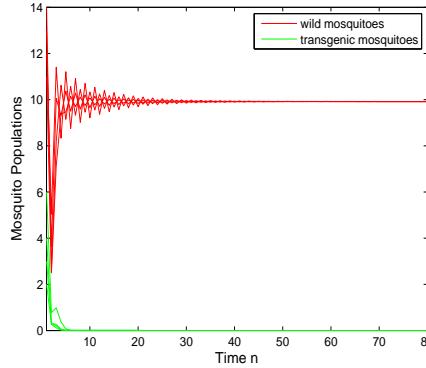


FIGURE 7. With the parameter $k = 0.2$, $a_1 = 8$, $a_2 = 3$, $a_3 = 5$, $b_1 = 1.1$, and $b_2 = 9.7$, there exist no positive fixed points. Two boundary fixed points $E_1^{\{1\}} = (0.1478, 0)$ and $E_1^{\{2\}} = (9.9168, 0)$ exist. $E_1^{\{1\}}$ is unstable, and $E_1^{\{2\}}$ is asymptotically stable.

Example 6. Using the parameters

$$a_1 = 8, \quad a_2 = 3, \quad a_3 = 5, \quad b_1 = 7, \quad b_2 = 9.7, \quad k = 0.2,$$

we have the same $P_i(k)$, $i = 1, 2$, as in Example 5. It follows again from $P_1(k) < a_1$ and $b_1 < a_1 < P_2(k)$ that there exist two boundary fixed points $E_1^{\{1\}} = (0.1478, 0)$ and $E_1^{\{2\}} = (9.9168, 0)$, where only $E_1^{\{2\}}$ is asymptotically stable. Conditions (3.15), (3.16), (4.8), and those in Theorem 4.3 d), are all satisfied. Hence there exist two positive

$$p_*^{\{1\}} = 0.8555, \quad p_*^{\{2\}} = 5.8445,$$

and four positive fixed points, two associated with $p_*^{\{1\}}$, denoted by $E_{*p1}^{\{i\}}$, and two associated with $p_*^{\{2\}}$, denoted by $E_{*p2}^{\{i\}}$, $i = 1, 2$:

$$\begin{aligned} E_{*p1}^{\{1\}} &= (0.0639, 0.0747), & E_{*p1}^{\{2\}} &= (4.7059, 5.5007), \\ E_{*p2}^{\{1\}} &= (0.1385, 0.0237), & E_{*p2}^{\{2\}} &= (8.1145, 1.3884), \end{aligned}$$

where $E_{*p1}^{\{2\}}$ is the only stable positive fixed point. Solution with different initial values approach either $E_1^{\{2\}}$ or $E_{*p1}^{\{2\}}$ as shown in Figure 8.

Example 7. Using the following parameters

$$a_1 = 12, \quad a_2 = 3, \quad a_3 = 5, \quad b_1 = 10, \quad b_2 = 9.7, \quad k = 0.2,$$

we have the same $P_i(k)$, $i = 1, 2$, as in Example 5. It follows again from $P_1(k) < a_1$ and $b_1 < a_1 < P_2(k)$ that there exist two boundary fixed points, but because of $a_1 > P_2(k)$, both boundary fixed points are unstable. Conditions in Theorem 4.3 d) are satisfied so that there exist four positive fixed points. However, it follows from

$$\frac{b_1 p_*^{\{1\}} + b_2}{1 + p_*^{\{1\}}} = 9.8586 > P_2(k) = 8.8368$$

that no positive fixed point is stable. With different initial values, solutions either approach a “boundary” 2-cycle where, asymptotically, the x -component is 2-cycle and the y component is zero as shown in the left figure, or approach a positive

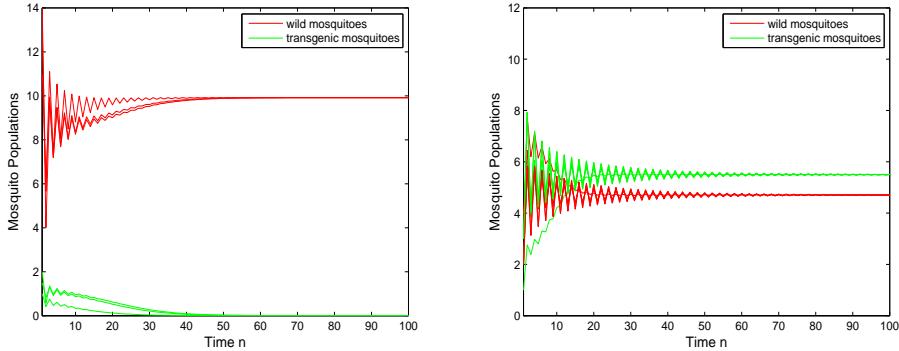


FIGURE 8. We use parameters $k = 0.2$, $a_1 = 8$, $a_2 = 3$, $a_3 = 5$, $b_1 = 7$, and $b_2 = 9.7$. There exist two boundary fixed points and four positive fixed points. However, only the boundary fixed point $E_1^{\{2\}} = (9.9168, 0)$ and the positive fixed point $E_*^{\{2\}} = (4, 7059, 5.5007)$ are asymptotically stable. The stability is local. With different initial values, solutions approach $E_1^{\{2\}}$ as shown on the left, or $E_*^{\{2\}}$ as shown on the right.

2-cycle where both x and y components are 2-cycles, as shown in the right figure, in Figure 9.

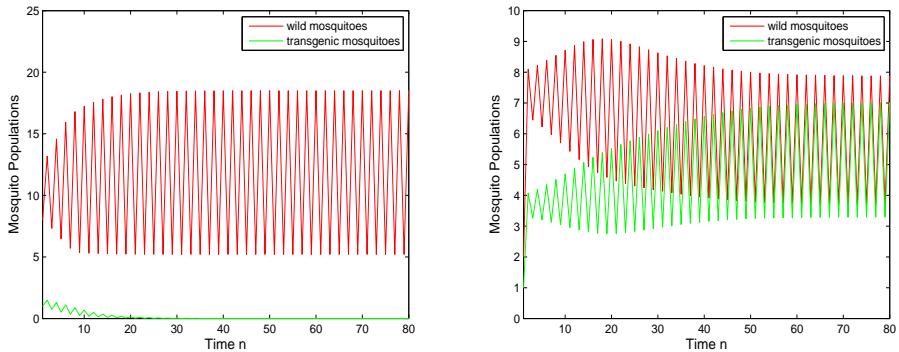


FIGURE 9. We use parameters $k = 0.2$, $a_1 = 12$, $a_2 = 3$, $a_3 = 5$, $b_1 = 10$, and $b_2 = 9.7$. There exist two boundary fixed points and four positive fixed points. However, all of these fixed points are unstable. Solutions either approach a “boundary” 2-cycle where the x -component is a 2-cycle and the y component is zero as shown in the left figure, or approach a positive 2-cycle where both x and y components are positive 2-cycles, as shown in the right figure.

Example 8. System (D2) with Allee effects exhibit similar period-doubling bifurcation features as system (D1) with constant mating rates. We use the parameters

$$a_1 = 2, \quad a_2 = 3, \quad a_3 = 5, \quad b_1 = 1, \quad k = 0.2,$$

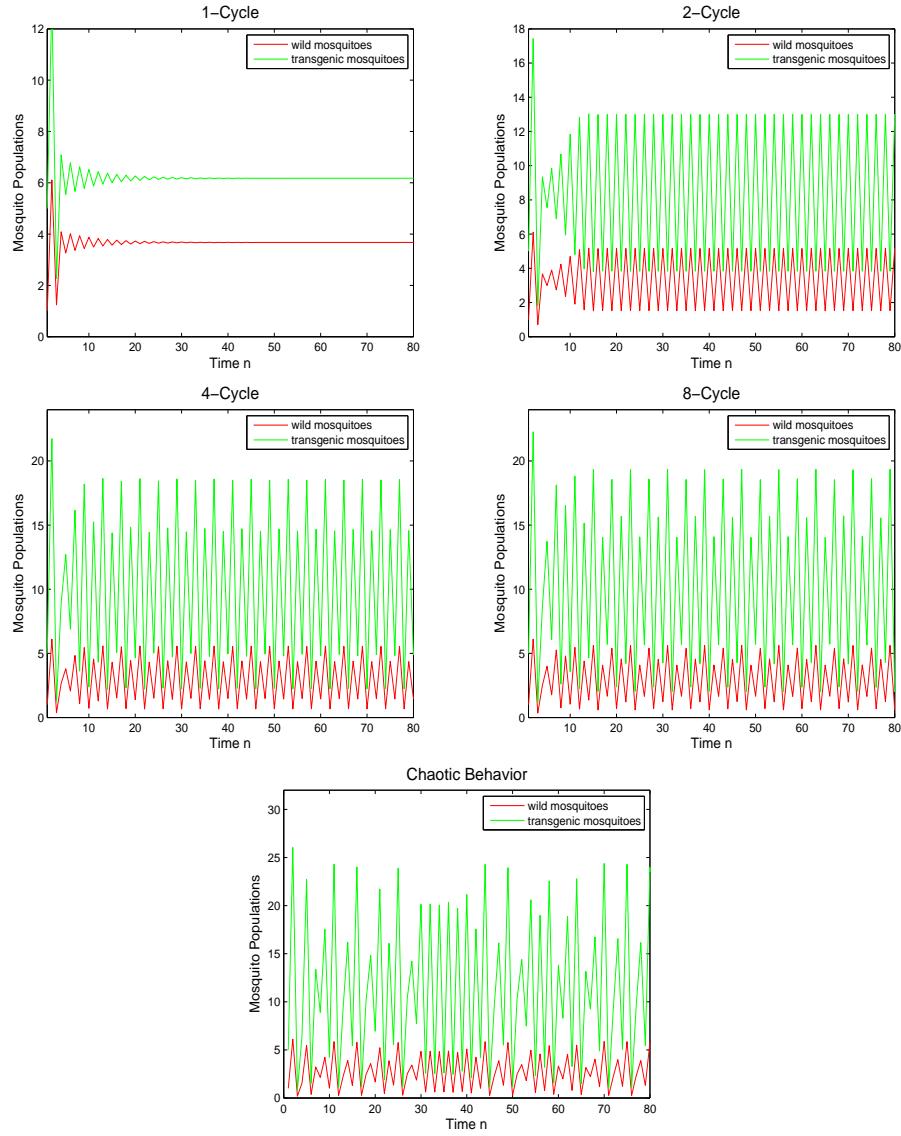


FIGURE 10. We use the parameters $k = 0.2$, $a_1 = 2$, $a_2 = 3$, $a_3 = 5$, $b_1 = 1$, and vary b_2 . We also fix initial value $x_0 = 1$ and $y_0 = 5$. As $b_2 = 12, 15, 20$, and 20.5 , there appear 1-, 2-, 4-, and 8-cycles, as shown in the upper four figures, respectively. When $b_2 = 24$, chaotic behavior occurs as shown in the lower figure.

and fix the initial value $(x_0, y_0) = (1, 5)$. We then vary parameter b_2 , from 12, 15, 20, 20.5, to 24, sequentially. 1-cycle, 2-cycle, 4-cycle, 8-cycle, and chaotic behavior occur, respectively, as shown in Figure 10.

5. Concluding remarks. To study the impact of releasing transgenic mosquitoes on malaria transmissions, we formulate discrete-time models, based on difference equations. We first include all homozygotously wild, heterozygous, and homozygotously

transgenic mosquitoes to formulate a three dimensional system of difference equations (2.1), which is similar to the system in [21] but with a more general setting. Our goal is to focus on the study of the impact on malaria transmissions. Then we consider the cases where the transgenes are either dominant or recessive such that heterozygous mosquitoes with one copy of a transgene is either resistant or unresistant to the malaria transmission. We divide the total mosquito population into two groups such that one group consists of only homozygotously wild mosquitoes and one group consists of heterozygous and homozygotously transgenic mosquitoes if the transgenes are dominant, and one group consists of homozygotously wild and heterozygous mosquitoes and one group consists of only homozygotously transgenic mosquitoes if the transgenes are recessive. The model system (2.1) is reduced to the two dimensional system (2.2) or (2.3). We then assume the mating rates to be constant in Section 3. While the model systems are similar to that studied in [20], we provide more details in the derivation and the model systems are more accurate to count in all components, whereas it was assumed in [20] that the wild and transgenic mosquitoes were two independent groups acting symmetrically, and hence there was no input term from the interaction between the transgenic mosquitoes into the wild mosquitoes for the case of dominant transgenes, nor input term from the interaction between the wild mosquitoes into the transgenic mosquitoes for the case of the recessive transgenes. We also consider the mating rates of the Holling-II type in this paper, to include the Allee effects in Section 4. We investigate the existence and stability of all fixed points for the models formulated in this paper, and obtain conditions that determine whether the boundary fixed points, in which one component is positive and the other is zero, and the positive fixed points, in which both components are positive, exist. We also obtain conditions that determine whether a boundary or positive fixed point, if it exists, is locally asymptotically stable. We provide numerical simulations for the models with constant or Holling-II type mating rates, in Sections 3.3 and 4.3, respectively, to verify our analytic results.

Our results provide insight into the dynamics of interacting wild and transgenic mosquitoes. In the case of dominant transgenes with either constant or Holling-II type mating rates, there exist no boundary fixed points in which the component for the wild mosquitoes is zero. This contrasts with the feature of the models studies in [20] where such boundary fixed points exist. Nevertheless, similarly as in [20], there exist boundary fixed points in which the component for the transgenic mosquitoes is zero. The unstable conditions for such boundary fixed points show that the transgenic mosquitoes with one or two copies of transgenes can survive only if the total death-adjusted number of offspring with one or two copies of the transgenes, through heterogeneous matings, exceeds the death-adjusted number of offspring with no transgenes, produced per wild mosquito ($b_1 > a_1$), or there are too many wild offspring so that they cause oscillations in the wild mosquito population ($a_1 > e^2$ for model (D1) and $a_1 > P_2(k)$ for model (D2)). On the other hand, even if the transgenes are recessive, they can still eventually drive wild mosquitoes to extinct and take over the mosquito population by wiping out the homozygotously wild and the heterozygous mosquitoes as shown in both models (R1) and (R2), based on the results for the boundary fixed points. This seems to imply that the dominance of the transgenes may not necessarily be the major factor in getting rid of wild mosquitoes.

Moreover, the stability results we obtain for all fixed points in all models are only local. Meeting conditions for the desired asymptotic behavior of the desired boundary fixed points may not be realistic in practice, and hence seeking coexistence may be a more feasible way in controlling of wild mosquitoes. We note that even there may exist two or four positive fixed points for the models with constant or Holling-II type mating rates, there is at most one stable fixed point for each model. The stability of the boundary or positive fixed point may be global if there exist no other fixed points for the models with constant mating rates although we are unable to prove it, whereas any fixed point cannot be globally stable for the models with Holling-II type mating rates because of the local stability of the origin. The models studied in this paper also exhibit other phenomena such as period-doubling bifurcations, which are common in discrete-time population models.

We need to point out that the nonexistence of such boundary fixed points with $x = 0$ and $y > 0$ for the dominant transgenes, and with $x > 0$ and $y = 0$ for the recessive transgenes, seems to come from the way of grouping the mosquitoes in our model formulations. As long as the heterozygous mosquitoes exist, they produce both homozygously wild and transgenic offspring. Then, to eliminate malaria unresistant mosquitoes, it needs also to completely eliminate the heterozygous mosquitoes even the transgenes are dominant such that the heterozygous mosquitoes are malaria resistant. This seems unreasonable and, therefore, to have a better understanding of the interactions between the two types of mosquitoes, we may need to go back to fully study the original three dimensional model (2.1) even the mathematical analysis is more difficult.

REFERENCES

- [1] W. C. Allee, "The Social Life of Animals," 2nd ed., Beacon Press, 1958.
- [2] R. M. Anderson and R. M. May, "Infectious Diseases of Humans," Dynamics and Control, Oxford Univ. Press, Oxford, 1991.
- [3] D. L. Capurro, J. Coleman J, B. T. Beerntsen, K. M. Myles, K. E. Olson, E. Rocha, A. U. Krettli and A. A. James, *Virus-expressed, recombinant single-chain antibody blocks sporozoite infection of salivary glands in Plasmodium gallinaceum-infected Aedes aegypti*, Am. J. Trop. Med. Hyg., **62** (2000), 427–433.
- [4] H. Caswell, "Matrix Population Models: From Fates of Individuals to the Dynamics of Populations," Sinauer Associates, Sunderland, 2001.
- [5] F. Catteruccia, T. Nolan, T. G. Loukeris, C. Blass, C. Savakis, F. C. Kafatos and A. Crisanti, *Stable germline transformation of the malaria mosquito Anopheles stephensi*, Nature, **405** (2000), 959–962.
- [6] J. D. Charlwood, R. Thompson and H. Madsen, *Observations on the swarming and mating behaviour of Anopheles funestus from southern Mozambique*, Malaria Journal, Feb., (2003), 2:2.
- [7] C. J. Coates, N. Jasinskiene, L. Miyashiro and A. A. James, *Mariner transposition and transformation of the yellow fever mosquito, Aedes aegypti*, Proc. Natl. Acad. Sci. USA, **95** (1998), 3743–3747.
- [8] J. M. Cushing, "An Introduction to Structured Population Dynamics," CBMS-NSF Regional Conference Series in Applied Mathematics, 71, Society for Industrial and Applied Mathematics (SIAM), Philadelphia, PA, 1998.
- [9] B. Dennis, *Allee-effects: Population growth, critical density, and the chance of extinction*, Nat. Res. Model, **3** (1989), 481–538.
- [10] C. Easmon, *The life cycle of the malarial parasite*, 2009, http://netdoctor.co.uk/travel/diseases/life_cycle_of_the_malarial_parasite.htm.
- [11] S. N. Elaydi, "An Introduction to Difference Equations," 3rd Ed., Undergraduate Texts in Mathematics, Springer, New York, 2005.
- [12] M. Enserink, *Two new steps toward a 'better mosquito'*, Science, **293** (2001), 2370–2371.
- [13] O. Galor, "Discrete Dynamical Systems," Springer, Berlin, New York, 2007.

- [14] A. K. Ghosh, P. E. M. Ribolla and M. Jacobs-Lorena, *Targeting Plasmodium ligands on mosquito salivary glands and midgut with a phage display peptide library*, Proc. Natl. Acad. Sci. USA, **98** (2001), 13278–13281.
- [15] C. S. Holling, *The components of predation as revealed by a study of small mammal predation of the European pine sawfly*, Canad. Entomol., **91** (1959), 293–320.
- [16] J. Ito, A. Ghosh, L. A. Moreira, E. A. Wilmmer and M. Jacobs-Lorena, *Transgenic anopheline mosquitoes impaired in transmission of a malaria parasite*, Nature, **417** (2002), 452–455.
- [17] E. I. Jury, *The inners approach to some problems of system theory*, IEEE, Trans. Automatic Contr., AC, **16** (1971), 233–240.
- [18] N. Keyfitz, *The mathematics of sex and marriage*, Proceedings of the Sixth Berkeley Symposium on Mathematical Statistics and Probability (Univ. California, Berkeley, Calif., 1970/1971), Vol. IV: Biology and health, 89–108, Univ. California Press, Berkeley, Calif., 1972.
- [19] Chaoyang Li, Mauro T. Marrelli, Guiyun Yan and M. Jacobs-Lorena, *Fitness of transgenic anopheles stephensi mosquitoes expressing the SM1 peptide under the control of a vitellogenin promoter*, Journal of Heredity, **99** (2008), 275–282.
- [20] Jia Li, *Simple mathematical models for interacting wild and transgenic mosquito populations*, Math. Biosci., **189** (2004), 39–59.
- [21] Jia Li, *Heterogeneity in modeling of mosquito populations with transgenic mosquitoes*, J. Diff. Eqns. Appl., **11** (2005), 443–457.
- [22] Jia Li, *Differential equations models for interacting wild and transgenic mosquito populations*, J. Biol. Dyn., **2** (2008), 241–258.
- [23] Jia Li, Baojun Song and Xiaohong Wang, *An extended Ricker population model with Allee effects*, J. Diff. Eqns. Appl., **13** (2007), 309–321.
- [24] G. J. Lycett and F. C. Kafatos, *Anti-malarial mosquitoes?* Nature, **417** (2002), 387–388.
- [25] “Malaria,” 2009, <http://www.who.int/mediacentre/factsheets/fs094/en/index.html>.
- [26] “Malaria Facts,” 2009, <http://www.cdc.gov/Malaria/facts.htm>
- [27] R. M. May, G. R. Conway, M. P. Hassell and T. R. E. Southwood, *Time delays, density-dependence and single-species oscillations*, J. Anim. Ecol., **43** (1974), 747–770.
- [28] L. A. Moreira, Jing Wang, F. H. Collins and M. Jacobs-Lorena, *Fitness of anopheline mosquitoes expressing transgenes that inhibit Plasmodium development*, Genetics, **166** (2004), 1337–1341.
- [29] J. Roughgarden, “Theory of Population Genetics and Evolutionary Ecology: An Introduction,” Macmillan Publ., New York, 1979.
- [30] W. H. Wernsdorfer, “The Importance of Malaria in the World,” in “Malaria,” Vol. 1, Epidemiology, Chemotherapy, Morphology, and Metabolism, Kreier, J. P. (ed.), Academic Press, New York, 1980.
- [31] World malaria report 2008, <http://www.malaria.org/malaria2008.pdf>.

Received June 22, 2009; Accepted August 24, 2009.

E-mail address: li@math.uah.edu