Mathematical modeling of the impact of periodic release of sterile male mosquitoes and seasonality on the population abundance of malaria mosquitoes

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Abstract

This study presents a new mathematical model for assessing the impact of sterile insect technology (SIT) and seasonal variation in local temperature on the population abundance of malaria mosquitoes in an endemic setting. Simulations of the model, using temperature data from Kipsamoite area of Kenya, show that a peak abundance of the mosquito population is attained in the Kipsamoite area when the mean monthly temperature reaches 30°C. Furthermore, in the absence of seasonal variation in local temperature, our results show that releasing more sterile male mosquitoes (e.g., 100,000) over a one year period with relatively short duration between releases (e.g., weekly, bi-weekly or even monthly) is more effective than releasing smaller numbers of the sterile male mosquitoes (e.g., 10,000) over the same implementation period and frequency of release. It is also shown that density-dependent larval mortality plays an important role in determining the threshold number of sterile male mosquitoes that need to be released in order to achieve effective control (or elimination) of the mosquito population in the community. In particular, low(high) density-dependent mortality requires high(low) numbers of sterile male mosquitoes to be released to achieve such control. In the presence of seasonal variation in local temperature, effective control of the mosquito population using SIT is only feasible if a large number of the sterile male mosquitoes (e.g., 100,000) is periodically released within a very short time interval (at most weekly). In other words, seasonal variation in temperature necessitates more frequent releases (of a large number) of sterile male mosquitoes to ensure the effectiveness of the SIT intervention in curtailing the targeted mosquito population.

Keywords: SIT; malaria; *Anopheles* mosquito; release effect statistic; seasonality.

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1 Introduction

Mosquitoes are the principal vectors of numerous mosquito-borne diseases (MBDs) of major public health **concern**, including malaria [1, 2, 3, 4], dengue [5, 6, 7], West Nile virus [8, 9, 10], Zika [8, 11] and Chikungunya [8, 11]. Of the over 3,500 described species of mosquitoes, about 200 are known to be capable of transmitting infectious diseases to humans [12]. Malaria is the most devastating of all the MBDs, accounting for approximately 214 (149-303) million cases and 438,000 (236,000-635,000) deaths annually, with the majority of deaths occurring in children under the age of five and in pregnant women [13]. Malaria parasites are transmitted to humans by adult female *Anopheles* mosquitoes and around 30-40 species in this genus have been shown to be vectors of at least one of the five human malaria species [12]. As with other mosquitoes, the lifecycle of *Anopheles* mosquitoes alternates between the free-flying adult stage and several aquatic juvenile stages, including the eggs, the larvae, and the pupae. Adult females require a blood meal for egg development and oviposit directly onto standing water, where the eggs hatch, releasing larvae that pass through four instars and then develop into pupae. Adult mosquitoes emerge from the pupae following metamorphosis and then fly away. Many aspects of this lifecycle, including adult and juvenile survival probabilities as well as the duration of each stage, are dependent on environmental conditions, most notably temperature [1, 3, 6, 7, 8, 14].

The control of MBDs (such as malaria) in endemic areas relies mainly on the implementation of mosquito-reduction strategies, such as the use of long-lasting insecticidal nets(LLINs) and indoor residual spraying (IRS) and treatment of confirmed cases [15, 16]. However, adult female mosquitoes have started developing resistance to the chemicals currently being used in the production of IRS and LLINs (Figure 1). Furthermore, in the context of malaria, the *Plasmodium* parasite has started developing resistance to the *artemisinin*-based therapy [17, 18, 19]. Hence, there is urgent need to explore other measures for vector control. Biological controls, such as sterile insect technology (SIT) [20, 21, 22, 23, 24, 25, 26], are being used to achieve this objective.

SIT is based on the repeated release of large numbers of sterile male mosquitoes aimed at disrupting the natural reproductive process of mosquitoes [20, 21, 25]. One key feature of SIT is that female mosquitoes that mate only with sterile males will produce no offspring. If sufficient numbers of wild females mate with sterile males, the target population will decline and possibly collapse. Sterile males can be mass produced using several different techniques, including exposure of male pupae to sterilizing radiation and infection with sterilizing vertically-transmitted bacteria such as *Wolbachia* [20, 21, 25, 27]. Although controversial, certain forms of gene drive, engineered using CRISPR-CAS9 technology, may also lead to population declines through male sterility [28].

SIT was first successfully implemented in Florida, USA, in 1958 to eradicate screwworm flies *Cochliomya omnivorax* [20, 27, 29, 30]. In this instance, about 50 million sterile flies were released each week over an 18 month period within an 85,000 square mile area [27]. The technique has also been successfully used against a range of agricultural pest insects, such as fruit flies, moths and tsetse flies [31]. Sterile mosquitoes have so far been used in the Cayman Islands, Brazil, USA, Panama and India [24]. Recently, the company Verily (formerly Google Life Sciences) released 20 million sterile male mosquitoes in two neighborhoods in Fresno County over a period of 20 weeks in an effort to reduce the population

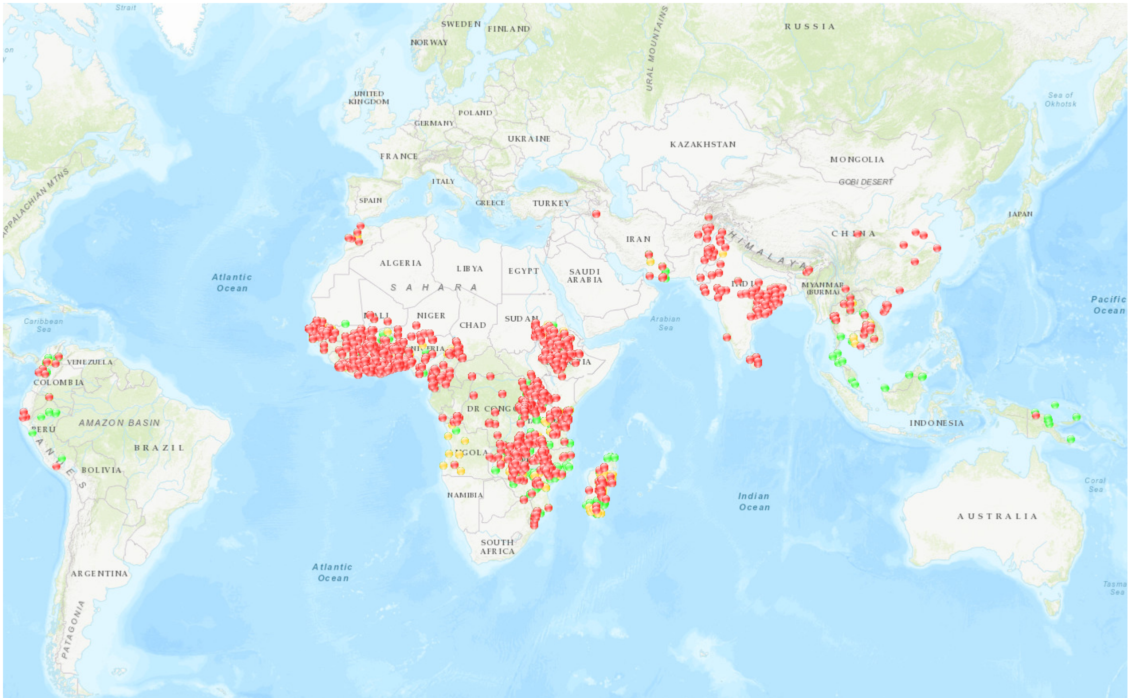


Figure 1: **Red: Confirmed resistance, Yellow: Possible resistance and Green: Susceptibility**. Source: `http://anopheles.irmapper.com/`

of *Aedes aegypti* mosquitoes (the primary vector of dengue, chikungunya, yellow fever and Zika viruses) which have been present in California's central valley since 2013 [22]. **Zheng *et al.* [26] recently studied the combined impact of using incompatible insect techniques (IIT) and SIT to control the population abundance of *Aedes albopictus* mosquitoes in Guangzhou province of China during the peak mosquito breeding seasons between 2016 and 2017 (based on the weekly release of over 160,000 of these mosquitoes *per* hectare)**.

Although the use of SIT has been proven to be effective (in reducing the abundance of the targeted mosquito species population in a community) under certain conditions, it comes with a number of challenges [20, 21, 24, 26, 27, 32, 33]. Depending on the distribution and abundance of the target species, large numbers of sterile males may have to be reared and released over a large area [24, 26, 27, 32, 33]. Even larger numbers of sterile males will be required if sterilization also reduces male mating fitness, since this will increase the likelihood of adult female mosquitoes mating with fertile adult wild male mosquitoes [32]. Furthermore, although SIT is highly species-specific and, therefore, less likely to have unintentional adverse environmental consequences [20, 21, 24, 26, 27, 32, 33], this specificity may be problematic in settings where there are multiple competent vector species requiring control.

Another important factor that affects the dynamics of mosquito population is the seasonal variabilities in climate factors, such as temperature and precipitation [6, 8, 14, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43]. In particular, changes in temperature is known to significantly affect the distribution and ecology of *Anopheles* mosquitoes by altering their maturation, survival and biting rates [8, 34, 35, 36, 37, 39, 41]. Consequently, this study will additionally assess how such seasonal variability will affect the effectiveness of the SIT program in curtailing the abundance of the targeted mosquito population.

Numerous mathematical models have been developed and used to assess the population-level effectiveness of SIT on the population abundance and dynamics of mosquito populations (see, for instance, [21, 25, 27, 32, 33, 44, 45]). Anguelov *et al.* [44] used a deterministic model to analyze the impact of the SIT as a measure for the control of *Anopheles* mosquito. Cai *et al.* [21] formulated a model of the interactive dynamics of wild and sterile mosquitoes by incorporating different strategies in releasing sterile mosquitoes. Dumont *et al.* [45] formulated and analysed a model of SIT to prevent, reduce, eliminate or stop an epidemic of Chikungunya. Esteva *et al.* [27] proposed a model to assess the effect of irradiated (or transgenic) male insect introduction in a previously infested region. Gentle *et al.* [32] used agent-based modelling of emerging and theoretical implementations of transgenic SIT in *Anopheles gambiae* for the control of malaria. Thome *et al.* [25] presented a mathematical model to describe the dynamics of mosquito population when sterile male mosquitoes (produced by irradiation) are introduced as a biological control along with the application of insecticide. Finally, White *et al.* [33] used a stage-structured model to explore the impact of pulsed releases of sterile males on a mosquito population in which sterilized males suffer a reduction in mating fitness.

The primary objective of the current study is to use mathematical modeling and simulations to assess the impact of the periodic release of sterile male mosquitoes (using SIT) on the local abundance of *Anopheles* mosquitoes. The potential impact of seasonal variations in temperature on the population-level effectiveness of the SIT control strategy will also be assessed. In other words, we will seek to determine whether or not local (seasonal) changes in temperature might affect the utility of the SIT vector control strategy. To achieve these objectives, a novel mathematical model, which takes the form of an impulsive, deterministic system of nonlinear differential equations, will be developed. The paper is organised as follows. The model is formulated in Section 2. Its basic qualitative features are also given. Simulations of the model, using temperature data from the Kipsamoite area of Kenya (an area with high *Anopheles* abundance), are reported in Section 3.

2 Model Formulation

The model to be formulated is based on the dynamics of *Anopheles* mosquitoes. The total mosquito (immature and mature) population at time t, denoted by $N_V(t)$, is subdivided into subpopulations of eggs ($E(t)$), larvae ($L(t)$), pupae ($P(t)$), unmated female adult mosquitoes ($F_u(t)$), female adult mosquitoes that mated with fertile wild males ($F_{m,w}(t)$), female adult mosquitoes that mated with sterile males ($F_{m,s}(t)$), wild adult male mosquitoes ($M_w(t)$) and sterile adult male mosquitoes ($M_s(t)$). Hence,

$$N_V(t) = E(t) + \sum_{j=1}^{4} L_j(t) + P(t) + F_u(t) + F_{m,w}(t) + F_{m,s}(t) + M_w(t) + M_s(t).$$

First of all, upon emergence, adult female mosquitoes search for male mosquitoes to mate [46]. Let β represent this (mating) rate. The mean time required for an adult female mosquito to find a mating partner (i.e., an adult male mosquito) is

inversely proportional to the local density of adult male mosquitoes that are able to mate [33, 47, 48]. It is assumed that while all wild-type adult male mosquitoes are able to mate, only a fraction, $0 < \eta \leq 1$, of adult sterile male mosquitoes are able to mate (this is due to a number of factors, such as development, culturing and production processes, including storage temperature and compaction rate [26, 31, 33, 49, 50, 51]). Therefore, once an adult male mosquito is found, it is assumed that the mating process is completed within ζ units of time [52]. Hence, the mean time for an adult female mosquito to find an adult male mosquito (and mate with it), denoted by $\mathcal{H}_{mean}$, is given by:

$$\mathcal{H}_{mean} = \zeta + \frac{1}{\beta(M_w + \eta M_s)}.$$

Furthermore, the *per capita* rate at which adult female mosquitoes mate with adult male mosquitoes (denoted by $\mathcal{Y}_a(t)$) is inversely proportional to this time. That is,

$$\mathcal{Y}_a(t) = -F_u \frac{1}{\mathcal{H}_{mean}} = -F_u \frac{\beta(M_w + \eta M_s)}{1 + \beta\zeta(M_w + \eta M_s)}.$$

Likewise, the rates at which adult female mosquitoes mate with adult male wild-type (denoted by $\mathcal{Y}_b(t)$) or sterile male mosquitoes (denoted by $\mathcal{Y}_c(t)$) are given, respectively, by

$$\mathcal{Y}_b(t) = \beta \left[\frac{M_w}{1 + \beta\zeta(M_w + \eta M_s)}\right] F_u \text{ and } \mathcal{Y}_c(t) = \beta \left[\frac{\eta M_s}{1 + \beta\zeta(M_w + \eta M_s)}\right] F_u.$$

Figure 2 depicts the possible mating outcomes between sterile male mosquitoes and adult wild female mosquitoes. It is worth emphasizing that the model to be designed in this study accounts for the seasonal fluctuations in temperature. In particular, fluctuations in both ambient/air temperature (denoted by $T_A(t)$) and water temperature (denoted by $T_W(t)$) will be incorporated into the model.

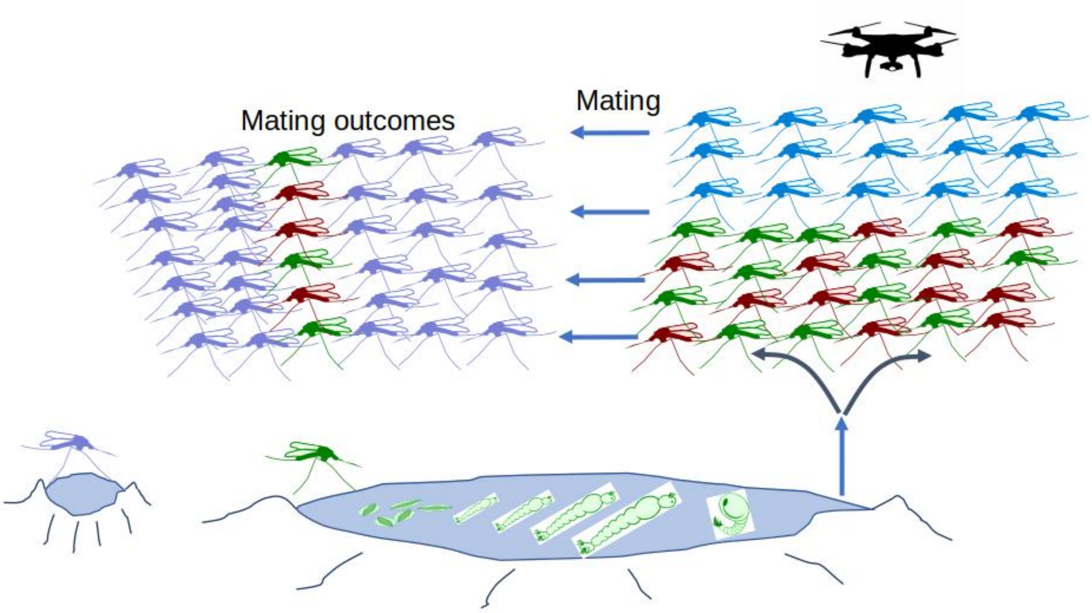


Figure 2: Mating outcomes between sterile male mosquitoes and wild adult female mosquitoes. Colors: Blue–Sterile male mosquitoes; Brown–Wild male mosquitoes; Green–Unmated female mosquitoes; Purple–Mated female mosquitoes that would be laying (nonhatching) eggs.

The model for the population dynamics of *Anopheles* mosquitoes, which incorporates, in addition to mosquito lifecycle dynamics, the intermittent release of sterile male mosquitoes and the seasonal fluctuation in temperature, is given by the following deterministic, impulsive, non-autonomous system of non-linear differential equations (where a dot represents differentiation with respect to time t):

$$
\left\{
\begin{array}{l}
\left.
\begin{aligned}
\dot{E} &= \phi_E\psi_E\left(1-\frac{E}{K_E}\right)_* F_{m,w} - \left[\sigma_{\mathbf{E}}(\mathbf{T_W}) + \mu_E(T_W)\right]E,\\
\dot{L}_1 &= \sigma_{\mathbf{E}}(\mathbf{T_W})E - \left[\sigma_{L_1}(T_W) + \mu_L(T_W) + \delta_L L\right]L_1,\\
\dot{L}_j &= \sigma_{L_{j-1}}(T_W)L_{j-1} - \left[\sigma_{L_j}(T_W) + \mu_L(T_W) + \delta_L L\right]L_j;\ \text{with } L=\sum_{j=1}^{4} L_j,\ \ j=2,3,4,\\
\dot{P} &= \sigma_{L4}(T_W)L_4 - \left[\sigma_{\mathbf{P}}(\mathbf{T_W}) + \mu_P(T_W)\right]P,\\
\dot{F}_u &= r\sigma_{\mathbf{P}}(\mathbf{T_W})P - \left[\frac{\beta(M_w+\eta M_s)}{1+\beta\zeta(M_w+\eta M_s)} + \mu_q(T_A)\right]F_u,\\
\dot{M}_w &= (1-r)\sigma_{\mathbf{P}}(\mathbf{T_W})P - \mu_q(T_A)M_w,\\
\dot{F}_{m,w} &= \left[\frac{\beta M_w}{1+\beta\zeta(M_w+\eta M_s)}\right]F_u - \mu_q(T_A)F_{m,w},\\
\dot{F}_{m,s} &= \left[\frac{\beta\eta M_s}{1+\beta\zeta(M_w+\eta M_s)}\right]F_u - \mu_q(T_A)F_{m,s},\\
\dot{M}_s &= -\mu_q M_s,
\end{aligned}
\right\} t \neq n\tau\\
\left.
\begin{aligned}
E(n\tau^+) &= E(n\tau),\\
L_1(n\tau^+) &= L_1(n\tau),\\
L_j(n\tau^+) &= L_j(n\tau),\\
P(n\tau^+) &= P(n\tau),\\
F_u(n\tau^+) &= F_u(n\tau),\\
M_w(n\tau^+) &= M_w(n\tau),\\
F_{m,w}(n\tau^+) &= F_{m,w}(n\tau),\\
F_{m,s}(n\tau^+) &= F_{m,s}(n\tau),\\
M_s(n\tau^+) &= M_s(n\tau) + C_R,
\end{aligned}
\right\} t = n\tau,\ \ n = 0,1,2,\cdots\ .
\end{array}
\right.
\tag{2.1}
$$

A schematic diagram of the model (2.1) is depicted in Figure 3, and the state variables and parameters of the model are described in Table 1.

In the formulation of the model (2.1), it is assumed, first of all, that only adult female mosquitoes that have mated with wild male mosquitoes (i.e., $F_{m,w}$ mosquitoes) lay eggs (i.e., adult female mosquitoes that mate with sterile male mosquitoes will not lay eggs, owing to the assumed 100% effectiveness of SIT to inhibit egg laying [27, 44]). Eggs laying occurs at a logistic rate $\phi_E\psi_E\left(1-\frac{E}{K_E}\right)_*$, where ϕ_E is the egg oviposition rate, ψ_E is the number of eggs laid *per* oviposition and K_E (the notation $r_* = \max\{0, r\}$ is used to ensure the non-negativity of the logistic term) is the carrying capacity for eggs (a measure of the exhaustion of space for laying the eggs) [6, 37, 38, 53, 54]. Eggs hatch into larvae **at a temperature-dependent rate** $\sigma_E(T_W)$, larvae mature into pupae at **temperature-dependent rates** $\sigma_{Lj}(T_W)$ (with $j = 1, 2, 3, 4$ accounting for the four larval instar stages), and pupae mature into adult mosquitoes **at a temperature-dependent rate** $\sigma_P(T_W)$. Among these newly emerging adult mosquitoes, it is assumed that a proportion, r $(0 < r < 1)$, are females (and the remaining proportion, $1-r$, are males). Natural mortality occurs in all mosquito life stages at a temperature-dependent rates $\mu_E(T_W), \mu_L(T_W), \mu_P(T_W)$ and $\mu_q(T_A)$, respectively, while larvae are also additionally lost due to density-dependent mortality at a rate $\delta_L L$ [8] (where $\delta_L = 1/K_L$, with K_L being the carrying capacity of larvae). Finally, sterile adult male mosquitoes are released to the environment periodically. That is [32, 45],

$$M_s(n\tau^+) = M_s(n\tau) + C_R,$$

where τ is the time lag between successive sterile male mosquito releases and $n\tau^+$ is the moment immediately after the nth sterile release. At each release time $n\tau$, a constant number of sterile male mosquitoes (C_R) are released to the environment. **For instance, during the summer of 2015, a joint US-China research team released 7,000 to 10,000 sterile male mosquitoes in the Sand island (a small island in Guandong province of China) thrice a week in March [23]. Similarly, in a more recent field study in Guangzhou province of China [26], over 160,000 sterile male mosquitoes were released *per* hectare every week (during the peak mosquito breeding seasons between 2016 and 2017). Sterile male mosquitoes are typically released in areas where the density of wild female mosquitoes reaches a certain threshold level [23].**

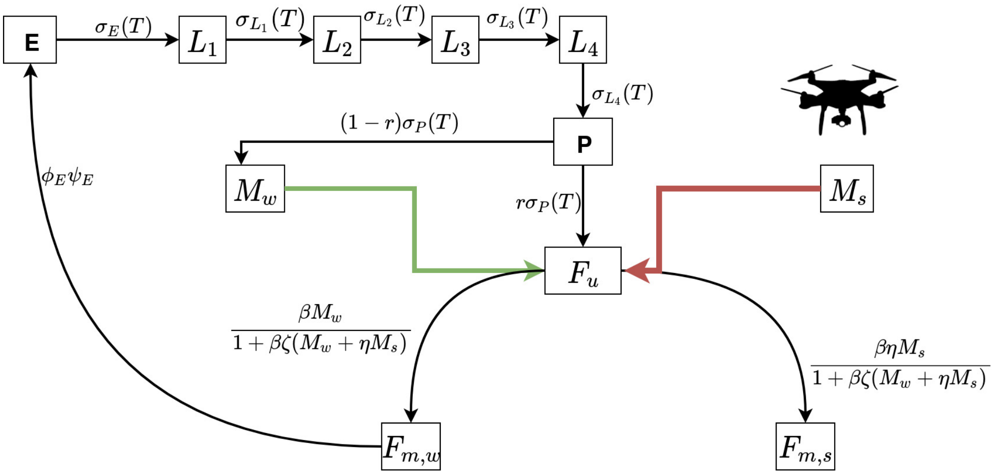


Figure 3: Flow diagram of the model.

The model (2.1) extends numerous mathematical models that incorporate the implementation of SIT vector control strategy, such as those in [21, 25, 27, 32, 33, 44, 45], in several ways. In particular,

(i) it extends the models in [21, 25, 27, 32, 33, 44, 45] by including the dynamics of immature mosquitoes (i.e., the compartments E, $L_j (j = 1, 2, 3, 4)$ and P);

(ii) it extends the models in [21, 25, 27, 32, 44] by including periodic releases of sterile male mosquitoes (i.e., $M_s(n\tau^+) = M_s(n\tau) + C_R$);

(iii) it extends the models in [21, 25, 27, 32, 33, 44, 45] by including a novel mating function that realistically accounts for the detailed mating processes and outcomes;

(iv) it extends all of the aforementioned studies by incorporating the effect of local (seasonal) temperature variability on the dynamics of the mosquito population (in fact, to the best of the authors' knowledge, seasonal variation in temperature has not previously been investigated in SIT-based mosquito control modeling studies, despite the fact that mosquito and many other arthropod populations are strongly affected by seasonal changes in temperature and precipitation) [1, 3, 6, 7, 8, 14, 55, 56].

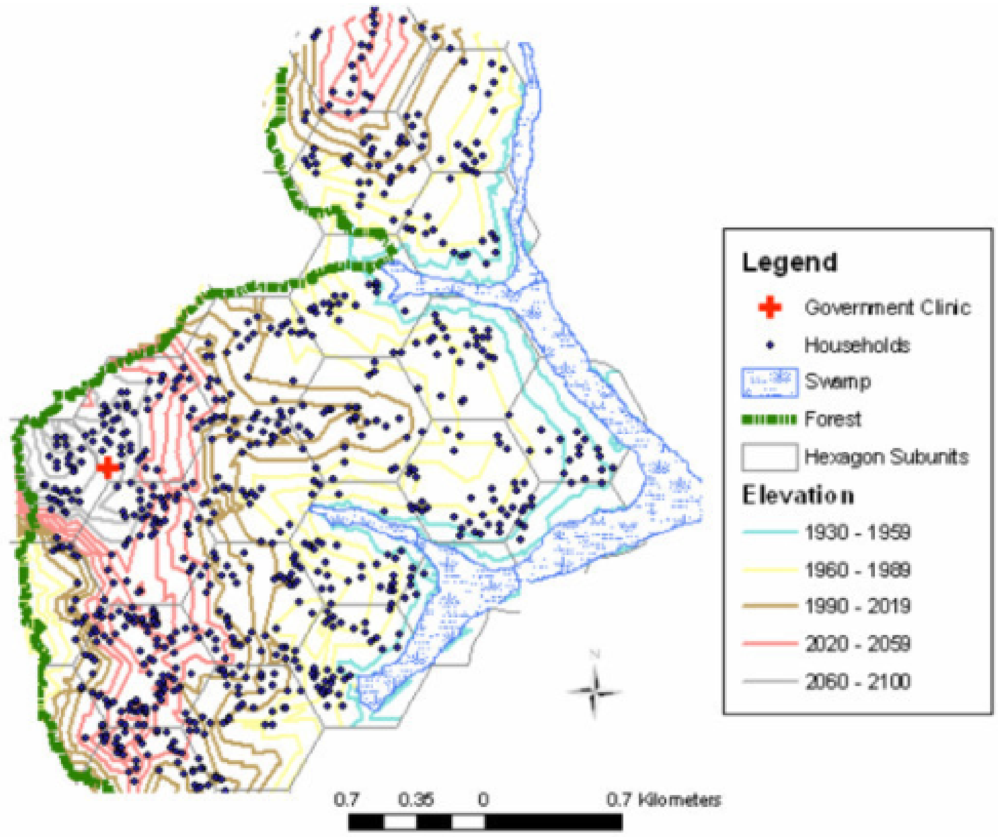


Figure 4: Geography and household locations in Kipsamoite area (within Nandi Hills District) of Kenya [57].

2.1 Formulation of Thermal-response Functions

The functional forms of the temperature-dependent parameters in the model (2.1) are based on the biology of *Anopheles* mosquitoes, and are formulated as follows. First of all, we adopt the relationship between water temperature and overall time from egg to adult, $\mathcal{D}_{EA}(T_W)$, given by Bayoh and Lindsay [56] (based on laboratory data):

$$\frac{1}{\mathcal{D}_{EA}(T_W)} = -0.05 + 0.005T_W - 2.139 \times 10^{-16}e^{T_W} - 2.81357 \times 10^5 e^{-T_W}.$$

For the parameters related to the mosquito development rates in the immature stages, we determined stage-specific development times as a function of water temperature from Figure 1 of Bayoh and Lindsay [56], as shown in Figure 5. It can be seen from Figure 5 that the development times are similar across all immature stages of the mosquito lifecycle, with appreciable overlap in the temperature-dependent curves. Hence, it is assumed that the average duration in all immature stages are the same. Further, the uniform temperature-dependent development rates are given as (recalling that $L = L_1 + L_2 + L_3 + L_4$):

$$\sigma_E(T_W) = \sigma_P(T_W) = \sigma_L(T_W) = 6\frac{1}{\mathcal{D}_{EA}(T_W)}. \tag{2.2}$$

It is worth mentioning that some field studies suggest that the distribution of hatching time in *Anopheles gambiae* is relatively constant [58].

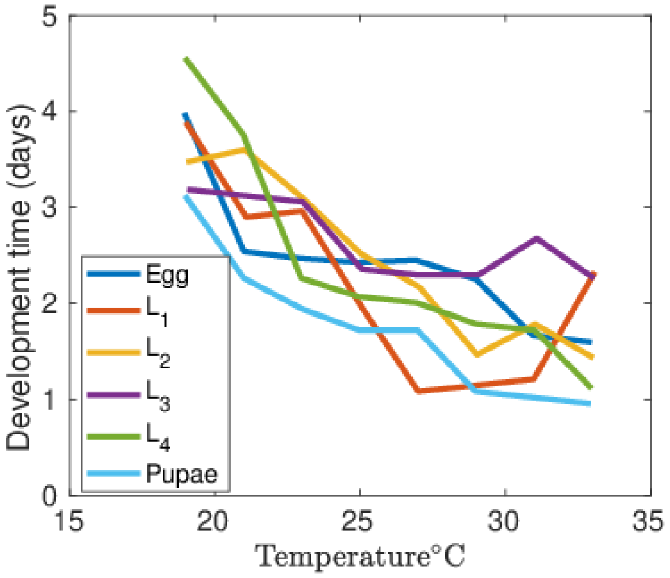


Figure 5: Development times in the immature mosquito stages. Data extracted from Figure 1 of Bayoh and Lindsay [56].

The functional forms of the *per capita* death rates (μ_E for eggs; μ_L for larvae and μ_P for pupae) are obtained by fitting the data on larval survival times reported by Bayoh and Lindsay [56], to the following quartic **polynomial** (note that survival time is the inverse of death rate):

$$\mu_i(T_W) = 8.929 \times 10^{-6}T_W^4 - 9.271 \times 10^{-4}T_W^3 + 3.536 \times 10^{-2}T_W^2 - 0.5814T_W + 3.509;$$

$i = E, L, P$. The temperature-dependent mortality rate of adult mosquitoes ($\mu_q(T_A)$) is given by [59]:

$$\frac{1}{\mu_q(T_A)} = \max(-11.8239 + 3.3292T_A - 0.0771T_A^2, 0.1).$$

In the formulation of the model (2.1), it is assumed, for simplicity, that near the surface of the water, air and water temperature are approximately equal [6, 14] (so that, $T_A(t) = T_W(t) = T(t)$). The following piecewise-constant function is proposed to model temperature variability:

$$T(t) = v(T_{obs} - T_{mean}) + T_{mean}, \tag{2.3}$$

where T_{mean} is the mean annual temperature in the chosen community, T_{obs} is the observed mean monthly temperature and v is a parameter that governs the amplitude of seasonal fluctuations around the mean annual temperature. The observed mean monthly temperature for Kipsamoite area of Kenya for the year 2016 is tabulated in Table 2 [60]. This formulation allows us to study the impact of increasing seasonal variation in temperature using temperature profiles typical of areas with moderate to high densities of wild adult female *Anopheles* mosquitoes. In particular, we note that the model (2.1) reduces to a non-seasonally-forced model when the parameter v is set to 0.

2.2 Timing of Release of Sterile Male Mosquitoes

Following White *et al.* [33], we define the *release effect statistic*, denoted by $R(t)$, given by:

$$R(t) = \frac{\int_{\tau}^{t+\tau} N_1(s)ds}{\int_{\tau}^{t+\tau} N_0(s)ds}, \tag{2.4}$$

where N_1 is the total abundance of adult females over a period of time with the control (SIT) and N_0 is the total abundance of adult females over that same period without the control. **Following White *et al.* [33], Equation (2.4) yields the following three ecological interpretations for the release statistic R:**

- **(i) If $R(t) < 1$, then the sterile male release (i.e., SIT control) has a negative (desirable) effect on the wild adult female mosquito population (i.e., the SIT control decreases the population abundance of the wild adult female mosquito).**
- **(ii) If $R(t) = 1$, then the SIT control has no relative effect on the wild adult female mosquito population (i.e., SIT control does not increase or decrease the wild adult female mosquito population).**
- **(iii) If $R(t) > 1$, then the SIT control has a positive (detrimental)effect on the wild adult female mosquito population (i.e., SIT increases the population abundance of the wild adult female mosquitoes).**

In other words, an SIT-based mosquito control strategy that has an associated release effect statistic value less than unity will lead to an effective control of the local abundance of the targeted (wild) adult mosquito population.

2.3 Basic Qualitative Properties of the Model

The basic qualitative properties of the model (2.1) will now be analysed. Let $\mathbb{R}_+ = [0, \infty)$, $\mathbb{R}_+^{11} = \{\mathcal{B} \in \mathbb{R}_+^{11} : \mathcal{B} \geq 0\}$, where

$$\mathcal{B} = (E(t), L_j(t), P(t), F_u(t), F_{m,w}(t), F_{m,s}(t), M_w(t), M_s(t));\ j = 1, 2, 3, 4.$$

Consider the following ecologically-feasible region of the model (2.1):

$$\begin{aligned}\Omega = \big\{\mathcal{B} \in \mathbb{R}_+^{11} : E(t) \leq K_E, L_1(t) \leq L_1^\diamond, L_2(t) \leq L_2^\diamond, L_3(t) \leq L_3^\diamond, L_4(t) \leq L_4^\diamond, P(t) \leq P^\diamond,\\ F_u \leq F_u^\diamond, M_w \leq M_w^\diamond, F_{m,w} \leq F_{m,w}^\diamond, F_{m,s} \leq F_{m,s}^\diamond, M_s \leq M_s^\diamond\big\},\end{aligned}$$

where,

$$\begin{aligned}
&L_1^\diamond = \frac{\sigma_E K_E}{\sigma_{L_1} + \mu_L},\ L_2^\diamond = \frac{\sigma_{L_1} L_1^\diamond}{\sigma_{L_2} + \mu_L},\ L_3^\diamond = \frac{\sigma_{L_2} L_2^\diamond}{\sigma_{L_3} + \mu_L},\ L_4^\diamond = \frac{\sigma_{L_3} L_3^\diamond}{\sigma_{L_4} + \mu_L},\ P^\diamond = \frac{\sigma_{L_4} L_4^\diamond}{\sigma_P + \mu_P},\\
&M_w^\diamond = \frac{(1-r)\sigma_P P^\diamond}{\mu_q},\ F_u^\diamond = \frac{r\sigma_P P^\diamond}{Q_1},\ F_{m,s}^\diamond = \frac{Q_2}{\mu_q},\ F_{m,w}^\diamond = \frac{Q_3}{\mu_q},\ M_s^\diamond = \frac{C_R e^{-\mu_q(t-n\tau)}}{1-e^{-\mu_q\tau}},\\
&\left[\frac{\beta(M_w^\diamond + \eta M_s^\diamond)}{1+\beta\zeta(M_w^\diamond + \eta M_s^\diamond)} + \mu_q\right] \leq Q_1,\ \frac{\beta M_w^\diamond}{1+\beta\zeta(M_w^\diamond + \eta M_s^\diamond)} \leq Q_2,\ \text{and}\\
&\frac{\beta\eta M_s^\diamond}{1+\beta\zeta(M_w^\diamond + \eta M_s)} \leq Q_3.
\end{aligned} \tag{2.5}$$

Furthermore, it is worth recalling the following definitions:

Definition 2.1 *[23, 61]. Let $r(t) = r(t, t_0, x_0)$ be a solution of (2.1) on $[t_0, t_0 + a)$. Then $r(t)$ is said to be a maximal solution of (2.1), if for any solution $x(t) = x(t, t_0, x_0)$ of (2.1) existing on $[t_0, t_0 + a)$, the inequality*

$$x(t) \leq r(t), t \in [t_0, t_0 + a) \tag{2.6}$$

holds. A minimal solution $\rho(t)$ may be defined in a similar way by reversing the inequality of (2.6)

Definition 2.2 *[23, 61]. Let $V : \mathbb{R}_+ \times \mathbb{R}_+^{11} \longrightarrow \mathbb{R}_+$. Then V is said to belong to a class V_0 if V satisfies:*

(i) V is continuous on $(n\tau, (n+1)\tau] \times \mathbb{R}_+^{11}$ and $\lim\limits_{(t,y)\to(n\tau^+,x)} V(t,x) = V(n\tau^+, x)$ for every $x \in \mathbb{R}_+^{11}, n \in N$;

(ii) V is locally Lipschitz continuous with respect to x.

Definition 2.3 *[23, 61]. Let $V \in V_0$, for $(t, x) \in (n\tau, (n+1)\tau] \times R^{11}$. Define the upper right derivative with respect to (2.1) as*

$$D^+V(t,x) = \lim_{h\to 0^+} \sup \frac{1}{h}[V(t+h, x+hf(t,x)) - V(t,x)].$$

Theorem 2.1 *[23, 61]. Let* $V : \mathbb{R}_+ \times \mathbb{R}_+^{11} \longrightarrow R_+$, $V \in V_0$. *Suppose*

$$\begin{aligned} D^+V(t,x) &\leq g(t, V(t,x)),\ t \neq t_n,\ n = 1, 2, \cdots, \\ V(t_n^+) &\leq m_n(V(t_k)),\ t = t_n,\ n = 1, 2, \cdots, \end{aligned} \tag{2.7}$$

where $g \in C(R_+ \times \mathbb{R}_+, \mathbb{R}), m_k \in C(\mathbb{R}, \mathbb{R})$ *and* $m_n(u)$ *is non-decreasing in* u *for each* $n = 1, 2, \ldots..$ *Let* $r(t)$ *be the maximal solution of the scalar impulsive differential equation*

$$\begin{aligned} \dot{u}(t) &= g(t,u),\ \ t \neq t_n, \\ u(t_n^+) &= m_n(u(t_n)),\ \ t = t_n \\ u(t_0) &= u_0, \end{aligned} \tag{2.8}$$

which exists on $[t_0, \infty)$. *Then,* $V(t_0^+, x_0) \leq u_0$ *implies that* $V(t, x(t)) \leq r(t)$ *for* $t \geq t_0$ *where* $x(t) = x(t, t_0, x_0)$ *is any solution of* (2.1) *on* $[t_0, \infty)$. *Similar result can be obtained when all the directions of the inequalities in Theorem 2.1 are reversed and* $m_n(u)$ *is non-increasing.*

Remark 2.1 *In Theorem 2.1, the function* g *must be smooth enough to guarantee the existence and uniqueness of solution for* (2.8). *Hence,* $r(t)$ *is indeed the unique solution of* (2.8).

Let $x(t) = (E(t), L_j(t), P(t), F_u(t), F_{m,w}(t), F_{m,s}(t), M_w(t), M_s(t))^T$, with $j = 1, 2, 3, 4$, be a continuous solution of the model (2.1) on $(n\tau, (n+1)\tau], n \in Z_+$, and $x(n\tau^+) = \lim\limits_{t \to n\tau^+} x(t)$ exists. Then, the global existence and uniqueness of solutions of the model (2.1) is determined by the smoothness of $f = (\mathbf{g})^T$ where $\mathbf{g}$ is the right-hand side vector of the model (2.1). Consider, now, the impulsive component of the model (2.1), given by:

$$\begin{aligned} \dot{M}_s &= -\mu_s M_s, & t &\neq n\tau, \\ M_s(n\tau^+) &= M_s(n\tau) + C_R, & t &= n\tau, \\ M_s(0^+) &\geq 0. \end{aligned} \tag{2.9}$$

We claim the following result.

Lemma 2.1 *The impulsive system* (2.9) *has a unique positive periodic solution and* $M_s^\diamond(t)$ *is globally-asymptotically stable, where*

$$\begin{aligned} M_s^\diamond(t) &= \frac{C_R e^{-\mu_q(t-n\tau)}}{1 - e^{-\mu_q\tau}},\quad n\tau < t \leq (n+1)\tau, \\ M_s^\diamond(0^+) &= \frac{C_R}{1 - e^{-\mu_q\tau}}. \end{aligned} \tag{2.10}$$

Proof. It follows from the first equation of system (2.9) that,

$$M_s(t) = M_s(n\tau^+) e^{-\mu_q(t-n\tau)},\quad n\tau < t \leq (n+1)\tau.$$

The following stroboscopic map can be established using the second equation of (2.9)[62]:

$$M_s[(n+1)\tau^+] = M_s[(n+1)\tau] + C_R = M_s(n\tau^+). \tag{2.11}$$

Hence, the unique positive (periodic) solution of (2.9) is given by

$$\begin{aligned} M_s^{\diamond}(t) &= \frac{C_R e^{-\mu_q(t-n\tau)}}{1-e^{-\mu_q\tau}}, \quad n\tau < t \leq (n+1)\tau, \\ M_s^{\diamond}(0^+) &= \frac{C_R}{1-e^{-\mu_q\tau}}. \end{aligned} \tag{2.12}$$

□

We further claim the following positivity result.

Theorem 2.2 Consider the model (2.1). *Each component of the solution of the model, with non-negative initial conditions, remains positive and bounded for all time $t > 0$.*

Proof. The positivity of $M_s(t)$ follows from Lemma 2.1. It should be noted that the right-hand side of each of the first ten equations of the model (2.1) is continuous and locally-Lipschitz at $t = 0$. Hence, a solution of the model with non-negative initial conditions exists and is unique for all time $t > 0$. Now, to show that the periodic solution $M_s(t)$ is bounded, it can be recalled from Lemma 2.1 that system (2.9) has a globally-asymptotically stable positive periodic solution. This solution satisfies $\lim\limits_{t\to\infty} M_s(t) \leq M_s^{\diamond}(t)$. Furthermore, since $\phi_E\psi_E\left(1-\frac{E}{K_E}\right)_* \geq 0$, it follows from the first equation of the model (2.1) that $E(t) \leq K_E$ for all time $t > 0$. Similarly, it follows from the second equation of the model (2.1) that

$$\dot{L}_1 = \sigma_E E - \left(\sigma_{L_1} + \mu_L\right) L_1 \leq \sigma_E K_E - \left(\sigma_{L_1} + \mu_L\right) L_1,$$

so that $\limsup\limits_{t\to\infty} L_1(t) \leq \dfrac{\sigma_E K_E}{\sigma_{L_1}+\mu_L} = L_1^{\diamond}$. Using a similar approach, it can be shown that $\limsup\limits_{t\to\infty} L_2(t) \leq \dfrac{\sigma_{L_1} L_1^{\diamond}}{\sigma_{L_2}+\mu_L} = L_2^{\diamond}$, $\limsup\limits_{t\to\infty} L_3(t) \leq \dfrac{\sigma_{L_2} L_2^{\diamond}}{\sigma_{L_3}+\mu_L} = L_3^{\diamond}$, $\limsup\limits_{t\to\infty} L_4(t) \leq \dfrac{\sigma_{L_3} L_3^{\diamond}}{\sigma_{L_4}+\mu_L} = L_4^{\diamond}$, $\limsup\limits_{t\to\infty} P(t) \leq \dfrac{\sigma_{L_4} L_4^{\diamond}}{\sigma_P+\mu_P} = P^{\diamond}$, $\limsup\limits_{t\to\infty} M_w(t) \leq \dfrac{(1-r)\sigma_P P^{\diamond}}{\mu_q} = M_w^{\diamond}$, $\limsup\limits_{t\to\infty} F_u(t) \leq \dfrac{r\sigma_P P^{\diamond}}{Q_1} = F_u^{\diamond}$, $\limsup\limits_{t\to\infty} F_{m,s}(t) \leq \dfrac{Q_2}{\mu_q} = F_{m,s}^{\diamond}$, $\limsup\limits_{t\to\infty} F_{m,w}(t) \leq \dfrac{Q_3}{\mu_q} = F_{m,w}^{\diamond}$, where

$$\left[\frac{\beta(M_w^{\diamond}+\eta M_s^{\diamond})}{1+\beta\zeta(M_w^{\diamond}+\eta M_s^{\diamond})} + \mu_q\right] \leq Q_1, \quad \frac{\beta M_w^{\diamond}}{1+\beta\zeta(M_w^{\diamond}+\eta M_s^{\diamond})} \leq Q_2 \text{ and } \frac{\beta\eta M_s^{\diamond}}{1+\beta\zeta(M_w^{\diamond}+\eta M_s)} \leq Q_3.$$

Hence, all solutions of the model (2.1) are bounded for all time $t > 0$. □

In summary, it follows from the above analyses that the model (2.1) is well-posed mathematically. Hence, it is sufficient to study its dynamics in the invariant region Ω.

3 Numerical Simulations

In this section, the model (2.1) will be simulated, using the mosquito ecology data in Table 3 (together with the mean monthly temperature data for **the Kipsamoite area in the Nandi Hills District of Kenya** in Table 2), to gain insight into the local mosquito dynamics in the absence or presence of SIT and seasonal variation in local temperature.

3.1 Mosquito Ecology in the Absence of SIT and Seasonality

Here, the model (2.1) is simulated in the absence of SIT (i.e., $C_R = 0$) and seasonal variation in temperature (i.e., $v = 0$). These simulations allow for the determination of the worst-case mosquito abundance (since $C_R = 0$) for the case where the mean annual temperature is used (i.e., no seasonal variation in temperature). That is, for these simulations, the temperature-dependent parameters of the model (2.1), given in Section 2, are computed using the mean annual temperature for the Kipsamoite area (which is 22.2°C [60]). The simulation results obtained show that the population of mosquitoes (both immature and adult) rapidly reaches a non-trivial (endemic) steady-state (Figures 6a-e). Since no sterile male mosquitoes are released in these simulations, the release effect statistic (R) is unity (Figure 6f).

The effect of mean monthly temperature on the local population abundance of immature and adult mosquitoes is monitored by simulating the model (2.1), using the various values of the mean monthly temperature for the Kipsamoite area given in Table 2. The results obtained (depicted in Figure 7) show that the maximum abundance of both the immature and adult mosquitoes is achieved when the mean monthly temperature is about 30°C (which is 7.2°C higher than the current mean annual temperature for the Kipsamoite area or Nandi Hill region [60]).

3.2 Assessment of the Impact of SIT on Mosquito Abundance

The model (2.1) is now simulated to assess the impact of SIT-based vector control on the local population abundance of the wild adult female *Anopheles* mosquitoes. The model is, first of all, ran for a period of one year (so that the system settles at its non-trivial (endemic) steady-state). A fixed number of sterile male mosquitoes (C_R) are then released after every release period (τ). For these simulations, C_R is initially set at 10,000 sterile male mosquitoes. Further, three periods of release (τ) are chosen, namely weekly (in line with the SIT-IIT implementation in two islands in Guangzhou province of China during peak mosquito seasons in 2016-2017 [26]), bi-weekly and every three weeks. For these simulations, we consider the cases with and without seasonal variation in temperature, as described below.

3.2.1 No seasonal variation in temperature ($v = 0$)

The model (2.1) is simulated using the parameter values tabulated in Table 3, for the case with no seasonal variation in temperature (i.e., $v = 0$). Furthermore, the temperature-dependent parameters of the model are evaluated at the mean annual temperature of 22.2°C. As stated above, the model, under this setting, is initially ran for a period of one year before the sterile male mosquitoes are released for another one year duration (Figure 8a). For these simulations, C_R is initially set to 10,000 sterile male mosquitoes. The simulation results obtained show a dramatic decrease in the population of eggs and the first three larval instars (from the pre-SIT baseline equilibrium values), before settling down to a positive (mosquito-persistent) steady-state following the release of the sterile male mosquitoes for a period of one year (Figures 8b-c). Surprisingly, such weekly release (of 10,000 sterile male mosquitoes) resulted in an increase (from the pre-SIT baseline) in the fourth larval instar and pupal stages, leading to convergence to a stable endemic level (Figure 8c).

Furthermore, an increase in the population abundance of the mated adult female mosquitoes was observed (Figure 8d). This is a direct consequence of the decrease in the population of fertilized wild adult female mosquitoes, and the increase in the population of fertilized female mosquitoes that would be laying nonhatching eggs (Figure 8e). Finally, for these simulations, the release effect statistic (R) exceeds unity (Figure 8f). Thus, it follows from the simulations in Figure 8 that the weekly release of 10,000 sterile male mosquitoes ($C_R = 10,000$ with $\tau = 7$) in the community, for the case when seasonal variation in temperature is not accounted for (i.e., $v = 0$), increases the population abundance of adult female mosquitoes. Hence, this level of sterile male release and frequency of release ($C_R = 10,000$ and $\tau = 7$) induces detrimental effect to the community (by increasing the local abundance of the mated adult mosquito population..... since both classes of mated adult female mosquitoes can transmit disease to humans, the epidemiological consequence of this SIT-induced increase in the mated adult female mosquito population is a corresponding increase in malaria burden in the community). Qualitatively similar trends were observed when the period of release is increased to bi-weekly, every three or four weeks (Figure 9). **This result differs from one of the main conclusions in the White *et al.* study [33], which suggests that the control of the *Anopheles* population is more effective when smaller numbers of sterile male mosquitoes are released more frequently (as against releasing larger numbers less frequently).**

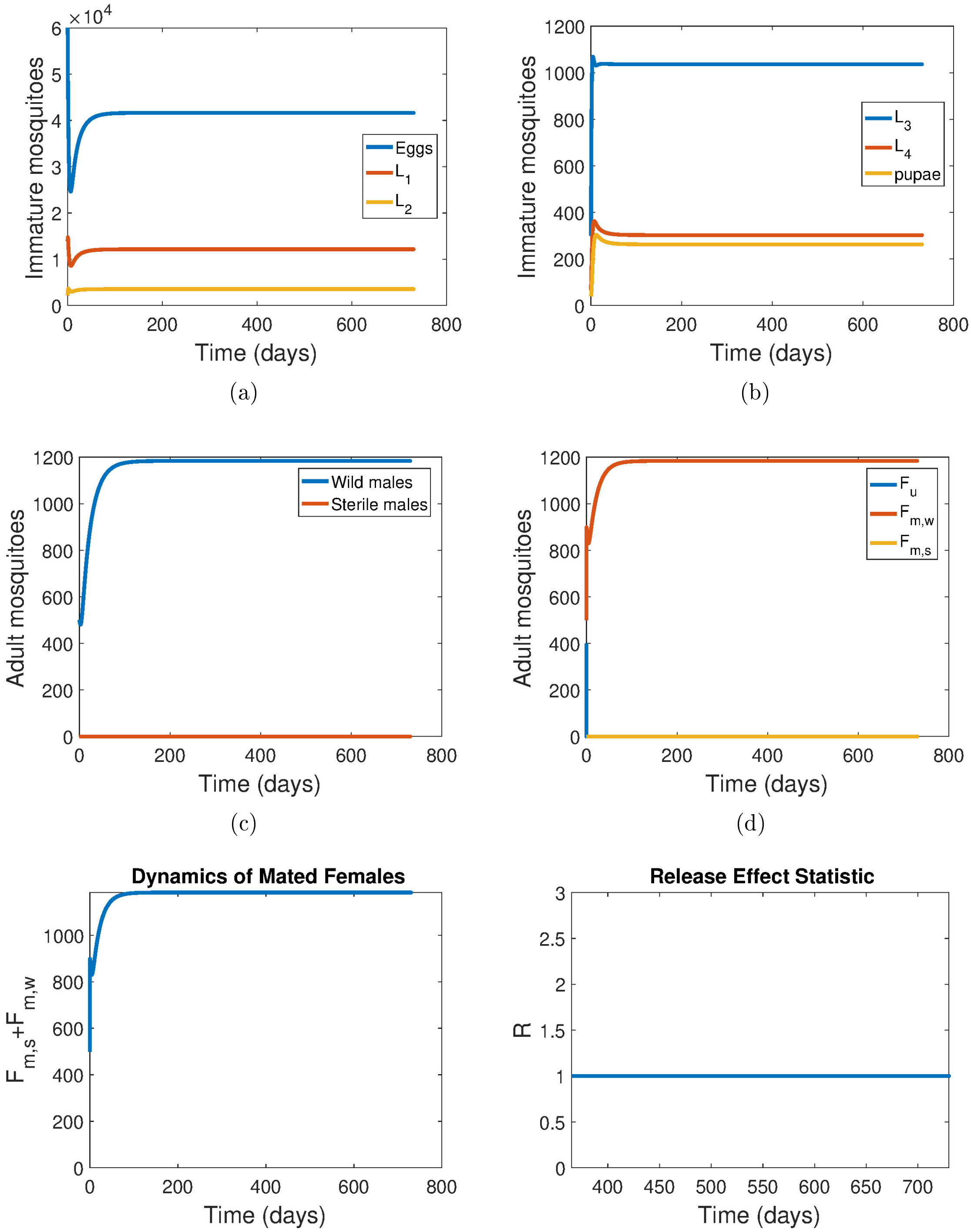
Additional simulations were carried out for the case when the number of sterile male mosquitoes released (C_R) is increased (from C_R = 10,000) to $C_R = 100,000$ (Figure 10a). These simulations (depicted in Figure 10) show qualitatively different dynamics, in comparison to the simulation results depicted in Figures 8 and 9. In particular, these simulations show a rapid decrease in the population of the immature mosquitoes, leading to extinction (Figures 10b and 10c). Furthermore, the population of mated adult female mosquitoes initially increases (during the first three to four months of SIT implementation), followed by a rapid decline leading to extinction (Figure 10d). This is a consequence of the rapid decrease in the population of the mated wild adult female mosquitoes, and the gradual decline (after three to four months of SIT implementation) in the population of mated adult female mosquitoes that will be laying nonhatching eggs (Figure 10e). Additionally, the release effect statistic (R) increases during the first three to four months of the one year SIT implementation period, and then significantly decreases for the remaining SIT implementation duration (Figure 10f).

In summary, the above simulations show that, when a large number of sterile male mosquitoes are released (e.g., $C_R = 100,000$) for a weekly period ($\tau = 7$ days), there is an initial time-lag (of about three to four months, on a one year SIT release protocol), before the full population-level impact of the SIT release (*vis a vis* reduction in local mosquito abundance) is achieved. In fact, this combination of C_R and τ values can lead to the extinction of the adult mosquito population if implemented weekly for a one year period (Figure 10). Unlike the case where only 10,000 sterile male mosquitoes were released (Figures 8-9), the weekly release of 100,000 sterile male mosquitoes can significantly reduce (and potentially lead to the extinction of) the adult mosquito population (while the former cannot eliminate the adult mosquito population). **It is worth mentioning that White *et al.* [33] and Dumont and Tchuenche [45] also showed that the control of the wild adult female mosquito population is highly dependent on the rate at which the sterile male**

mosquitoes are released, with only high release rates giving sufficient control. Our result is also consistent with that reported in the field study conducted in Guangzhou province of China by Zheng *et al.* **[26] (based on the weekly release of over 160,000 sterile male mosquitoes during the SIT implementation period).**

Although similar qualitative trends were observed when the period between releases (τ) is increased from weekly to bi-weekly, every three and four weeks (Figure 11), such scenario, while greatly reducing the population abundance of the adult mosquitoes, does not lead to the extinction of the adult mosquito population. In general, the simulations in Figures 8-11 show that, for the case when no seasonal variation in temperature is allowed, releasing more sterile male mosquitoes (e.g., $C_R = 100,000$) over a one year period with relatively shorter duration between releases (e.g., weekly, bi-weekly or even monthly) does better (in terms of reducing the population abundance of mosquitoes) than releasing smaller numbers of sterile male mosquitoes (e.g., $C_R = 10,000$) over the same time period and frequency of release. **The modeling studies in [23, 33, 45] also advocate for more frequent (but smaller) sterile male releases.**

The effect of density-dependent mortality in the larval stage (δ_L)on the population dynamics of the mosquito and the effectiveness of SIT is monitored by simulating the model (2.1) using various values of δ_L for different quantities of sterile male mosquito released (C_R). The results obtained, depicted in Figure 12, show that, for relatively small values of δ_L (such as $\delta_L = 0.00002$), the biweekly release of the sterile male mosquitoes (below a certain threshold value) initially increases the total mated female population until a peak is reached and decreases briefly before settling to a positive (mosquito persistent) state. However, when larval density-dependent mortality is increased (e.g, to $\delta_L = 0.0001$ or $\delta_L = 0.001$), the release also led to a dramatic increase in the population abundance, but followed by a rapid decrease, which may result in extinction depending on the amount released. Furthermore, much higher values of sterile release amount (C_R) are needed to achieve mosquito elimination for small values of δ_L. In particular, while about $300,000$ mosquitoes need to be released to achieve elimination when $\delta_L = 0.00002$ (Figure 12a), only about $50,000$ need to be released to achieve such elimination if δ_L is increased to $\delta_L = 0.0001$ (Figure 12b). For $\delta_L = 0.001$, however, elimination can be achieved by releasing only $10,000$ sterile male mosquitoes weekly for one year (Figure 12c). In other words, this study shows that larval density-dependent mortality decreases the number of sterile male mosquitoes that need to be released to achieve effective mosquito control or extinction. **Hence, SIT-based mathematical models for mosquito (immature and adult) population dynamics that do not incorporate density-dependence in the larval stage of the immature mosquito lifecycle may under-estimate or over-estimate the effectiveness of SIT implementation on the local mosquito population abundance**.

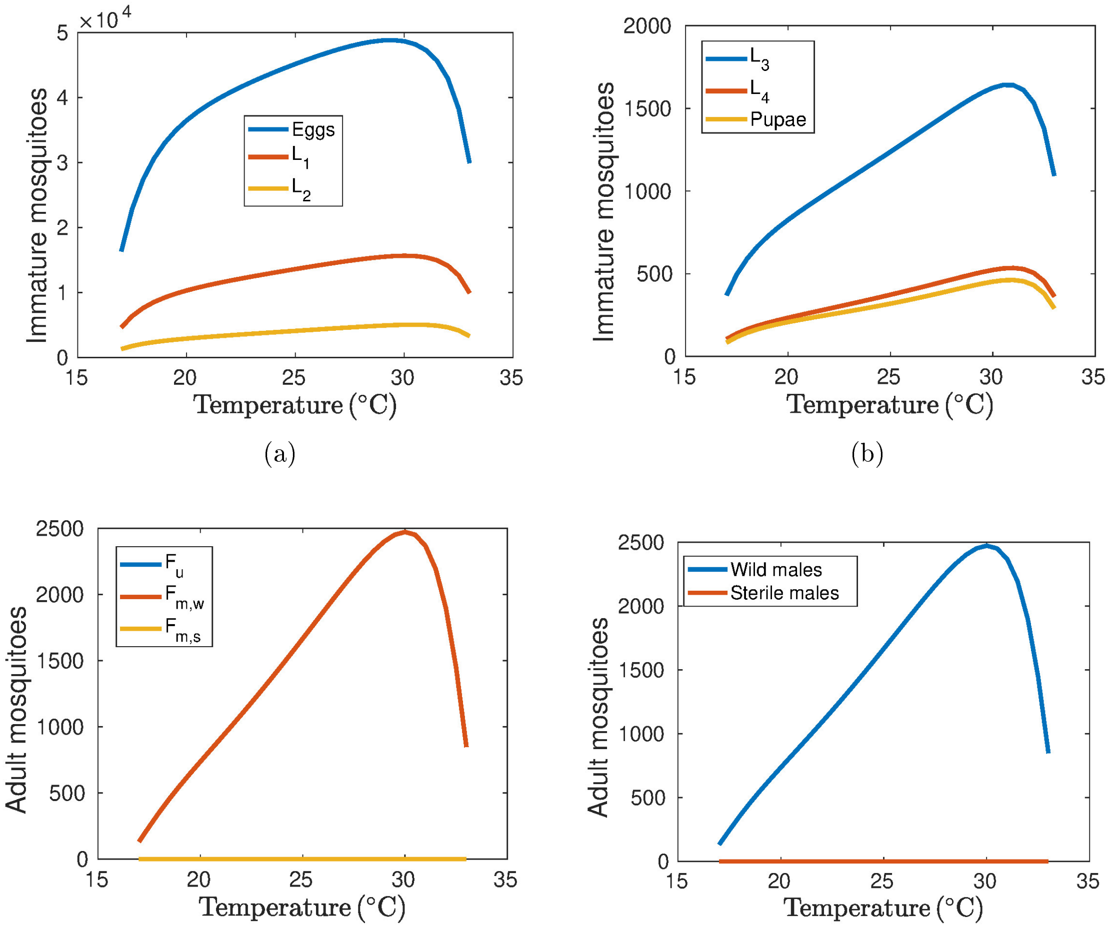


(a) (b)

(c) (d)

(e) (f)

Figure 6: Simulations of the model (2.1), showing the dynamics of the various mosquito lifecycle stages in the absence of SIT (i.e., $C_R = 0$) and seasonal variation in temperature (i.e., $v = 0$), as a function of time. Other parameter values used are as given in Table 3.



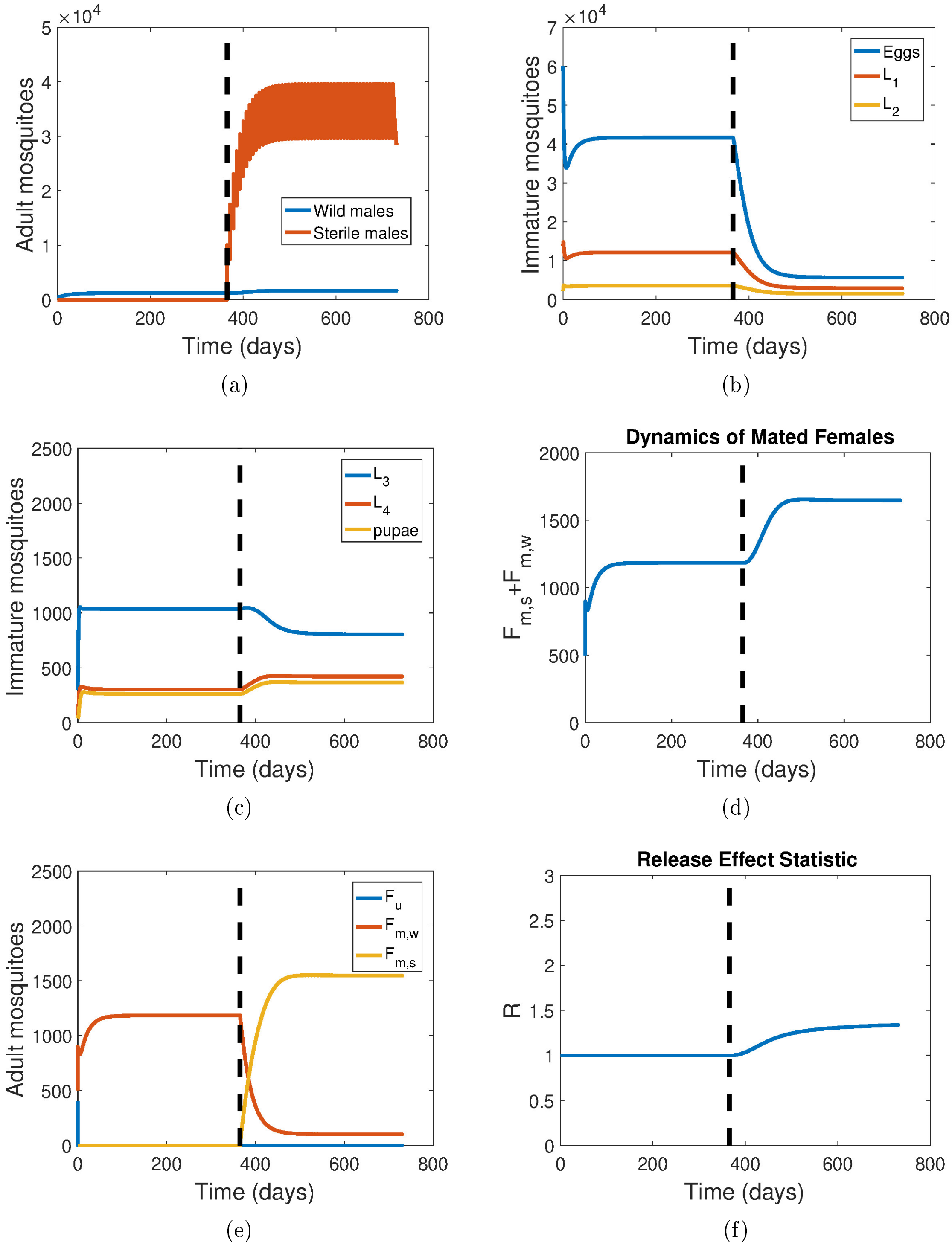
(a) (b)

(c) (d)

Figure 7: Simulations of the model (2.1), showing the dynamics of the various mosquito lifecycle stages as a function of the mean monthly temperature (for Kipsamoite area of Kenya) in the absence of SIT release (i.e., $C_R = 0$) and seasonal variation in temperature (i.e., $v = 0$). Other parameter values used are as given in Table 3.

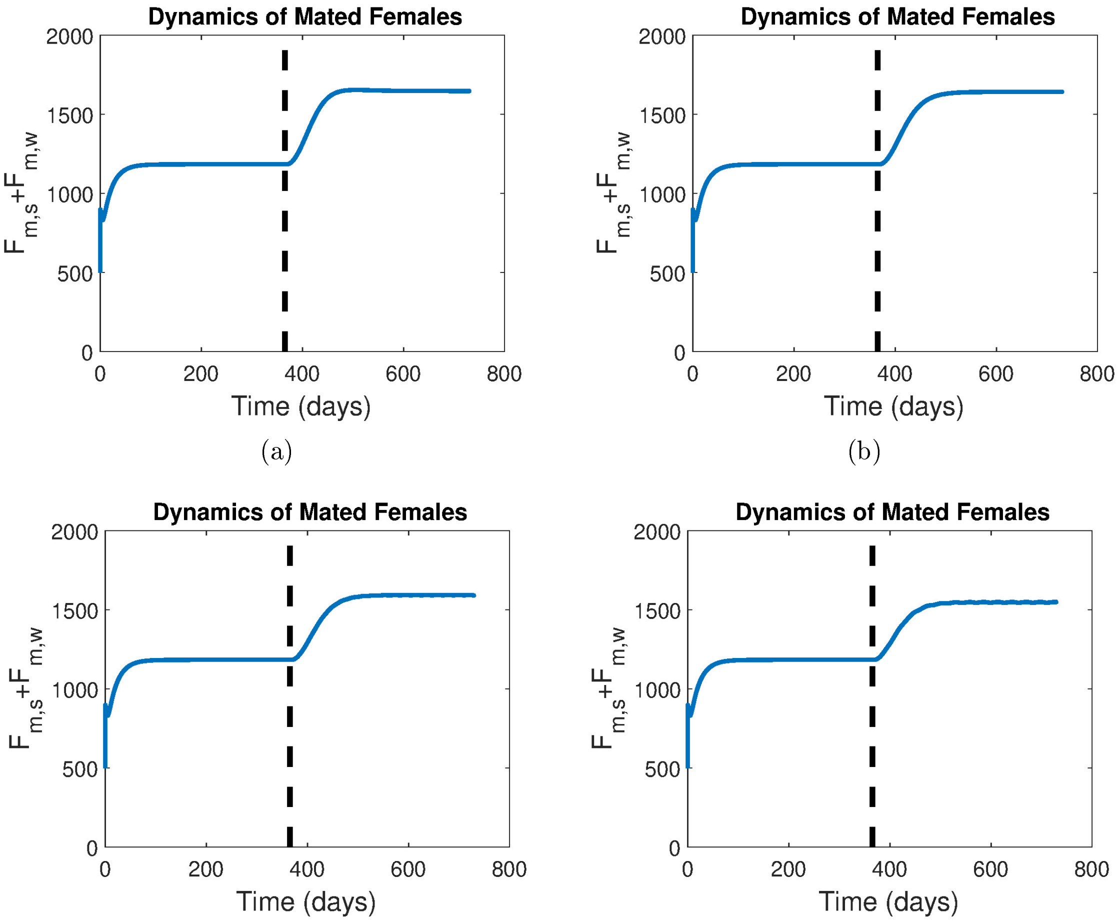
3.2.2 Seasonal variation in temperature ($v \neq 0$)

The effect of SIT implementation will now be assessed for the case when the assumption for no seasonal variation in temperature ($v = 0$) is relaxed. That is, the model (2.1) will now be simulated for the case when $v \neq 0$. In particular, we set $v = 1$ (i.e., the temperature at time t equals the actual observed temperature at time t, as given in equation (2.3)). Here, too, the model is, first of all, simulated for one year prior to the release of the sterile male mosquitoes, followed by the release of $10,000$ sterile male mosquitoes weekly for a one year duration (Figure 13a). The simulation results obtained, depicted in Figures 13b-e, show oscillatory dynamics in the mosquito population (unlike the monotone dynamics observed in Figures 8-11). Further, although this strategy leads to the overall decline in some of the mosquito populations (Figures 13b-c), it also resulted in an overall increase in some of the other mosquito populations (Figures 13c-e). For these simulations, the release effect statistic (R) always exceeds unity (Figure 13e). Thus, for the case when seasonal variation in temperature is accounted for (i.e., $v \neq 0$), the weekly release of 10,000 sterile male mosquitoes will not lead to the effective control of the mosquito population (since it resulted in an overall increase in the mated adult female mosquito population). Similar trends were observed when the period between releases was increased to bi-weekly and every three weeks (Figure 14). However, when the number of sterile male mosquitoes released is increased to $100,000$, the simulation results obtained show that mosquito extinction is feasible if such release is made on a weekly basis for one year (Figure 15a). However, when such release is made bi-weekly (Figure 15b), every three (Figure 15c) or every four (Figure 15d) weeks, mosquito extinction is not feasible. Thus, this study shows that seasonal fluctuation in mean monthly temperature ($v \neq 0$) necessitates more frequent releases of the sterile male mosquitoes (in comparison to the corresponding case where such seasonal variation is not incorporated into the numerical simulation of the model) to achieve effective control or extinction of the local mosquito population.



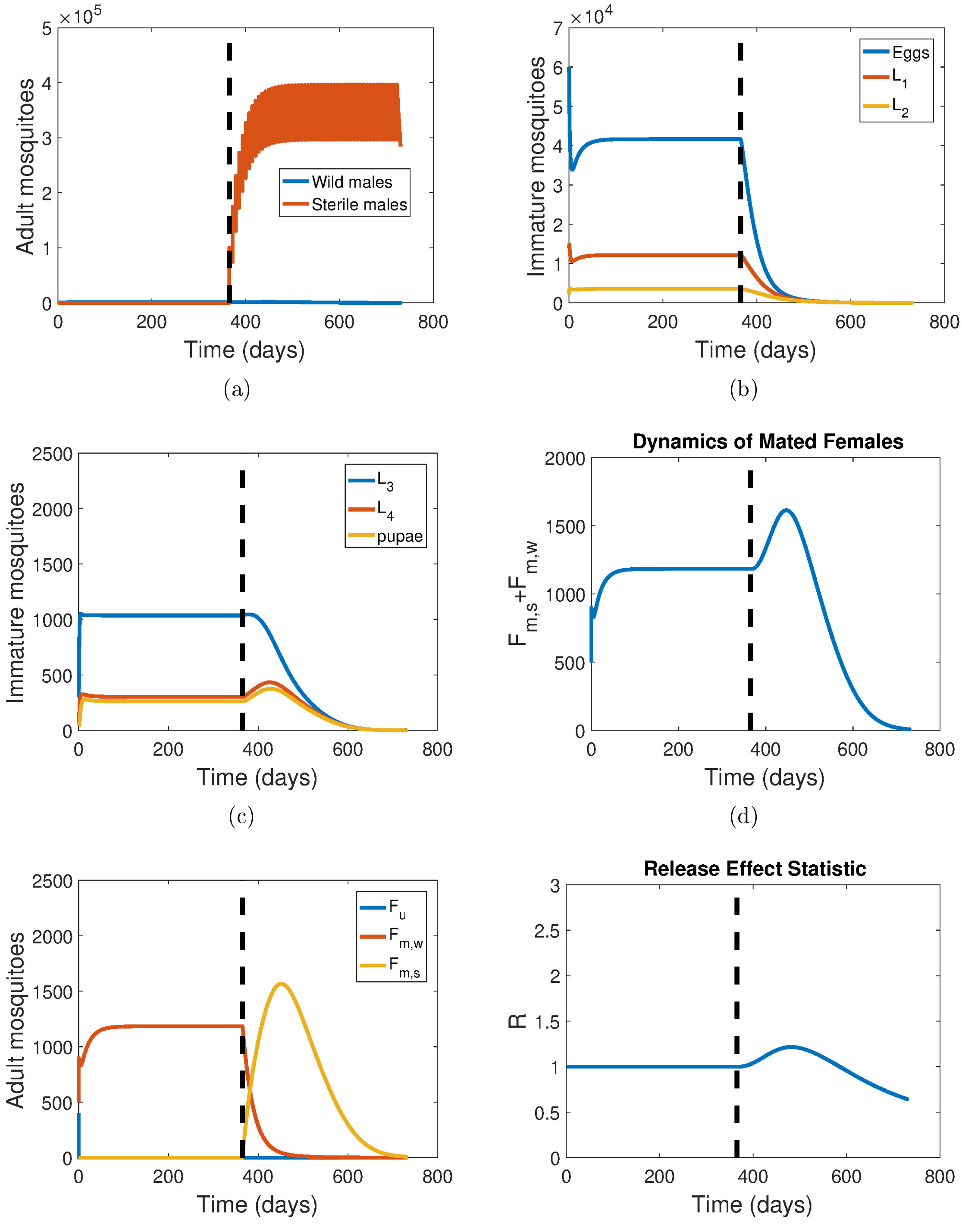
(a) (b) (c) (d) (e) (f)

Figure 8: Simulations of the model (2.1), showing the dynamics of the various mosquito lifecycle stages in the presence of SIT (with $C_R = 10,000$) and no seasonal variation in temperature ($v = 0$). The simulations were ran for one year without the release of the sterile male mosquitoes, after which the sterile male mosquitoes are released weekly for a period of one year ($\tau = 7$ days). Notation: dashed vertical lines represent the time for the onset of the release of sterile male mosquitoes. The shaded area depicts the periodic releases of sterile male mosquitoes weekly for a period of one year. Parameter values used are as given in Table 3, with $C_R = 10,000, v = 0$ and $\tau = 7$ days.



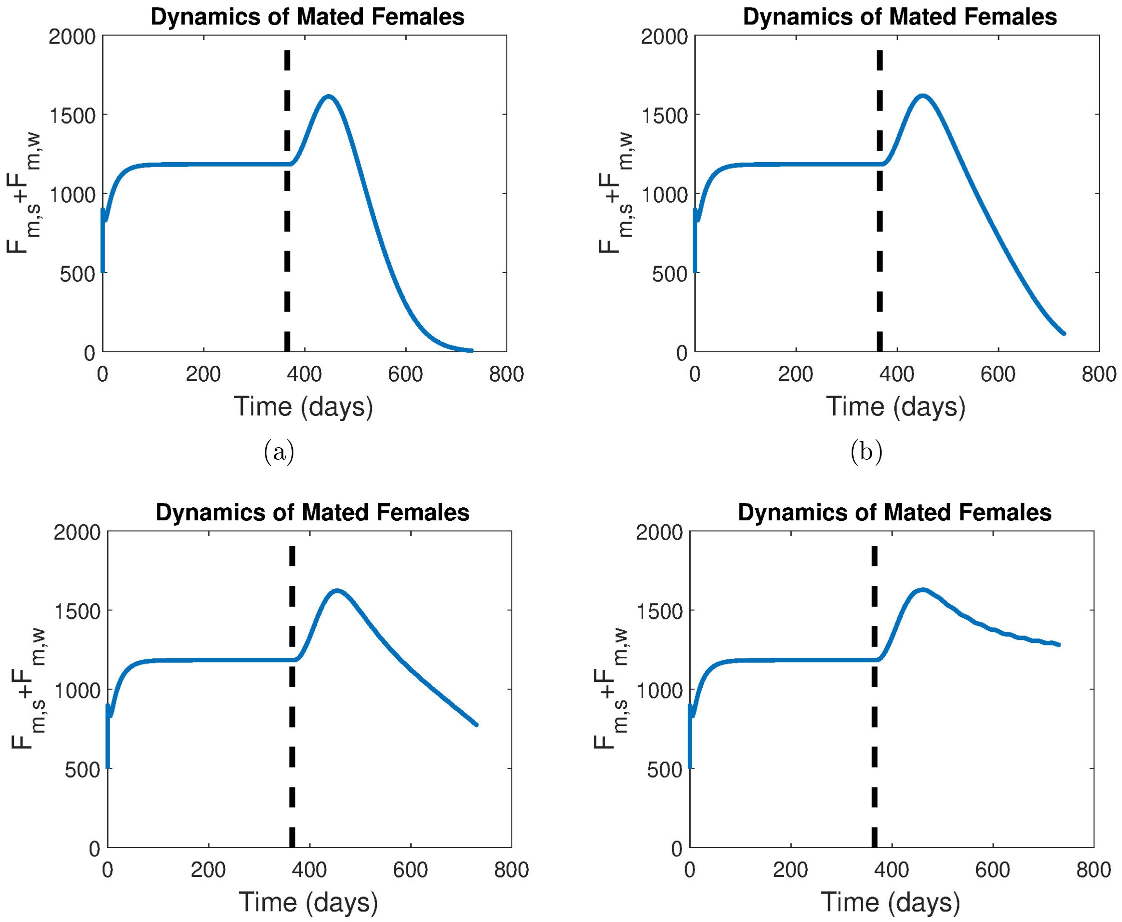
(a) (b) (c) (d)

Figure 9: Simulations of the model (2.1), showing the effect of the frequency of release of sterile male mosquitoes (τ) on the dynamics of mated female mosquitoes. (a) $\tau = 7$ days (b) $\tau = 14$ days (c) $\tau = 21$ days and (d) $\tau = 28$ days. The simulations were ran for one year without the release of the sterile male mosquitoes, followed by the release of sterile male mosquitoes for a period of 1 year. Parameter values used are as given in Table 3, with $C_R = 10,000$ and $v = 0$.



(a) (b) (c) (d) (e) (f)

Figure 10: Simulations of the model (2.1), showing the dynamics of the various mosquito lifecycle stages in the presence of SIT (with $C_R = 100,000$) and the seasonal variation in temperature ($v = 0$). The simulations were ran for one year without the release of the sterile male mosquitoes, after which the sterile male mosquitoes are released for a period of one year. Notation: dashed vertical lines represent the time for the onset of the release of sterile male mosquitoes. The shaded area depicts the periodic releases of sterile male mosquitoes weekly for a period of one year. Other parameter values used are as given in Table 3, with $\tau = 7$ days.



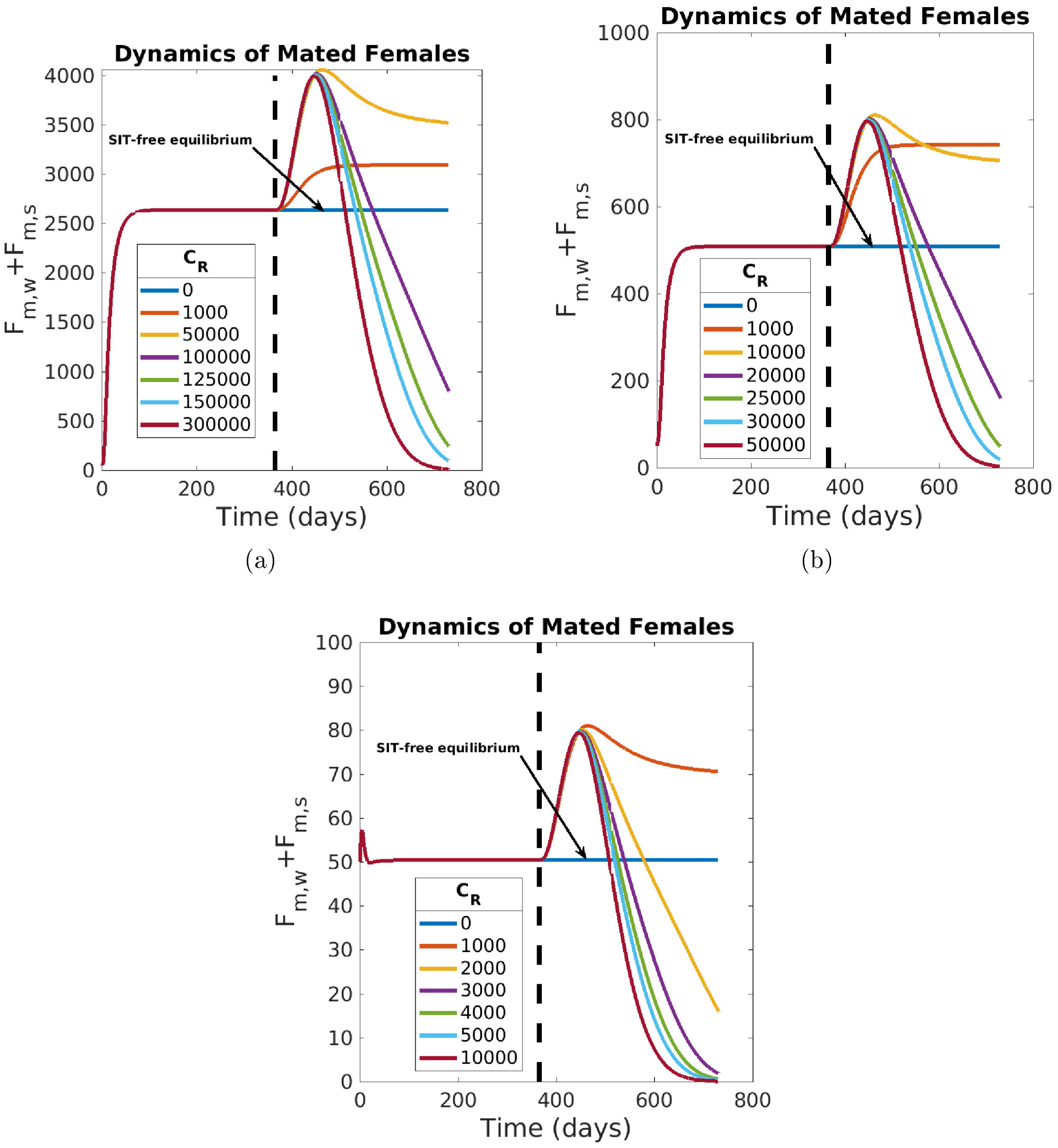
(a)

(b)

(c)

(d)

Figure 11: Simulations of the model (2.1), showing the effect of the frequency of release of sterile male mosquitoes (τ) on the dynamics of mated female mosquitoes. (a) $\tau = 7$ days (b) $\tau = 14$ days (c) $\tau = 21$ days and (d) $\tau = 28$ days. The simulations were ran for one year without the release of the sterile male mosquitoes, followed by the release of sterile male mosquitoes for a period of 1 year. Parameter values used are as given in Table 3, with $C_R = 100,000$ and $v = 0$.

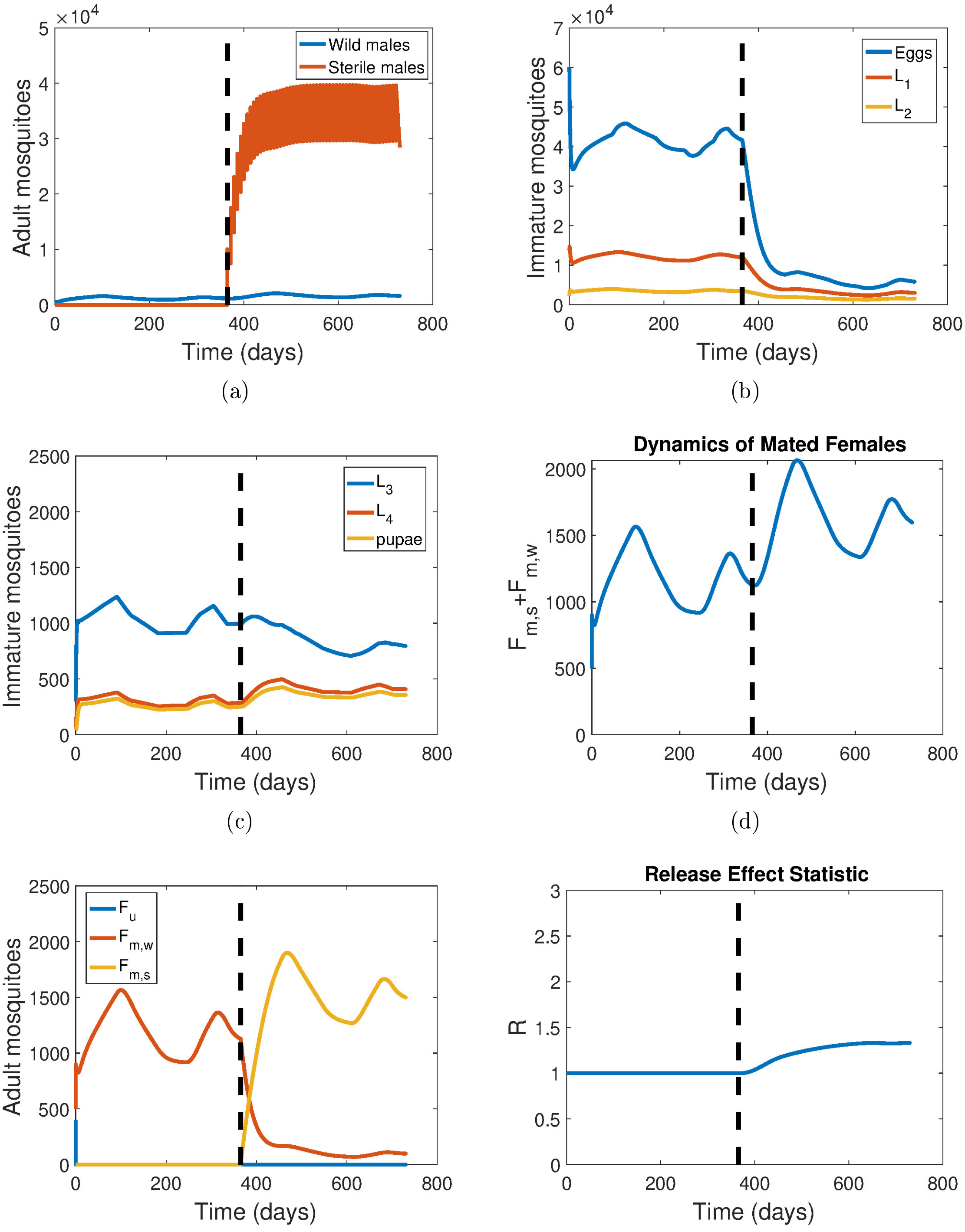


(a)

(b)

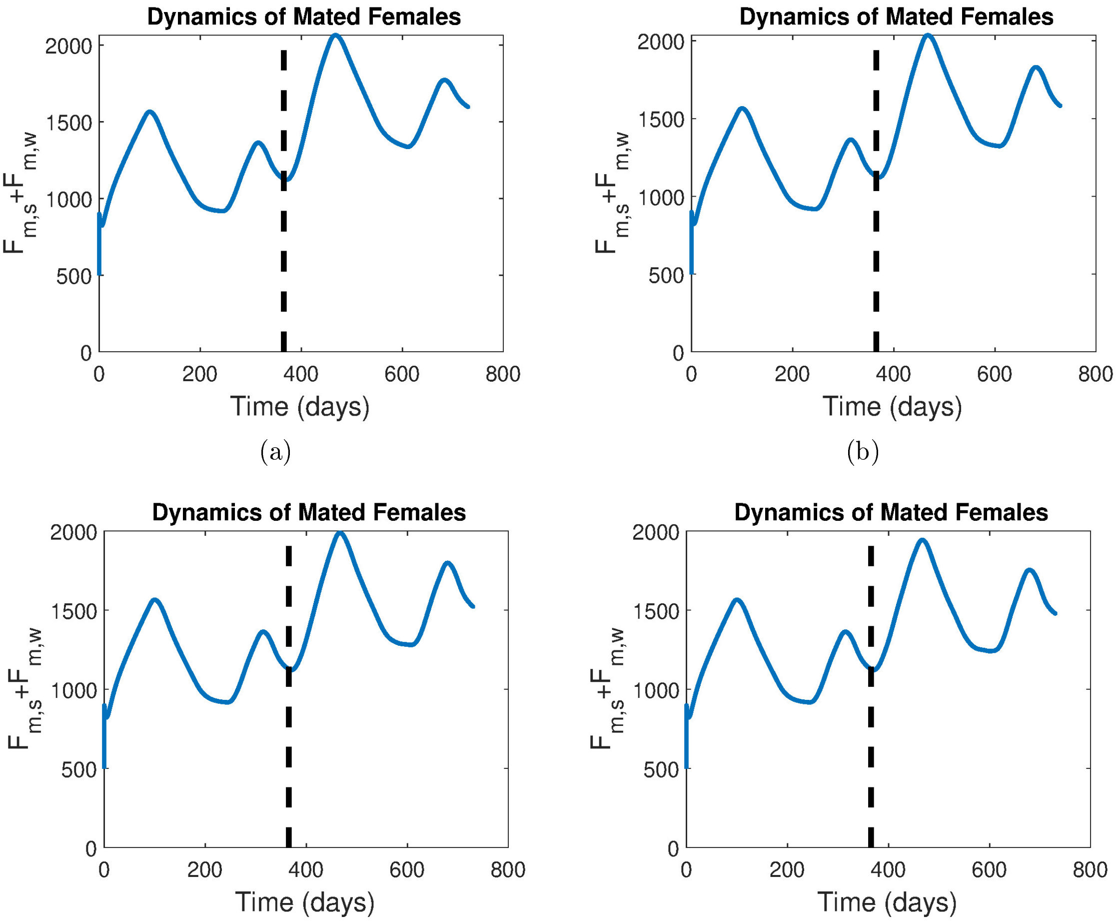
(c)

Figure 12: Simulations of the model (2.1), showing the dynamics of the total number of mated female mosquitoes for several different choices of C_R. (a) $\delta_L = 0.00002$. (b) $\delta_L = 0.0001$ and (c) $\delta_L = 0.001$. The simulations were ran for one year without the release of the sterile male mosquitoes (to reach the mosquito-present endemic equilibrium), followed by the release of sterile male mosquitoes for a period of one year. Other parameter values used are as given in Table 3.



(a) (b) (c) (d) (e) (f)

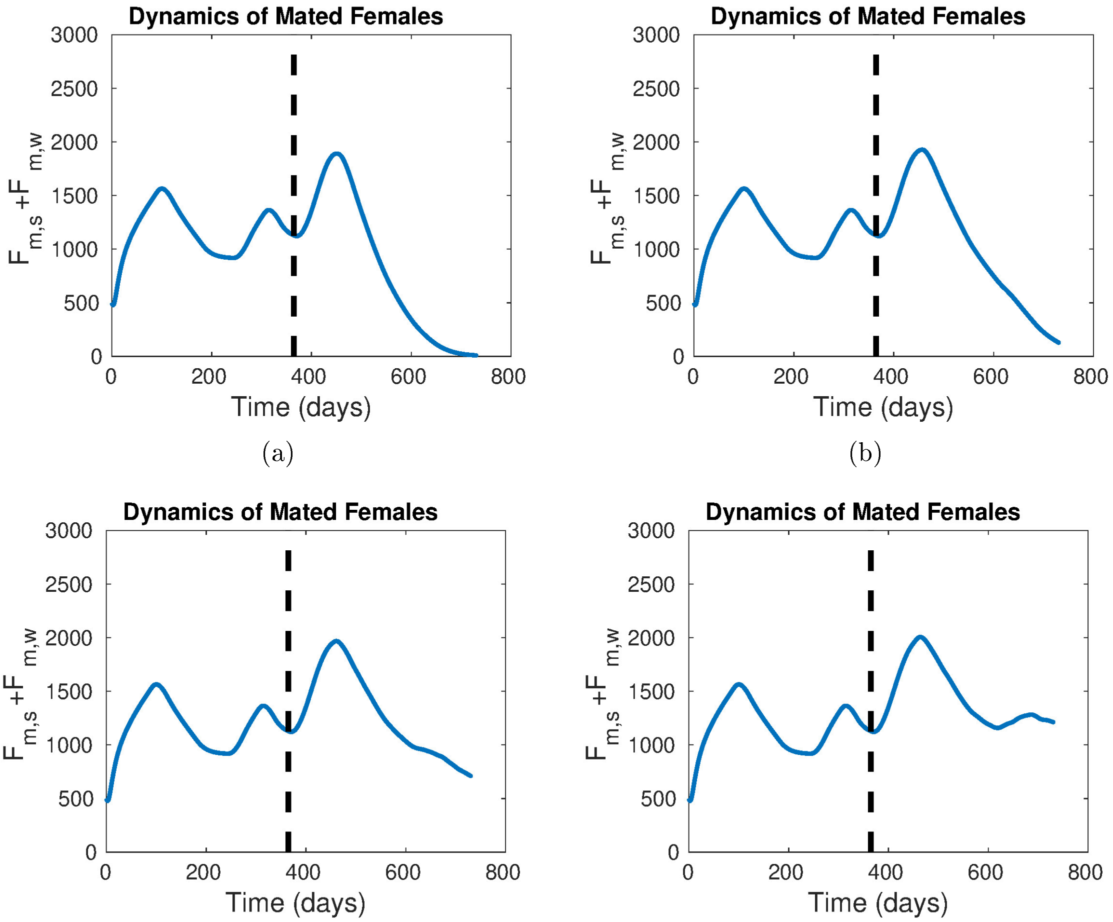
Figure 13: Simulations of the model (2.1), showing the effect of seasonal fluctuation in temperature ($v = 1$), and SIT (with $C_R = 10,000$) on mosquito abundance. The simulations were ran for one year without the release of the sterile male mosquitoes, followed by the release of the sterile male mosquitoes for a period of one year. The shaded area depicts the periodic releases of sterile male mosquitoes weekly for a period of one year. Parameter values used are as given in Table 3, with $\tau = 7$ days.



(a) (b)

(c) (d)

Figure 14: Simulations of the model (2.1), showing the effect of the frequency of release of sterile male mosquitoes (τ) on the dynamics of mated female mosquitoes. (a) $\tau = 7$ days (b) $\tau = 14$ days (c) $\tau = 21$ days and (d) $\tau = 28$ days. The simulations were ran for one year without the release of the sterile male mosquitoes, followed by the release of sterile male mosquitoes for a period of 1 year. Parameter values used are as given in Table 3, with $C_R = 10,000$ and $v = 1$.



(a)

(b)

(c)

(d)

Figure 15: Simulations of the model (2.1), showing the effect of the frequency of release of sterile male mosquitoes (τ) on the dynamics of mated female mosquitoes. (a) $\tau = 7$ days (b) $\tau = 14$ days (c) $\tau = 21$ days and (d) $\tau = 28$ days. The simulations were ran for one year without the release of the sterile male mosquitoes, followed by the release of sterile male mosquitoes for a period of 1 year. Parameter values used are as given in Table 3, with $C_R = 100,000$ and $v = 1$.

Discussion and Conclusions

Diseases caused by mosquitoes, such as chikungunya, dengue fever, malaria, West Nile virus and Zika, continue to pose major public health challenges in areas inhabited by more than one-third of the world's population. These diseases are transmitted to humans *via* the bite of infected adult female mosquitoes (in search of blood needed for egg development and oviposition). Malaria is the deadliest of all mosquito-borne diseases (accounting for over 500,000 deaths every year, mostly in children under the age of five [23]). In the absence of a safe and effective vaccine for use in humans against some of these diseases (particularly malaria), control measures against diseases vectored by the mosquito are mostly limited to implementing strategies that target the mosquito population. These strategies primarily include the use of insecticides (for example, in the form of IRS and LLINs in the context of malaria) to reduce the local population abundance of the mosquito in the targeted community. Unfortunately, the widespread use of these insecticides in endemic areas has resulted in the emergence of insecticide resistance in the adult mosquito population (Figure 1). Consequently, other alternative methods for mosquito control (notably using biological measures [21, 22, 24, 25, 26]) are urgently needed

Sterile insect technology (SIT), based on the release of sterile male mosquitoes into a wild adult female mosquito population, is one of the promising mosquito-reduction strategies being advocated in many endemic regions for mosquito-borne diseases [21, 25]. SIT which entails the periodic release of sterile male mosquitoes, into the wild mosquito population, targets the population of the wild (i.e., susceptible to biological control) adult female mosquitoes. SIT is a biological control mechanism that entails the alteration of the natural reproductive process of the target mosquito population (by chemical or physical means [23]). In particular, it is associated with the genetic modification of adult male mosquitoes to be sterile, while still being able to be sexually active. The sterile male mosquitoes are then periodically released into the environment, typically into areas with abundance of adult wild female mosquitoes, and the expectation is that an adult wild female mosquito that mates with the released sterile adult male mosquito will either not reproduce at all or produce eggs that do not hatch into larvae [23]. Ultimately, the hope is that the release of the sterile male mosquitoes may eventually lead to the effective control of the abundance of (or even eliminating) the adult wild female mosquitoes (thereby eliminating the disease(s) they vector).

This study aimed to provide insight into the effectiveness of such biological control strategy in combating the targeted mosquito population. This was achieved *via* the development, analysis and simulations of a novel mathematical model for the temporal dynamics of the mosquito (both immature and adult) population in a community. In addition to incorporating many pertinent features of the mosquito population dynamics (such as the entire lifecycle of the mosquito, density-dependent larval mortality etc.), the model developed in this study also incorporated the effect of seasonality in the mosquito dynamics (to account for the fact that seasonal variations in local climate variables, such as temperature, significantly affect many aspects of the mosquito dynamics, such as reproduction, parasite development, larval and adult survival etc. [1, 3, 6, 7, 8, 14, 23].

The developed model was used to assess the impact of such changes on the population abundance of mosquitoes in Kipsamoite area of Kenya. The simulation results obtained show that maximum population of both the immature and adult female mosquito is recorded in the Kipsamoite area whenever the mean monthly temperature is about 30°C. This value is 7.2°C greater than the current mean annual temperature for the province. The implication of this result is that increases in mean annual temperature (due to global warming) could make the province more vulnerable to increased malaria burden.

The model developed in this study was also used to assess the population-level impact of the release of a certain number of sterile male mosquitoes (with a certain frequency) on the population biology of *Anopheles* mosquitoes in a malaria-endemic community. Simulations were carried out for the case where local seasonal variation in temperature is (or is not) accounted for. In the absence of the seasonal variation in temperature, numerical simulations of the model showed that the weekly release of 10,000 sterile male mosquitoes, over a one year period, induces a detrimental effect to the malaria-endemic community. This is because such release resulted in an increase in the population of mated adult female mosquitoes. Similar qualitative result was obtained when the release period was increased to bi-weekly or every three or four weeks. **This result differs from that reported by White *et al.* [33], which showed that control is more effective if smaller numbers of sterile male mosquitoes are released more frequently (rather than larger and less frequent releases).** However, when the number of sterile male mosquitoes released was increased to 100,000, the population of the mated adult female mosquitoes initially increased (for a period of 3 to 4 months) followed by a rapid decline (leading to extinction) for the reminder of the one year sterile release duration. The ecological implication of this result is that, when seasonal variation in temperature is not accounted for, effective control or extinction of the mosquito population is feasible by releasing a large number of sterile male mosquitoes for a very short frequency of release period (e.g., weekly). **White *et al.* [33] and Dumont and Tchuenche [45] also emphasized the importance of larger sterile male releases on mosquito control.** Although (for this level of sterile male release) the population of mosquitoes is greatly reduced when the frequency of release is increased from weekly to bi-weekly or every three weeks or monthly, such does not result in mosquito extinction.

The model was also used to study the effect of density-dependent larval mortality on the population abundance of mosquitoes and the effectiveness of the SIT-based mosquito control strategy. Such density-dependence occurs when larvae compete for space and nutrients [6, 8]. Simulations of the model, for the case with no seasonal variations in temperature, showed that for small values of the larval density-dependent mortality, the bi-weekly release of sterile male mosquitoes resulted in an increase in the population abundance of mated adult female mosquitoes. On the other hand, higher values of density-dependent mortality rates could lead to mosquito extinction depending on the number of the sterile male mosquitoes released. The implication of this result is that the effect of (higher values of) larval density-dependent mortality is to decrease the number of sterile male mosquitoes that need to be released in order to achieve effective control or extinction of the mosquito population.

For the case where seasonal variation in temperature is accounted for, the simulations of the model showed very different qualitative dynamics than the case without such variation. For instance, unlike the monotone dynamics observed for the case with no seasonal variations, rich oscillatory dynamics were observed when such variations are taken into account. Here, too, the release of 10,000 sterile male mosquitoes failed to result in the extinction of the mosquito population. However, when 100,000 sterile male mosquitoes were released (under this scenario with seasonal temperature variation), our simulation results showed that mosquito extinction is feasible if the sterile male mosquitoes are released weekly (such extinction is not feasible if the frequency of release exceeds a week). The implication of this result is that incorporating seasonal variation in temperature necessitate more frequent releases of the (large number) of the sterile male mosquitoes. In summary, our simulations for the population-level impact of SIT suggest that the prospects of an SIT-based mosquito control strategy (for a one-year duration) are very bright if large numbers of the sterile male mosquitoes ($C_R = 100,000$) are released.

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Table 1: Description of state variables and parameters for the model (2.1)

Variables	**Interpretation**
E	Total number of eggs
$L = \sum_{j=1}^{4} L_j$	Total number of larvae
P	Total number of pupae
F_u	Population of new unmated wild adult female mosquitoes
M_w	Population of wild adult male mosquitoes
$F_{m,w}$	Population of fertilized wild adult female mosquitoes that have mated
$F_{m,s}$	Population of fertilized female mosquitoes that would be laying (nonhatching) eggs
M_s	Population of sterile male mosquitoes released
Parameters	**Interpretation**
β	Mating rate of wild female mosquitoes with males (either M_w or M_s)
η	Fraction of sterile males that are able to mate
ζ	Time required for mating to be completed
r	Proportion of new adult mosquitoes (based on gender status)
ϕ_E	Egg oviposition rate
ψ_E	Number of eggs laid *per* oviposition
$\sigma_E(T_W)$	Maturation rate from egg to larvae
$\sigma_L(T_W)$	Maturation rate from larvae to pupae
$\sigma_P(T_W)$	Maturation rate from pupae to adult mosquitoes
$\mu_E(T_W)$	Natural mortality rate of eggs
$\mu_L(T_W)$	Natural mortality rate of larvae
$\mu_P(T_W)$	Natural mortality rate of pupae
δ_L	Density-dependent mortality rate of larvae
$\mu_q(T_A)$	Natural mortality rate of adult female and male mosquitoes
C_R	Rate of release of sterile male mosquitoes

Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Temperature (^{0}C)	24	26	25	23	21	20	20	21	21	22	21	22

Table 2: Mean monthly temperature (in ^{0}C) for Kipsamoite, Kenya for the year 2019 [60].

Parameters	Values	Reference
ψ_E	65	[55, 37]
ϕ_E	0.4	[55, 37]
β	0.7	[27]
ζ	0.000174	Estimated
η	0.75	[33]
C_R	10^4	Variable
δ_L	0.00005	Assumed
r	0.5	[39]

Table 3: Values of temperature-independent parameters of the model (2.1).