A malaria transmission model with seasonal mosquito life-history traits

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Abstract

In this paper we develop and analyse a malaria model with seasonality; periodic-mosquitoes per capita birth rate, mosquitoes death rate, -infectivity of humans and mosquitoes, and -mosquitoes biting rate. All these parameters are assumed to be time dependent leading to a nonautonomous differential equations system. We provide a global analysis of the model depending on some threshold $\mathcal{R}_0$. When $\mathcal{R}_0 < 1$, then the disease-free equilibrium is globally asymptotically stable and the disease died out from the host population. On the contrary, if $\mathcal{R}_0 > 1$, the disease persists in the host population in the long term and the model admits at least one positive periodic solution. The simulation results are in accordance with the seasonal variation of the reported cases of a malaria-epidemic region in Mpumalanga province in South Africa.

Keywords: Seasonal pattern; Periodic solution; Basic reproduction ratio; Global stability; Uniform persistence

1 Introduction

Malaria is a potentially deadly disease caused by infection with *Plasmodium* protozoa transmitted by an infective female *Anopheles* mosquito. Globally, an estimated 216 million malaria cases was recorded in 2016 which is an increase of

about 5 million cases over 2015 (WHO, 2017). In the same year, almost 445,000 individuals lost their lives to the life-threatening disease (WHO, 2017).

Despite more than a century of research, there is a dearth of information on the mechanistic link between environmental variables, such as temperature and malaria risk (Lafferty, 2009; Paaijmans *et al.*, 2009; Alonso *et al.*, 2011). Temperature is fundamentally linked to malaria mosquito and parasite vital rates, and understanding the role of temperature in malaria transmission is particularly important in light of climate change. Using mathematical model, several attempts have been made to highlight some of the importance of climate variables on malaria transmission. Mordecai *et al.* (2013) built nonlinear thermal-response models to understanding the effects of current and future temperature regimes on malaria transmission. The models, which include empirically derived nonlinear thermal responses, predicts optimal malaria transmission at 25°C (6°C lower than previous models).

Dembele *et al.* (2009) proposed an ordinary differential equation (ODE) compartmental model for the spread of malaria with susceptible-infectious-recovered (SIRS) pattern for humans and a susceptible-infectious (SI) pattern for mosquitoes with mosquitoes periodic birth rate and death rate. More recently, Abiodun *et al.* (2017) developed and analysed a comprehensive mosquito-human dynamical model. The model was validated by Abiodun et *al.* (2018) over KwaZulu-Natal province – one of the epidemic provinces in South Africa. Several other studies (Craig *et al.*, 1999; Laneri *et al.*, 2015; Roy *et al.*, 2015; Abiodun *et al.*, 2016; Okuneye & Gumel, 2017; Abdelrazec & Gumel, 2017; Eikenberry & Gumel, 2018; Beck-Johnson *et al.*, 2017; Hoshen & Morse, 2004) have explored the impacts of environmental variables on malaria transmission and mosquito abundance. However, little has been done with regard to mosquito-human malaria transmission model with time dependent parameters with periodic variations. For instance, let us mention the work of Dembele *et al.* (2009) with periodic mosquito per capita death and birth rate; and the recent work of Bakary *et al.* (2018) with periodic mosquito biting rate. However, many other mosquito life-history traits (including larval development rate, larval survival, adult survival, biting rate, fecundity, and vector competence) are well known to have seasonal variation (Mordecai *et al.*, 2013; Eikenberry & Gumel, 2018). This present study aims to (i) proposed and analyze a human-mosquito malaria transmission model including all these life-history traits with periodic variation and (ii) validate the model proposed over a malaria-epidemic region in Mpumalanga province in South Africa.

The model proposed in this paper divides the human population into four classes: susceptible-exposed-infectious-recovered (SEIRS) and mosquitoes population into three classes: susceptible-exposed-infectious (SEI). The SEIRS pattern for humans and SEI pattern for mosquito model have been also proposed by Chitnis and collaborators (Chitnis *et al.*, 2006, 2008). Human migration is present throughout the world and plays a large role in the epidemiology of diseases, including malaria. In many parts of the developing world, there is rapid urbanization as many people leave rural areas and migrate to cities in search of employment. We include this movement as a constant immigration rate into

the human susceptible class. We make a simplifying assumption that there is no immigration of recovered humans and also include the direct infectious-to-susceptible recovery as in the model of Ngwa & Shu (2000).

This work is organized as follows: In Section 2, we fully describe the malaria seasonal model studied in this paper as Section 3 describes the main results. Section 4.1 is devoted for deriving preliminary results and remarks that will be used to study the long-term behavior of the problem. Section 4.2 is concerned with the proof of the main result that, roughly speaking, states that when some threshold (explicitly expressed using the parameters of the system) $\mathcal{R}_0 < 1$ the disease die out from the host population; and when $\mathcal{R}_0 > 1$ the disease persists in the host population in the long term and the model admits at least one positive periodic solution. The numerical simulations and discussion are given in Sections 5 with a concluding remark in Section 6.

2 The malaria seasonal model

The model sub-divides the total human population at time t, denoted by $N_h(t)$, into the following sub-populations of susceptible $S_h(t)$, exposed (infected but not infectious) $E_h(t)$, infectious $I_h(t)$ and recovered individuals with temporary immunity $R_h(t)$. So that $N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$.

The total vector (mosquito) population at time t, denoted by $N_v(t)$, is subdivided into susceptible $S_v(t)$, exposed $E_v(t)$ and infectious mosquitoes $I_v(t)$. Thus, $N_v(t) = S_v(t) + E_v(t) + I_v(t)$.

Susceptibles individuals are recruited at a constant rate Λ_h. We define the force of infection from mosquitoes to humans by $(\beta_1(t)\alpha\theta(t)I_v/N_v)$ as the product of the transmission rate per contact with infectious mosquitoes $\beta_1(t)$, the mosquito contact rate α, the mosquito biting rates $\theta(t)$ and the probability that the mosquito is infectious I_v/N_v. Then infected individuals move to the exposed class at a rate $(\beta_1(t)\alpha\theta(t)I_vS_h/N_v)$. The natural death rate of human is μ_h. The rate of progression from exposed class to infectious individuals class is σ_h while infectious individuals recovered due to treatment at a rate γ_h. The infectious humans after recovery without immunity become immediately susceptible again at rate $(1-r)$, where r is the proportion of infectious humans who recovered with temporary immunity. Recovered individual loses immunity at a rate k_h.

Susceptible mosquitoes are generated at a per capita rate $b_v(t)$ at time t and acquire malaria through contacts with infectious humans with the force of infection $(\beta_2(t)\alpha\theta(t)I_h/N_h)$ as the product of the probability of disease transmission from human to the mosquito $\beta_2(t)$, the mosquito contact rate α and the probability that human is infectious I_h/N_h. Hence, newly infected mosquitoes are moved into the exposed class at a rate $(\beta_2(t)\alpha\theta(t)I_hS_v/N_h)$ and progress to the class of infectious mosquitoes at a rate σ_v. Mosquitoes are assumed to suffer death due to natural causes at a rate $\mu_v(t)$ at time t.

The non-autonomous model has time-dependent ω-periodic coefficients which account for the environmental variations in the infectivity of both human and mosquitoes populations, the birth rate of the mosquitoes population, the biting

rate of the mosquitoes population and the death rates of mosquitoes. Setting $\dot{y} := \frac{dy}{dt}$, the resulting system of equation is shown below:

$$
\begin{cases}
\dot{S}_h = \Lambda_h - \alpha\beta_1(t)\theta(t)\dfrac{I_v}{N_v}S_h + k_h R_h + (1-r)\gamma_h I_h - \mu_h S_h; \\[2mm]
\dot{E}_h = \alpha\beta_1(t)\theta(t)\dfrac{I_v}{N_v}S_h - (\sigma_h + \mu_h)E_h; \\[2mm]
\dot{I}_h = \sigma_h E_h - (\gamma_h + \rho_h + \mu_h)I_h; \\[2mm]
\dot{R}_h = r\gamma_h I_h - (k_h + \mu_h)R_h; \\[2mm]
\dot{S}_v = b_v(t)Nv - \alpha\beta_2(t)\theta(t)\dfrac{I_h}{N_h}S_v - \mu_v(t)S_v; \\[2mm]
\dot{E}_v = \alpha\beta_2(t)\theta(t)\dfrac{I_h}{N_h}S_v - (\sigma_v + \mu_v(t))E_v; \\[2mm]
\dot{I}_v = \sigma_v E_v - \mu_v(t)I_v; \\[2mm]
\dot{N}_h = \Lambda_h - \mu_h N_h - \rho_h I_h; \\[2mm]
\dot{N}_v = (b_v(t) - \mu_v(t))N_v.
\end{cases}
\tag{2.1}
$$

Table 1: Parameter description

Constant parameters	
Λ_h	human recruitment rate.
μ_h	human per capita death rate.
α	mosquitoes contact.
k_h	rate of loss of immunity.
γ_h	human recovery rate.
r	rate of recovered with temporary immunity.
σ_h	progression rate from exposed class to infectious individuals.
σ_v	progression rate from exposed class to infectious mosquitoes.
ρ_h	human disease induce mortality rate.
ω-Periodic parameters	
$b_v(t)$	mosquitoes per capita birth rate.
$\mu_v(t)$	mosquitoes per capita death rate.
$\beta_1(t)$	infectivity of humans.
$\beta_2(t)$	infectivity of mosquitoes.
$\theta(t)$	biting rate of mosquitoes.

To simplify the analysis of the malaria model (2.1), we work with fractional quantity instead of actual populations by scaling the population of each by the total species population. We let

$$
\begin{aligned}
s_h = S_h/N_h, \quad e_h = E_h/N_h, \quad i_h = I_h/N_h, \quad r_h = R_h/N_h, \\
s_v = S_v/N_v, \quad e_v = E_v/N_v, \quad i_v = I_v/N_v.
\end{aligned}
\tag{2.2}
$$

Differentiating the scaling equations (2.2) and solving for the derivatives of scaled variables, we obtain for example

$$\frac{de_h}{dt} = \frac{1}{N_h}\left[\frac{dE_h}{dt} - e_h\frac{dN_h}{dt}\right] \quad \text{and} \quad \frac{de_v}{dt} = \frac{1}{N_v}\left[\frac{dE_v}{dt} - e_v\frac{dN_v}{dt}\right]$$

and so on for the other variables.

This creates a new seven-dimensional system of equations with two dimensions for the two total population variables, N_h and N_v, and five dimensions for the fractional population variables, e_h, i_h, r_h, e_v, and i_v. For convenience we still use $s_h = S_h$, $e_h = E_h$, $i_h = I_h$, $s_v = S_v$, $e_v = E_v$ and $i_v = I_v$. Since the compartment $(e_h, i_h, r_h, e_v, i_v, N_h)$ does not include the N_v-compartment, we have:

$$\begin{cases} \dot{E}_h = \alpha\beta_1(t)\theta(t)I_v(1 - E_h - I_h - R_h) - (\sigma_h + \frac{\Lambda_h}{N_h})E_h + \rho_h E_h I_h; \\[2mm] \dot{I}_h = \sigma_h E_h - (\gamma_h + \rho_h + \frac{\Lambda_h}{N_h})I_h + \rho_h I_h^2; \\[2mm] \dot{R}_h = r\gamma_h I_h - (k_h + \frac{\Lambda_h}{N_h})R_h + \rho_h I_h R_h; \\[2mm] \dot{E}_v = \alpha\beta_2(t)\theta(t)I_h(1 - E_v - I_v) - (\sigma_v + b_v(t))E_v; \\[2mm] \dot{I}_v = \sigma_v E_v - b_v(t)I_v; \\[2mm] \dot{N}_h = \Lambda_h - \mu_h N_h - \rho_h I_h N_h; \end{cases} \qquad (2.3)$$

and

$$E_h(0) \geq 0;\ I_h(0) \geq 0;\ R_h(0) \geq 0;\ E_v(0) \geq 0;\ I_v(0) \geq 0,\ N_h(0) > 0. \qquad (2.4)$$

The variables of the model are resumed in Table 1.

In what follow we shall discuss the asymptotic behavior of system (2.3)-(2.4) and we will make use the following assumption.

Assumption 2.1 *We assume that, Λ_h, μ_h, α, k_h, γ_h, r, σ_h and σ_v are positives constants with the exception of the disease-induced death rate ρ_h, which is non-negative constant. The functions $b_v(.)$, $\mu_v(.)$, $\beta_1(.)$, $\beta_2(.)$ and $\theta(.)$ are ω-periodic and belong to $L_+^\infty(0, \omega, \mathbb{R}_+)$.*

3 Main results

In what follows, we introduce the basic reproduction ratio $\mathcal{R}_0$ for system (2.3) according to general procedure presented in (Wang & Zhao, 2008; Liu *et al.*, 2010) and references therein. The positive equilibrium human and mosquito population, in the absence of disease, for system (2.3) is $M_0 = (0, 0, 0, 0, 0, N_h^*)$; where $N_h^* = \Lambda_h/\mu_h$.

The equation for exposed and infectious for both human and mosquitoes populations of the linearized system of model (2.3) at M_0 is

$$\frac{d}{dt}(E_h, I_h, E_v, I_v)^T = (F(t) - V(t)).(E_h, I_h, E_v, I_v)^T;$$

where

$$F(t) = \begin{pmatrix} 0 & 0 & 0 & \alpha\beta_1(t)\theta(t) \\ 0 & 0 & 0 & 0 \\ 0 & \alpha\beta_2(t)\theta(t) & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix};$$

and

$$V(t) = \begin{pmatrix} \sigma_h + \mu_h & 0 & 0 & 0 \\ -\sigma_h & \gamma_h + \rho_h + \mu_h & 0 & 0 \\ 0 & 0 & \sigma_v + b_v(t) & 0 \\ 0 & 0 & -\sigma_v & b_v(t) \end{pmatrix}$$

(3.5)

Let $\Phi_V(t)$ and $\rho(\Phi_V(\omega))$ be the monodromy matrix of the linear ω-periodic system $\frac{dz}{dt} = V(t)z$ and the spectral radius of $\Phi_V(\omega)$, respectively. Assume $Y(t, s)$, $t \geq s$, is the evolution operator of the linear ω-periodic system

$$\frac{dz}{dt} = -V(t)z.$$

(3.6)

That is, for each $s \in \mathbb{R}$, the 4×4 matrix $Y(t, s)$ satisfies

$$\frac{d}{dt}Y(t, s) = -V(t)Y(t, s), \ \ \forall t \geq s, \ Y(s, s) = I,$$

where I is the 4×4 identity matrix. Thus, the monodromy matrix $\Phi_{-V}(t)$ of (3.6) is equal to $Y(t, 0)$ for $t \geq 0$.

Now, we deal with disease-free equilibrium invasion process (Van den Driessche & Watmough, 2008) and references therein. Let $\phi(s)$ the initial distribution of infectious individuals. Then $F(s)\phi(s)$ is the rate of new infections produced by the infected individuals who were introduced at time s. Given $t \geq s$, then $Y(t, s)F(s)\phi(s)$ gives the distribution of those infected individuals who were newly infected at time s and remain in the infected compartments at time t. It follows that

$$\psi(t) := \int_{-\infty}^{t} Y(t, s)F(s)\phi(s)ds = \int_{0}^{\infty} Y(t, t-s)F(t-s)\phi(t-s)ds$$

is the distribution of accumulative new infections at time t produced by all those infected individuals $\phi(s)$ introduced at time previous to t.

Let $\mathcal{C}_\omega(\mathbb{R}, \mathbb{R}^4)$ be the ordered Banach space of all ω-periodic functions from $\mathbb{R}$ to $\mathbb{R}^4$ which is equipped with the maximum norm $||.||$ and the positive cone

$\mathcal{C}_\omega^+(\mathbb{R}, \mathbb{R}^4) = \{\phi \in \mathcal{C}_\omega(\mathbb{R}, \mathbb{R}^4) : \phi(t) \geq 0\}$. Then we can define a linear operator $L : \mathcal{C}_\omega(\mathbb{R}, \mathbb{R}^4) \to \mathcal{C}_\omega(\mathbb{R}, \mathbb{R}^4)$ by

$$L\phi(t) = \int_0^\infty Y(t, t-s)F(t-s)\phi(t-s)ds, \ \forall t \in \mathbb{R}, \phi \in \mathcal{C}_\omega(\mathbb{R}, \mathbb{R}^4). \quad (3.7)$$

Following (Wang & Zhao, 2008), we call L the next generation operator, and define the basic reproduction ratio as $\mathcal{R}_0 = \rho(L)$, the spectral radius of L.

In the special case of $\beta_1(t) \equiv \beta_1$, $\beta_2(t) \equiv \beta_2$, $b_v(t) \equiv b_v$ and $\theta(t) \equiv \theta$ $\forall t \geq 0$, we obtain $F(t) \equiv F$ and $V(t) \equiv V$. By Van den Driessche & Watmough (2008), the basic reproduction ratio is:

$$\mathcal{R}_0 = \sqrt{\frac{\alpha^2 \theta^2 \beta_1 \beta_2 \sigma_h \sigma_v}{(\sigma_h + \mu_h)(\gamma_h + \rho_h + \mu_h)(\sigma_v + b_v)b_v}}. \quad (3.8)$$

As pointed in (Chitnis $et\ al.$, 2006), The original definition of the reproductive number of the Ross-Macdonald model (Anderson & May, 1992) and the Ngwa and Shu model (Ngwa & Shu, 2000), is equivalent to the square of this $\mathcal{R}_0$. Anderson and Ngaw use the traditional definition of the reproductive number, which approximates the number of secondary infections in humans caused by one infected human, while the $\mathcal{R}_0$ used here is consistent with the definition given by the next generation operator approach (Van den Driessche & Watmough, 2008) which approximates the number of secondary infections due to one infected individual (be it human or mosquito). Moreover, the number of new infections in humans that one human causes through his/her infectious period is $\mathcal{R}_0^2$, not $\mathcal{R}_0$. Because this definition of $\mathcal{R}_0$ (3.8) is based on the next generation operator approach, it counts the number of new infections from one generation to the next. That is, the number of new infections in mosquitoes counts as one generation.

For any ω-periodic function $z(t)$, we define the avaerage of the function z by setting

$$\langle z \rangle = \frac{1}{\omega} \int_0^\omega z(t)dt.$$

We further define the average basic reproduction ratio (according to the periodic parameters)

$$\langle \mathcal{R}_0 \rangle = \sqrt{\frac{\alpha^2 \langle \theta \rangle^2 \langle \beta_1 \rangle \langle \beta_2 \rangle \sigma_h \sigma_v}{(\sigma_h + \mu_h)(\gamma_h + \rho_h + \mu_h)(\sigma_v + \langle b_v \rangle)\langle b_v \rangle}}.$$

In general, $\mathcal{R}_0 \neq \langle \mathcal{R}_0 \rangle$. For example, in a tuberculosis model it was shown, in (Liu $et\ al.$, 2010), that $\mathcal{R}_0 < \langle \mathcal{R}_0 \rangle$, and in Dengue fever model it was shown in (Wang & Zhao, 2008) that $\mathcal{R}_0 > \langle \mathcal{R}_0 \rangle$. We can also consult Friedman (2013) for more details.

To deal with model (2.3), some notations will be given. Let us identify x_h together with $(E_h, I_h, R_h, N_h)^T$ and x_v together with $(E_v, I_v)^T$ and set $x =$

$(x_h^T, x_v^T)^T$. Define

$$\Omega = \left\{ (x_h^T, x_v^T)^T \in \mathbb{R}^6 \left| \begin{array}{l} E_h \geq 0; \ I_h \geq 0; \ R_h \geq 0; \ E_v \geq 0; \ I_v \geq 0, \ N_h > 0, \\ E_h + I_h + R_h \leq 1; \quad E_v + I_v \leq 1 \end{array} \right. \right\},$$

$$X_0 := \{ (x_h^T, x_v^T)^T \in \Omega : E_h + I_h + E_v + I_v > 0 \} \text{ and } \partial X_0 := \Omega \setminus X_0.$$

Using the above notations the main result of this work is the following theorem.

Theorem 3.1 *Let Assumption 2.1 be satisfied.*

(i) *The disease-free equilibrium M_0 for System (2.3)-(2.4) is globally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.*

(ii) *If $\mathcal{R}_0 > 1$, then system (2.3)-(2.4) is uniformly persistence with respect to the pair $(X_0, \partial X_0)$, in the sense that there exists $\delta > 0$, such that for any $x_0 \in X_0$ we have,*

$$\liminf_{t \to \infty} d(x(t, x_0), \partial X_0) \geq \delta,$$

and system (2.3) admits at least one positive periodic solution; where $x(t, x_0)$ is the unique solution of (2.3) with $x(0, x_0) = x_0$.

This result says that when $\mathcal{R}_0 < 1$ the disease die out from the host population; and when $\mathcal{R}_0 > 1$ the disease persists in the human host population in the long term.

4 Preliminary and proof of Theorem 3.1

The aim of this section is to derive preliminary remarks on (2.3)-(2.4). These results include the existence of the unique maximal non-autonomous semiflow associated with this system and technical Lemmas that will be used to prove Theorem 3.1.

4.1 Preliminary results

As in (Hirsch & Smith, 2006), the following vector order in $\mathbb{R}^n$ will be used. For $u, v \in \mathbb{R}^n$, we write

$$\begin{aligned} u \leq v &\Leftrightarrow u_i \leq v_i, \\ u < v &\Leftrightarrow u_i \leq v_i, u \neq v, \\ u \ll v &\Leftrightarrow u_i < v_i, \end{aligned}$$

where $i = 1, \ldots, n$.

Definition 4.1 *Consider two maps $\tau : [0, \infty) \times \Omega \to (0, \infty]$ and $\mathcal{U} : D_\tau \to \Omega$, where $D_\tau = \{ (t, s, \mathbf{v}) \in [0, \infty)^2 \times \Omega : s \leq t \leq s + \tau(s, \mathbf{v}) \}$. We say that $\mathcal{U}$ is a maximal non-autonomous semiflow on Ω if U satisfies the following properties:*

(i) $\tau(r, \mathcal{U}(r, s)\mathbf{v}) + r = \tau(s, \mathbf{v}) + s, \forall s \geq 0, \forall \mathbf{v} \in \Omega, \forall r \in [s, s + \tau(s, \mathbf{v}))$.

(ii) $\mathcal{U}(s, s)\mathbf{v} = \mathbf{v}, \forall s \geq 0, \forall \mathbf{v} \in \Omega$.

(iii) $\mathcal{U}(t, r)\mathcal{U}(r, s)\mathbf{v} = \mathcal{U}(t, s)\mathbf{v}, \forall s \geq 0, \forall \mathbf{v} \in \Omega, \forall t, r \in [s, s + \tau(s, \mathbf{v}))$ *with*
$t \geq r$.

(iv) *If* $\tau(s, \mathbf{v}) < +\infty$, *then* $\lim_{t \to (s + \tau(s, \mathbf{v}))^-} \|\mathcal{U}(t, s)\mathbf{v}\|_\Omega = +\infty$.

We first derive that the Cauchy problem (2.3)-(2.4) generates a unique globally defined and positive non-autonomous semiflow.

Theorem 4.2 *Let Assumption 2.1 be satisfied. Then there exits a map* $\tau :$
$[0, \infty) \times \Omega \to (0, \infty]$ *and a maximal non-autonomous semiflow* $U : D_\tau \to \Omega$, *such that for each* $x_0 := x(0) \in \Omega$ *and each* $s \geq 0$, $U(., s)x_0 \in \mathcal{C}\left([s, s + \tau(s, x_0)), \Omega\right)$ *is a unique maximal solution of* (2.3)-(2.4). *The map* $U(t, s)x_0 := (x_h(t)^T, x_v(t)^T)^T$
satisfied the following properties: The subsets X_0 *and* ∂X_0 *are both positively invariant under the non-autonomous semiflow* U; *in other words,*

$$U(t, s)X_0 \subset X_0 \quad and \quad U(t, s)\partial X_0 \subset \partial X_0, \quad \forall(t, s) \in D_\tau.$$

Proof. The proof of this result is rather standard. Standard methodology apply to provide the existence and uniqueness of the semiflow of system (2.3)-(2.4) (Wanner & Hairer, 1991; Hartman, 1964; Katok & Hasselblatt, 1997; Morris *et al.*, 1973).

Let us check the positive invariance of Ω with respect to the semiflow $U(t)$. To do so, let $x_0 = (E_h(0), I_h(0), R_h(0), E_v(0), I_v(0), N_h(0))^T \in \Omega$, we shall prove that $U(t, s)x_0 = (E_h(t), I_h(t), R_h(t), E_v(t), I_v(t), N_h(t))^T \in \Omega$ for all $(t, s) \in D_\tau$. Recalling Assumption 2.1 we easily find that $N_h(t) > 0$ for all $t \geq 0$.

For the other variables, we consider first the case where $I_h(0) > 0$. Using the continuity of the semiflow we find $t_0 > 0$ such that $I_h(t) > 0$ for $t \in [0, t_0]$. If there is $t_1 \in [0, t_0]$ such that $E_h(t_1) + I_h(t_1) + R_h(t_1) = 1$, then $\dot{E}_h(t_1) + \dot{I}_h(t_1) + \dot{R}_h(t_1) < 0$. Therefore $E_h(t) + I_h(t) + R_h(t) \leq 1$ for all $t \in [0, t_0]$. Similarly, $E_v(t) + I_v(t) \leq 1$ for all $t \in [0, t_0]$. If $E_v(t_1) = 0$ for $t_1 \in [0, t_0]$, then E_v-equation of system (2.3) gives $\dot{E}_v(t_1) = \alpha\beta_2(t_1)\theta(t_1)I_h(t_1)(1 - I_v(t_1)) \geq 0$. Thus $E_v(t) \geq 0$ for all $t \in [0, t_0]$. The same arguments give successively that $R_h(t) \geq 0$, $I_v(t) \geq 0$ and $E_h(t) \geq 0$, for $0 < t \leq t_0$.

We next show that $I_h(t)$ remains positive for all $t \geq t_0$. Proceeding by contradiction we suppose that $I_h(t) > 0$ for $0 \leq t < t_0$ and $I_h(t_0) = 0$. Then $\dot{I}_h(t_0) \leq 0$. On the other hand, by I_h-equation of System (2.3), $\dot{I}_h(t_0) = \sigma_h E_h(t_0) > 0$, which is a contradiction. This complete the proof of the first part of theorem in the case $I_h(0) > 0$. It remains to consider the case $I_h(0) = 0$. In this case, recalling $E_h(0) + R_h(0) \leq 1$ so that either $E_h(0) > 0$ or $R_h(0) > 0$. Without loss of generality, we suppose $E_h(0) > 0$ and denote by $x^\delta(t)$ the solution (δ-solution) of System (2.3) with $E_h^\delta(0) = E_h(0) - \delta$, $I_h^\delta(0) = \delta$, $R_h^\delta(0) = R_h(0)$, $E_v^\delta(0) = E_v(0)$, $I_v^\delta(0) = I_v(0)$; $N_h(0)^\delta = N_h(0)$; where $0 < \delta < E_h(0)$. By what we have already proved, the δ-solution $x^\delta(t)$ remains on Ω for all $t > 0$. Taking $\delta \to 0$, the first part of the theorem follows.

To end the proof of the theorem, let

$$x_0 = (E_h(0), I_h(0), R_h(0), E_v(0), I_v(0), N_h(0))^T \in X_0$$

be given and let us denote for each $(t, s) \in D_\tau$,

$$U(t,s)x_0 = (E_h(t), I_h(t), R_h(t), E_v(t), I_v(t), N_h(t))^T,$$

the orbit of system (2.3) passing through x_0. Let us set $y_h(t) = E_h(t) + I_h(t)$ and $y_v(t) = E_v(t) + I_v(t)$. It follows from system (2.3) that $\dot{y}_h(t) \geq -f_h(t)y_h(t)$ and $\dot{y}_v(t) \geq -f_v(t)y_v(t)$; with $f_h(t) = \alpha\beta_1(t)\theta(t)I_v + \Lambda_h/N_h + \rho_h + \gamma_h$ and $f_v(t) = \alpha\beta_2(t)\theta(t)I_h + b_v(t)$. That is

$$y_h(t) \geq y_h(0)e^{-\int_0^t f_h(\eta)d\eta} \quad and \quad y_v(t) \geq y_v(0)e^{-\int_0^t f_v(\eta)d\eta}.$$

This end the proof of the fact that $U(t,s)X_0 \subset X_0$.

Now, let $x_0 \in \partial X_0$. We have $\dot{y}_h(t) + \dot{y}_v(t) \leq f_{h+v}(t)(y_h(t) + y_v(t))$, where $f_{h+v}(t) = \alpha\beta_1(t)\theta(t) + \alpha\beta_2(t)\theta(t) + \rho_h(I_h + E_h)$. Then,

$$(y_h(t) + y_v(t)) \leq (y_h(0) + y_v(0))e^{-\int_0^t f_{h+v}(\eta)d\eta}.$$

Since $y_h(0) + y_v(0) = 0$, we find that $y_h(t) + y_v(t) = 0$. Therefore, $U(t,s)\partial X_0 \subset \partial X_0$. ∎

Recalling (3.5), we now deal with the spectral properties of the linearized system of model (2.3) at the disease-free equilibrium M_0.

In the periodic case, we let $W_\lambda(t,s)$, $t \geq s$, $s \in \mathbb{R}$, be the evolution operator of the linear ω-periodic system

$$\frac{dz}{dt} = \left(\frac{1}{\lambda}F(t) - V(t)\right)z, \ t \in \mathbb{R}$$

with parameter $\lambda \in (0, \infty)$. Clearly, $\Phi_{F-V}(t) = W_1(t,0)$, $\forall t \geq 0$. Note that $\frac{1}{\lambda}F(t) - V(t)$ is cooperative. Thus, the Perron-Frobenius theorem (see Smith & Waltman (1995), Theorem A.3) implies that $\rho(W_\lambda(\omega,0)$ is an eigenvalue of $W_\lambda(\omega,0)$ with nonnegative eigenvector. We can easily find that the matrix $W_\lambda(s + \omega, s)$ is similar to the matrix $W_\lambda(\omega,0)$, and hence $\sigma(W_\lambda(s + \omega, s)) = \sigma(W_\lambda(\omega,0))$ for any $s \in \mathbb{R}$, where $\sigma(D)$ denotes the spectrum of the matrix D. It is easy to verify that system (2.3) satisfies assumptions (A1)-(A7) in Wang & Zhao (2008). Thus, recalling (3.7), we have the following two results.

Lemma 4.3 *(Wang & Zhao (2008), Theorem 2.1). The following statements are valid:*

1. *If $\rho(W_\lambda(\omega,0) = 1$ has a positive solution λ_0, then λ_0 is an eigenvalue of operator L, and hence $\mathcal{R}_0 > 0$.*

2. *If $\mathcal{R}_0 > 0$, then $\lambda = \mathcal{R}_0 > 0$ is the unique solution of $\rho(W_\lambda(\omega,0) = 1$.*

3. *$\mathcal{R}_0 = 0$ if and only if $\rho(W_\lambda(\omega,0) < 1$ for all $\lambda > 0$.*

Lemma 4.4 *(Wang & Zhao (2008), Theorem 2.2). The following statements are valid:*

1. $\mathcal{R}_0 = 1$ if and only if $\rho(\Phi_{F-V}(\omega)) = 1$.

2. $\mathcal{R}_0 > 1$ if and only if $\rho(\Phi_{F-V}(\omega)) > 1$.

3. $\mathcal{R}_0 < 1$ if and only if $\rho(\Phi_{F-V}(\omega)) < 1$.

Let $P : \Omega \to \Omega$ be the Poincaré map associated with system (2.3), that is $Px_0 = x(\omega, x_0)$ where $x(\omega, x_0)$ is the unique solution of system (2.3) with $x(0, x_0) = x_0$. We easily find that $P^n x_0 = x(n\omega, x_0)$, for all $n \geq 0$.

The following lemma will be useful later to derive the malaria persistence in the host population when the basic reproduction ratio $\mathcal{R}_0 > 1$.

Lemma 4.5 *If $\mathcal{R}_0 > 1$, then there exists $\epsilon > 0$, such that for any $x_0 := (E_h^0, I_h^0, R_h^0, E_v^0, I_v^0, N_h^0) \in X_0$ with $||x_0 - M_0|| \leq \epsilon$, we have*

$$\limsup_{n \to \infty} ||P^n x_0 - M_0|| \geq \epsilon.$$

Proof. Since $\mathcal{R}_0 > 1$, Lemma 4.4 implies that $\rho(\Phi_{F-V}(\omega) > 1$. We can choose $\eta > 0$ small enough such that $\rho(\Phi_{F-V-A_{3\eta}}(\omega)) > 1$, where

$$A_\eta(t) := \eta F(t).$$

The perturbed system

$$\frac{d\hat{N}_h}{dt} = \Lambda_h - (\mu_h + \eta\rho_h)\hat{N}_h; \tag{4.9}$$

admits a unique solution

$$\hat{N}_h(t, \eta) = e^{-(\mu_h+\eta)t} \left(\hat{N}_h(0, \eta) + \frac{\Lambda_h}{\mu_h + \eta\rho_h}(e^{(\mu_h+\eta)t} - 1) \right)$$

trough the arbitrary initial value $\hat{N}_h(0, \eta)$, and has a unique periodic attractive solution in $\mathbb{R}_+$

$$\hat{N}_h^\perp(t, \eta) = \frac{\Lambda_h}{\mu_h + \eta\rho_h}.$$

It follows that $\left| \hat{N}_h^\perp(t, \eta) - \hat{N}_h(t, \eta) \right| \to 0$ as $t \to \infty$. Thus $\hat{N}_h^\perp(t, \eta)$ is globally attractive on $\mathbb{R}_+$. It is obvious that $\hat{N}_h^\perp(t, \eta)$ is continuous with respect to η. By the continuity of the solutions with respect to the initial values, we find $\epsilon > 0$ such that for all $x_0 \in X_0$ with $||x_0 - M_0|| \leq \epsilon$, there holds $||x(t, x_0) - x(t, M_0)|| < \eta$, $\forall t \in [0, \omega]$. We further claim that

$$\limsup_{n \to \infty} ||x(n\omega, x_0) - M_0|| \geq \epsilon. \tag{4.10}$$

Assume by contradiction that (4.10) does not hold. Then without loss of generality, we assume that $||x(n\omega, x_0) - M_0|| < \epsilon$, for all $n \geq 0$ and for some $x_0 \in X_0$. It follows that

$$||x(t, P^n x_0) - x(t, M_0)|| < \eta, \quad \forall n \geq 0, \forall t \in [0, \omega].$$

For any $t \geq 0$, let $t = n\omega + s$ and n is the largest integer less than or equal to t/ω. Therefore, we have

$$||x(t, x_0) - M_0|| = ||x(s, P^n x_0) - x(s, M_0)|| < \eta, \ \forall t \geq 0.$$

Recalling that $x(t, x_0) = (E_h(t), I_h(t), R_h(t), E_v(t), I_v(t), N_h(t))^T$, and since $x(t, M_0) \in \partial X_0$ for all $t \geq 0$ (see Theorem 4.2); it then follows that $E_h(t) < \eta$, $I_h(t) < \eta$, $R_h(t) < \eta$, $E_v(t) < \eta$, $I_v(t) < \eta$ for all $t \geq 0$. Since the periodic solution $\hat{E}_h^\perp(t, \eta)$ of system (4.9) is globally attractive on $\mathbb{R}_+$ and $\hat{N}_h^\perp(t, \eta) < N_h^*$, we have $N_h(t) < N_h^*$, for sufficiently large t. From the E_h, I_h, E_v and I_v equations of system (2.3), we obtain, for sufficiently large t,

$$\frac{d}{dt}(E_h, I_h, E_v, I_v)^T \geq (F(t) - V(t) - A_{3\eta}(t))(E_h, I_h, E_v, I_v)^T. \qquad (4.11)$$

We then consider the following system

$$\frac{d}{dt}(\hat{E}_h, \hat{I}_h, \hat{E}_v, \hat{I}_v)^T = (F(t) - V(t) - A_{3\eta}(t))(\hat{E}_h, \hat{I}_h, \hat{E}_v, \hat{I}_v)^T. \qquad (4.12)$$

By Zhang & Zhao (2007), Lemma 2.1, it follows that there exists a positive ω-periodic function $\bar{z}(t)$ such that $\hat{z}(t) = e^{\xi t}\bar{z}(t)$ is a solution of system (4.12), with $\xi = \frac{1}{\omega} \ln \rho(\Phi_{F-V-A_{3\eta}}(\omega))$. Since $\rho(\Phi_{F-V-A_{3\eta}}(\omega)) > 1$, ξ is a positive constant. Let $t = n\omega$ and n be nonnegative integer and get

$$\hat{z}(n\omega) = e^{\xi n\omega}\bar{z}(n\omega) \to (\infty, \infty, \infty, \infty)^T$$

as $n \to \infty$, since $\omega\xi > 0$ and $\bar{z}(t) > 0$. For any nonnegative initial condition $(E_h(0), I_h(0), E_v(0), I_v(0))$ of system (4.11), there exists a sufficiently small $n_0 > 0$ such that $(E_h(0), I_h(0), E_v(0), I_v(0))^T > n_0\bar{z}(0)$. By the comparison principle (Theorem B.1, Smith & Waltman (1995)) we have $(E_h(t), I_h(t), E_v(t), I_v(t))^T > n_0\hat{z}(t)$, for all $t > 0$. Thus, we obtain $(E_h(n\omega), I_h(n\omega), E_v(n\omega), I_v(n\omega))^T \to (\infty, \infty, \infty, \infty)^T$ as $n \to \infty$, a contradiction with the first part of Theorem 4.2. ∎

4.2 Proof of Theorem 3.1

Proof of Theorem 3.1 (i). From Lemma 4.4, it follows that the disease-free equilibrium for System (2.3)-(2.4) is asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. In the sequel, we check the global stability of the disease-free equilibrium when $\mathcal{R}_0 < 1$.

Since $N_h(t) < N_h^*$ for all t sufficiently large (see the proof of Lemma 4.5); we then have for sufficiently large t,

$$
\begin{cases}
\dot{E}_h \leq \alpha\beta_1(t)\theta(t)I_v - (\sigma_h + \mu_h)E_h + \rho_h E_h; \\
\dot{I}_h \leq \sigma_h E_h - (\gamma_h + \rho_h + \mu_h)I_h + \rho_h I_h; \\
\dot{R}_h \leq r\gamma_h I_h - (k_h + \mu_h)R_h + \rho_h R_h; \\
\dot{E}_v \leq \alpha\beta_2(t)\theta(t)I_h - (\sigma_v + b_v(t))E_v; \\
\dot{I}_v \leq \sigma_v E_v - b_v(t)I_v; \\
\dot{N}_h \leq \Lambda_h - \mu_h N_h.
\end{cases}
$$

Therefore, for all t sufficiently large, we obtain that

$$\frac{d}{dt}(E_h, I_h, E_v, I_v)^T \leq [F(t) - V(t) + \rho_h.diag(1, 1, 0, 0,)](E_h, I_h, E_v, I_v)^T.$$

We introduce the solution z^δ of

$$\frac{dz^\delta}{dt} = [F(t) - V(t) + \rho_h.diag(1, 1, 0, 0) + \delta I]z^\delta,$$
$$z^\delta(0) = (E_h(0) + \delta, I_h(0) + \delta, E_v(0) + \delta, I_v(0) + \delta)^T, \quad (4.13)$$

for any $\delta > 0$. Then $z^\delta(t) > (E_h(t), I_h(t), E_v(t), I_v(t))^T$ for small t. We claim that this inequality holds for all $t > 0$. To check this assertion we apply the comparison principle (Theorem B.1, Smith & Waltman (1995)).

Indeed, otherwise there is a smallest $\bar{t}$ such that at least one of the strict inequalities is violated at $t = \bar{t}$. Suppose $z_1^\delta(\bar{t}) = E_h(\bar{t})$. Then $dz_1^\delta(\bar{t})/dt \leq dE_h(\bar{t})/dt$. We also have $z_4^\delta(\bar{t}) \geq I_v(\bar{t})$. Hence

$$\frac{dz_1^\delta(\bar{t})}{dt} \leq \frac{dE_h(\bar{t})}{dt} \leq \alpha\beta_1(\bar{t})\theta(\bar{t})z_4^\delta(\bar{t}) - (\sigma_h + \mu_h)z_1^\delta(\bar{t}) + \rho_h z_1^\delta(\bar{t}),$$

which contradict the z_1^δ-equation of system (4.13). By a similar argument one derives a contradiction in cases $z_2^\delta(\bar{t}) = I_h(\bar{t})$, $z_3^\delta(\bar{t}) = E_v(\bar{t})$ and $z_4^\delta(\bar{t}) = I_v(\bar{t})$.

Taking $\delta \to 0$ we conclude that

$$E_h(t) \leq z_1(t), \ I_h(t) \leq z_2(t), \ E_v(t) \leq z_3(t), \ I_v(t) \leq z_4(t), \quad \forall t > 0, \quad (4.14)$$

where $z(t) = (z_1, z_2, z_3, z_4)^T$ is the solution of

$$\frac{dz}{dt} = [F(t) - V(t) + \rho_h.diag(1, 1, 0, 0)]z,$$
$$z(0) = (E_h(0), I_h(0), E_v(0), I_v(0))^T. \quad (4.15)$$

Applying Lemma 4.4, we know that $\mathcal{R}_0 < 1$ if and only if $\rho(\Phi_{F-V}(\omega)) < 1$. By Zhang & Zhao (2007), Lemma2.1, it follows that there exists a positive ω-periodic function $\bar{z}(t)$ such that $z(t) = e^{\tau t}\bar{z}(t)$ is a solution of system (4.15), with $\tau = \frac{1}{\omega}\ln\rho(\Phi_W(\omega))$, with $W = F - V + \rho_h.diag(1, 1, 0, 0)$. Since $\rho(\Phi_W(\omega) < \rho(\Phi_{F-V}(\omega)) < 1$, τ is a negative constant. Therefore, we have $z(t) \to 0$ as $t \to +\infty$. This implies that the zero solution of system (4.15) is globally stable. Thus, equation (4.14) gives that $(E_h(t), I_h(t), E_v(t), I_v(t))^T \to (0, 0, 0, 0)^T$ as $t \to +\infty$. It is easy to find that $N_h(t) \to N_h^*$ as $t \to +\infty$. Then we can choose $\eta > 0$ small enough such that $\dot{R}_h \leq \eta - (k_h + \mu_h)R_h$ for all sufficiently large t. From where $R_h(t) \to 0$ as $t \to +\infty$. This end the proof of the first part of the theorem.

Proof of Theorem 3.1 (ii). By Theorem 4.2, the discrete system $\{P^n\}_{n\in\mathbb{N}}$ admits a global attractor in Ω. For any $x_0 := (E_h^0, I_h^0, R_h^0, E_v^0, I_v^0, N_h^0) \in X_0$, Let

$x(t, x_0) = (E_h(t), I_h(t), R_h(t), E_v(t), I_v(t), N_h(t))^T$ be the orbit of (2.3) passing through x_0.

We have show that, both Ω, X_0 and ∂X_0 are positively invariant with respect to the non-autonomous semiflow U (Theorem 4.2). Clearly, ∂X_0 is relatively closed in Ω, and there is exactly one fixed point $M_0 = (0, 0, 0, 0, 0, N_h^*)$ of P in ∂X_0.

Note that the linear system

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - \rho_h I_h N_h, \quad N_h(0) > 0;$$

admits a global asymptotic equilibrium N_h^*. Lemma 4.5 implies that $\{M_0\}$ is an isolated invariant set in Ω and $W^s(\{M_0\}) \cap X_0 = \emptyset$. We can also note that every orbit in ∂X_0 approches to M_0 and M_0 is acyclic in ∂X_0. By Zhao (2003), Theorem 1.3.1, it follows that P is uniformly persistence with respect to the pair $(X_0, \partial X_0)$. That is, there exists a $\delta > 0$ such that any solution $x(t, x_0)$ of system (2.3) with initial value $x_0 \in X_0$ satisfies $\liminf_{t \to \infty} d(x(t, x_0), \partial X_0) \geq \delta$.

Furthermore, Zhao (2003), Theorem 1.3.6, implies that the discrete system $\{P^n\}_{n \in \mathbb{N}}$ has a fixed point $x_0^\dagger = (E_h^\dagger(0), I_h^\dagger(0), R_h^\dagger(0), E_v^\dagger(0), I_v^\dagger(0), N_h^\dagger(0))^T \in X_0$. Then, by $(E_h, I_h, R_h, E_v, I_v)$-equation of system (2.3) and the irreducibility of the cooperative matrix

$$A^\dagger(t) = \begin{pmatrix} -(\sigma_h + \frac{\Lambda_h}{N_h^\dagger}) & 0 & 0 & 0 & \alpha\beta_1(t)\theta(t)g_h^\dagger \\ \sigma_h & -(\gamma_h + \rho_h + \frac{\Lambda_h}{N_h^\dagger}) & 0 & 0 & 0 \\ 0 & r\gamma_h & -(k_h + \frac{\Lambda_h}{N_h^\dagger}) & 0 & 0 \\ 0 & \alpha\beta_2(t)\theta(t)g_v^\dagger & 0 & -(\sigma_v + b_v(t)) & 0 \\ 0 & 0 & 0 & \sigma_v & -b_v(t) \end{pmatrix},$$

it follows that $(E_h^\dagger(t), I_h^\dagger(t), R_h^\dagger(t), E_v^\dagger(t), I_v^\dagger(t))^T \gg 0$ for all $t \geq 0$. Where $g_h^\dagger = (1 - E_h^\dagger - I_h^\dagger - R_h^\dagger)$ and $g_v^\dagger = (1 - E_v^\dagger - I_v^\dagger)$

Therefore, $(E_h^\dagger(t), I_h^\dagger(t), R_h^\dagger(t), E_v^\dagger(t), I_v^\dagger(t), N_h^\dagger(t), N_v^\dagger(t))$ is a positive ω-periodic solution of system (2.3). This end the proof of the second part of Theorem 3.1.

5   Numerical results and discussion

Thermal-response curves.   A collection of data to derive functions relating vector and parasite parameters to temperature was updated by Mordecai *et al.* (2013). As all rate parameters in the temperature-dependent are expected to be unimodal with respect to temperature, Mordecai *et al.* (2013) fit quadratic and Brière functions to each life-history parameter, as well as a linear function for comparison (Table 2). The Brière function is a left-skewed unimodal curve with three parameters, which represent the minimum temperature, maximum temperature and a rate constant (Briere *et al.*, 199). The unimodal functions are defined as Brière $[c(T_0 - T(t))(Tm - T(t))^{1/2}]$ and quadratic $[qT^2(t) + rT(t) + s]$, where $T(t)$ is temperature in degrees Celsius at time t. Constants c, T_0, T_m,

q, r and s are fitting parameters. In this paper, mosquitoes per capita birth rate (b_v), per capita death rate (μ_v), infectivity (β_2) and biting rate (θ) are estimated from thermal performance curves and summarized in Table 2.

Nkomazi (South Africa) climate data. For all simulations, we incorporate the daily climate data (temperature) of Nkomazi from 1997 to 2005 into our model to estimate time dependent parameters of model (2.1), namely b_v, μ_v, β_2 and θ (Figure 1). The temperature data were extracted from the National Centers for Environmental Prediction (NCEP) Climate Forecast System Reanalysis (CFSR). The 6-hourly climate dataset was converted to daily with $0.5° \times 0.5°$ resolution for the purpose of this study. Conversely, the malaria data sourced from the provincial Integrated Malaria Information System (IMIS) of the malaria control program in the Mpumalanga Provincial Department of Health, was obtained from the South African Weather Service (SAWS) through its collaborative research with the University of Pretoria Institute for Sustainable Malaria Control (UP ISMC). The locally recorded cases with minimal imported cases were extracted from Nkomazi – a local municipality in Mpumalanga province (one of the epidemic provinces in South Africa). In the province, malaria distribution is mainly in Nkomazi, Bushbuckridge, Mbombela, Umjindi and Thaba Chewu local municipalities, with suitable climate conditions for malaria transmission (Sila *et al.*, 2013; Adeola *et al.*, 2016). Of all the municipalities, Nkomazi has been identified as the most epidemic region in the province (Sila *et al.*, 2013; Adeola *et al.*, 2016).

The risk of outbreak in Nkomazi is underestimated when using the average basic reproduction number. Using parameters given by Tables 2 and 3, then by numerical computation, we get the curve of the basic reproduction number $\mathcal{R}_0$ (applying Lemma 4.3 item (ii)) and the curve of the average basic reproduction number $\langle \mathcal{R}_0 \rangle$ with respect to the mosquitoes contact rate α in Figure 2A. We can see that the average basic reproduction number $\langle \mathcal{R}_0 \rangle$ is always lower than the basic reproduction number $\mathcal{R}_0$ with α ranging from 0 to 1. Therefore, using $\langle \mathcal{R}_0 \rangle$ rather than $\mathcal{R}_0$ underestimates the outbreak of the disease in Nkomazi. Indeed, taking $\alpha = 0.2$, numerical computation leads to $\langle \mathcal{R}_0 \rangle = 0.8 < 1$, suggesting that there is no epidemic into the host population, and $\mathcal{R}_0 = 1.4 > 1$, suggesting that there is an epidemic into the host population (Figure 2B–C).

Illustration of disease extinction and persistence stated by Theorem 3.1. From Theorem 3.1, $\mathcal{R}_0$ is a threshold parameter to determine whether or not malaria persists in the population. We choose the total number of human and mosquitoes at initial time ($t = 0$) to be $N_h(0) = 1000$ and $N_v(0) = 2000$ respectively. Two sets of initial values are considered and given in Table 3. The number of mosquitoes per human host could be various, we take here $m^* = 2$ (Harada, 1998; Ishikawa *et al.*, 2003; Ruan *et al.*, 2008); therefore, the recruitment rate of human host is $\Lambda_h = N_v(0)\mu_h/m^* \approx 0.046$ per day. Tak-

Figure 1: Time performance curves of mosquitoes traits using daily temperature of Nkomazi (South Africa) and thermal performance curves summarized in Table 2.

Figure 2: **A** Comparison between the basic reproduction number ($\mathcal{R}_0$) and and the average basic reproduction number ($\langle \mathcal{R}_0 \rangle$) for range of the mosquitoes contact rate (α). **B-C** The long term dynamics of infectious human and infectious mosquitoes with $\rho_h = 0.01$, $\gamma_h = 0.01$, $\alpha = 0.2$, $r = 0.9$ and $\Lambda_h = 0.05$. We use the temperature data of Nkomazi (South Africa) and find that $\langle \mathcal{R}_0 \rangle = 0.8 < 1$; $\mathcal{R}_0 = 1.4 > 1$. Other parameters are given by Tab. 3 and Tab. 2. We illustrate the behavior of the model using time dependent parameters b_v, μ_v, β_2, θ (solid line) and average constant parameters $\langle b_v \rangle$, $\langle \mu_v \rangle$, $\langle \beta_2 \rangle$, $\langle \theta \rangle$ (dot line).

Figure 3: The long term behaviours (for two initial values) of four classes of population illustrated that the disease free state M_0 is globally stable. Here, we use $\Lambda_h \approx 0.046$ per day, $\rho_h = 0.01$, $\gamma_h = 0.01$, $r = 0.9$ and $\alpha = 0.1$ per day, $\mathcal{R}_0 = 0.7 < 1$ and $\langle \mathcal{R}_0 \rangle = 0.4 < 1$. Other parameters and initial values are given by Tab. 3 and Tab. 2. We illustrate the behavior of the model using time dependent parameters b_v, μ_v, β_2, θ (solid line) and average constant parameters $\langle b_v \rangle$, $\langle \mu_v \rangle$, $\langle \beta_2 \rangle$, $\langle \theta \rangle$ (dotted line).

Figure 4: The long term behaviors of four classes of population illustrated that the disease is endemic. Here, we use $\Lambda_h \approx 0.046$ per day, $\rho_h = 0.01$, $\gamma_h = 0.01$, $r = 0.9$ and $\alpha = 0.4$ per day, $\mathcal{R}_0 = 2.8 > 1$ and $\langle \mathcal{R}_0 \rangle = 1.6 > 1$. Other parameters and initial values are given by Tab. 3 and Tab. 2. We illustrate the behavior of the model using time dependent parameters b_v, μ_v, β_2, θ (solid line) and average constant parameters $\langle b_v \rangle$, $\langle \mu_v \rangle$, $\langle \beta_2 \rangle$, $\langle \theta \rangle$ (dotted line).

Figure 5: Daily malaria cases: reported number in Nkomazi (red dot line) and simulation curve (blue solid line) from October 1, 1997 to December 31, 2005. Here, we use $\alpha \approx 0.15$, $\Lambda \approx 0.595$, $\gamma_h \approx 0.01$, $\rho_h \approx 0.007$ and $r \approx 0.99$ per day. We find $\mathcal{R}_0 = 1.16 > 1$ and $\langle \mathcal{R}_0 \rangle = 0.65 < 1$. Other parameters are given by Tab. 3 and Tab. 2.

ing $\rho_h = 0.01$, $\gamma_h = 0.01$, $r = 0.9$ and $\alpha = 0.1$ per day, Figure 3 supports the theoretical fact that the disease-free equilibrium M_0 is globally asymptotically stable when $\mathcal{R}_0 = 0.7 < 1$. If the mosquitoes contact rate per human host is increased to $\alpha = 0.4$ per day, numerical simulations complete the theoretical analysis that there exists a global attractive positive periodic solution when $\mathcal{R}_0 = 2.8 > 1$ (Figure 4).

A case study. In this section, we estimate parameters of model (2.1)-(2.4) which are assumed to be variable (namely the human recuitement, disease induce mortality and recovery rate, Λ, ρ_h, γ_h and r; and the mosquitoes contact rate per human α) and study the transmission trend of malaria in Nkomazi, South Africa. Simulation results are given to show that our model with periodic parameters matches the seasonal fluctuation data reasonably well.

The daily numbers of human malaria cases from the study region correspond to the term $I_h(t)$ of model (2.1). Since we assume five model parameters to be variable, $\pi := (\Lambda, \rho_h, \gamma_h, r, \alpha)$, we then find the value $\pi^* = (\Lambda^*, \rho_h^*, \gamma_h^*, r^*, \alpha^*)$ which minimize the difference ($\Delta[\pi]$) between model prediction (I_h) and the malaria cases of Nkomazi (I_{cases}) from day d_S to day

d_F: $\Delta[\pi] := \left(\sum_{t=d_S}^{d_F} |I_h(t) - I_{\text{cases}}(t)|^2 \right)^{1/2}$. The value π^* is identified with the MATLAB nonlinear programming solver FMINCON. Taking October 1, 1997 and December 31, 2005 as the start and end time of simulation respectively, Nkomazi malaria cases and the model fit well with $\alpha^* \approx 0.15$, $\Lambda^* \approx 0.595$, $\gamma_h^* \approx 0.01$, $\rho_h^* \approx 0.007$ and $r^* \approx 0.99$ (Figure 5). The simulation result based on our model exhibits the seasonal fluctuation and matches the data reasonably well. We estimate the basic reproduction ratio and the average basic reproduction ratio $\mathcal{R}_0 = 1.16$ and $\langle \mathcal{R}_0 \rangle = 0.65$ respectively. Furthermore, the value of $\langle \mathcal{R}_0 \rangle < 1$ suggests that the epidemic is not endemic in Nkomazi leading to a wrong interpretation as illustrated by Figure 5.

6   Conclusion

We have developed a compartmental model to describe malaria seasonal incidence rate by incorporating periodic coefficients. We define the basic reproduction ratio $\mathcal{R}_0$ and prove that the unique disease-free equilibrium M_0 is globally asymptotically stable if $\mathcal{R}_0 < 1$; while the disease is uniformly persistent and there exists at least one positive periodic solution if $\mathcal{R}_0 > 1$. Numerical simulations show that there is only one positive periodic solution which is globally asymptotically stable in the case where $\mathcal{R}_0 > 1$. We observe a significant difference on the behaviour of the model without treating seasonality and with seasonality. We further provide some illustrations of the model without treating seasonality using the average numbers of the periodic parameters of the model. The performance of the model was also investigated with both Nkomazi climate and malaria data.

Table 2: The relationships between temperature and the mosquito and parasite life-history traits that determine malaria risk. Thermal performance curves were fitted to the data assuming Brière $[c(T_0 - T(t))(T_m - T(t))^{1/2}]$, **B**, or Quadratic $[qT^2(t) + rT(t) + s]$, **Q**, functions; in which $T(t)$ is temperature ($^\circ C$) at time t. Standard deviations for the parameters are listed in parentheses alongside parameter values. (see Mordecai et al. (2013) and references therein).

Parameters	Definition	Fit	Fit parameters (standard deviation)		
θ	Biting rate	**B**	$c = 0.000203(0.0000576)$	$T_m = 42.3(3.53)$	$T_0 = 11.7(2.47)$
$\beta_1 * \beta_2$	Vector competence	**Q**	$q = -0.54(0.18)$	r$= 25.2(9.04)$	$s = -206(108)$
$e^{-\mu_v}$	Daily adult survival probability	**Q**	$q = -0.000828(0.0000519)$	$r = 0.0367(0.00239)$	$s = 0.522(0.0235)$
Mdr	Mosquito development rate	**B**	$c = 0.000111(0.00000954)$	$T_m = 34(0.000106)$	$T_0 = 14.7(0.831)$
pEA	Egg-to-adult survival probability	**Q**	$q = -0.00924(0.00123)$	$r = 0.453(0.0618)$	$s = -4.77(0.746)$
EFD	Egg laid per adult female per day	**Q**	$q = -0.153(0.0307)$	$r = 8.61(1.69)$	$s = -97.7(22.6)$
PDR	Parasite development rate	**B**	$c = 0.000111(0.0000161)$	$T_m = 34.4(0.000176)$	$T_0 = 14.7(1.48)$

Using the above notations, the mosquitoes per capita birth rate b_v is given by
$$\dot{b}_v(t) = EFD(t) * Mdr(t) * pEA(t) * e^{-\mu_v(t)}.$$

Table 3: Parameter and initial values

Parameter	Description	Estimated value	Ref.
Λ	Human recruitment rate	variable	
α	Mosquitoes contact rate per human	variable: 0-1	Aron & May (1982)
ρ_h	Human disease induce mortality rate	variable: 0-1	Bray & Garnham (1982)
r	Rate of recovered with temporary immunity	variable: 0-1	Burkot et al. (1990)
γ_h	Human recovery rate	variable: 0.01-0.05/day	Craig et al. (1999)
μ_h	Natural death rate in humans	$1/(60*365)$/day	Blayneh et al. (2009)
k_h	Rate of loss of immunity	$1/(2*365)$/day	Blayneh et al. (2009)
σ_h	Humans progression rate to infectious	$1/17$	Blayneh et al. (2009)
σ_v	Mosquitoes progression rate to infectious	$1/18$	Beier (1998)
β_1	Rate of human getting infected	0.5	Bray & Garnham (1982)
			Burkot et al. (1990)

Initial values	Description	Ref.
Set 1	$N_h(0) = 1000; N_v(0) = 2000$	Assumed
	$(S_h(0), E_h(0), I_h(0), R_h(0)) = (0.4, 0.3, 0.2, 0.1) * N_h(0)$	
	$(S_v(0), E_v(0), I_v(0)) = (0.5, 0.3, 0.2) * N_v(0)$	
Set 2	$N_h(0) = 1000; N_v(0) = 2000$	Assumed
	$(S_h(0), E_h(0), I_h(0), R_h(0)) = (0.72, 0.05, 0.03, 0.2) * N_h(0)$	
	$(S_v(0), E_v(0), I_v(0)) = (0.94, 0.04, 0.02) * N_v(0)$	

Acknowledgements

GJA acknowledges the support of the Fogarty International Center (FIC) of the National Institutes of Health (NIH) under Award Number D43TW009343 and the University of California Global Health Institute (UCGHI).

References

Abdelrazec, A., Gumel, A. B. (2017). Mathematical assessment of the role of temperature and rainfall on mosquito population dynamics. Journal of mathematical biology, 74(6), 1351-1395.

Abiodun G.J., Okosun O.K., Witbooi P.J., Maharaj, R (2018). Exploring the impact of climate variability on malaria transmission using a dynamic mosquito-human malaria model. The Open Infectious Diseases Journal. https://www.benthamopen.com/EPUB/BMS-TOIDJ-2018-17.

Abiodun, G. J., Witbooi, P. J., Okosun, K. O. (2017). Mathematical modelling and analysis of mosquito-human malaria model. International Journal of Ecological Economics and Statistics™, 38(3), 1-22.

Abiodun, G. J., Maharaj, R., Witbooi, P., & Okosun, K. O. (2016). Modelling the influence of temperature and rainfall on the population dynamics of Anopheles arabiensis. Malaria journal, 15(1), 364.

Adeola, A. M., Botai, O. J., Olwoch, J. M., Rautenbach, C. D. W., Adisa, O. M., Taiwo, O. J., Kalumba, A. M. (2016). Environmental factors and population at risk of malaria in N komazi municipality, South Africa. Tropical Medicine and International Health, 21(5), 675-686.

Alonso, D., Bouma, M. J., Pascual, M. (2011). Epidemic malaria and warmer temperatures in recent decades in an East African highland. Proceedings of the Royal Society of London B: Biological Sciences, 278(1712), 1661-1669.

Anderson, R. M., May, R. M. (1992). Infectious diseases of humans: dynamics and control. Oxford university press.

Aron, J. L., May, R. M. (1982). The population dynamics of malaria. In The population dynamics of infectious diseases: theory and applications (pp. 139-179). Springer, Boston, MA.

Bakary, T., Boureima, S., Sado, T. (2018). A mathematical model of malaria transmission in a periodic environment. Journal of biological dynamics, 12(1), 400-432.

Beck-Johnson, L. M., Nelson, W. A., Paaijmans, K. P., Read, A. F., Thomas, M. B., Bjørnstad, O. N. (2013). The effect of temperature on Anopheles mosquito population dynamics and the potential for malaria transmission. PLOS one, 8(11), e79276.

Beier, J. C. (1998). Malaria parasite development in mosquitoes. Annual review of entomology, 43(1), 519-543.

Bray, R. S., Garnham, P. C. C. (1982). The life-cycle of primate malaria parasites. British Medical Bulletin, 38(2), 117-122.

Briere, J. F., Pracros, P., Le Roux, A. Y., Pierre, J. S. (1999). A novel rate model of temperature-dependent development for arthropods. Environmental Entomology, 28(1), 22-29.

Burkot, T. R., Graves, P. M., Paru, R., Battistutta, D., Barnes, A., Saul, A. (1990). Variations in malaria transmission rates are not related to anopheline survivorship per feeding cycle. The American journal of tropical medicine and hygiene, 43(4), 321-327.

Chitnis, N., Cushing, J. M., Hyman, J. M. (2006). Bifurcation analysis of a mathematical model for malaria transmission. SIAM Journal on Applied Mathematics, 67(1), 24-45.

Chitnis, N., Hyman, J. M., Cushing, J. M. (2008). Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. Bulletin of mathematical biology, 70(5), 1272.

Craig, M. H., Snow, R. W., le Sueur, D. (1999). A climate-based distribution model of malaria transmission in sub-Saharan Africa. Parasitology today, 15(3), 105-111.

Dembele, B., Friedman, A., Yakubu, A. A. (2009). Malaria model with periodic mosquito birth and death rates. Journal of biological dynamics, 3(4), 430-445.

Eikenberry, S. E., Gumel, A. B. (2018). Mathematical modeling of climate change and malaria transmission dynamics: a historical review. Journal of mathematical biology, 1-77.

Friedman, A. (2013). Epidemiological models with seasonality. In Mathematical Methods and Models in Biomedicine (pp. 389-410). Springer, New York, NY.

Wanner, G., Hairer, E. (1991). Solving ordinary differential equations II. Stiff and Differential-Algebraic Problems.

Harada, M. (1998). Studies on vector control by "Mosquito Candle". Malaria research in the Solomon Islands, 120-125.

Hartman P, Ordinary Differential Equations. John Wiley and Sons, New-York, 1964.

Hirsch, M. W., Smith, H. (2006). Monotone dynamical systems. In Handbook of differential equations: ordinary differential equations (Vol. 2, pp. 239-357). North-Holland.

Morris W.. Hirsch, Smale, S. (1973). Differential equations, dynamical systems and linear algebra. Academic Press college division.

Hoshen, M. B., Morse, A. P. (2004). A weather-driven model of malaria transmission. Malaria Journal, 3(1), 32.

Ishikawa, H., Ishii, A., Nagai, N., Ohmae, H., Harada, M., Suguri, S., Leafasia, J. (2003). A mathematical model for the transmission of Plasmodium vivax malaria. Parasitology International, 52(1), 81-93.

Katok, A., Hasselblatt, B. (1997). Introduction to the modern theory of dynamical systems (Vol. 54). Cambridge university press.

Blayneh, K., Cao, Y., Kwon, H. D. (2009). Optimal control of vector-borne diseases: treatment and prevention. Discrete and Continuous Dynamical Systems B, 11(3), 587-611.

Lafferty, K. D. (2009). The ecology of climate change and infectious diseases. Ecology, 90(4), 888-900.

Laneri, K., Paul, R. E., Tall, A., Faye, J., Diene-Sarr, F., Sokhna, C., ... Rodó, X. (2015). Dynamical malaria models reveal how immunity buffers effect of climate variability. Proceedings of the National Academy of Sciences, 112(28), 8786-8791.

Liu, L., Zhao, X. Q., Zhou, Y. (2010). A tuberculosis model with seasonality. Bulletin of Mathematical Biology, 72(4), 931-952.

Mordecai, E. A., Paaijmans, K. P., Johnson, L. R., Balzer, C., Ben-Horin, T., de Moor, E., ... Lafferty, K. D. (2013). Optimal temperature for malaria transmission is dramatically lower than previously predicted. Ecology letters, 16(1), 22-30.

Ngwa, G. A., Shu, W. S. (2000). A mathematical model for endemic malaria with variable human and mosquito populations. Mathematical and Computer Modelling, 32(7-8), 747-763.

Okuneye, K., Gumel, A. B. (2017). Analysis of a temperature-and rainfall-dependent model for malaria transmission dynamics. Mathematical biosciences, 287, 72-92.

Paaijmans, K. P., Read, A. F., Thomas, M. B. (2009). Understanding the link between malaria risk and climate. Proceedings of the National Academy of Sciences, 106(33), 13844-13849.

Roy, M., Bouma, M., Dhiman, R. C., Pascual, M. (2015). Predictability of epidemic malaria under non-stationary conditions with process-based models combining epidemiological updates and climate variability. Malaria journal, 14(1), 419.

Ruan, S., Xiao, D., Beier, J. C. (2008). On the Delayed Ross–Macdonald Model for Malaria Transmission. Bulletin of Mathematical Biology, 70(4), 1098–1114.

Silal, S. P., Barnes, K. I., Kok, G., Mabuza, A., Little, F. (2013). Exploring the Seasonality of Reported Treated Malaria Cases in Mpumalanga, South Africa. PLoS ONE, 8(10), e76640.

Smith, H. L., Waltman, P. (1995). The theory of the chemostat: dynamics of microbial competition (Vol. 13). Cambridge university press.

Van den Driessche, P., Watmough, J. (2008). Further notes on the basic reproduction number. In Mathematical epidemiology (pp. 159-178). Springer, Berlin, Heidelberg.

Wang, W., Zhao, X. Q. (2008). Threshold dynamics for compartmental epidemic models in periodic environments. Journal of Dynamics and Differential Equations, 20(3), 699-717.

World Health Organization (2017). World Malaria Report 2017. http://www.who.int/malaria/publications/world-malaria-report-2017/en/ (Accessed: June 2018)

Zhang, F., Zhao, X. Q. (2007). A periodic epidemic model in a patchy environment. Journal of Mathematical Analysis and Applications, 325(1), 496-516.

Zhao, X.Q. (2003) Dynamical Systems in Population Biology. Springer-Verlag, New York.