Journal of Biological Dynamics

ISSN: 1751-3758 (Print) 1751-3766 (Online) Journal homepage: http://www.tandfonline.com/loi/tjbd20

A mathematical model for the dynamics of malaria in mosquitoes feeding on a heterogeneous host population

Nakul Chitnis , Thomas Smith & Richard Steketee

To cite this article: Nakul Chitnis , Thomas Smith & Richard Steketee (2008) A mathematical model for the dynamics of malaria in mosquitoes feeding on a heterogeneous host population, Journal of Biological Dynamics, 2:3, 259-285, DOI: 10.1080/17513750701769857

To link to this article: http://dx.doi.org/10.1080/17513750701769857

Journal of Biological Dynamics
Vol. 2, No. 3, July 2008, 259–285

Taylor & Francis
Taylor & Francis Group

A mathematical model for the dynamics of malaria in mosquitoes feeding on a heterogeneous host population

Nakul Chitnis[a]*, Thomas Smith[a] and Richard Steketee[b]

[a]*Department of Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland;* [b]*MACEPA, PATH-Europe, Ferney-Voltaire, France*

(*Received 01 June 2007; final version received 03 October 2007*)

We describe and develop a difference equation model for the dynamics of malaria in a mosquito population feeding on, infecting and getting infected from a heterogeneous population of hosts. Using the force of infection from different classes of humans to mosquitoes as parameters, we evaluate a number of entomological parameters, indicating malaria transmission levels, which can be compared to field data. By assigning different types of vector control interventions to different classes of humans and by evaluating the corresponding levels of malaria transmission, we can compare the effectiveness of these interventions. We show a numerical example of the effects of increasing coverage of insecticide-treated bed nets in a human population where the predominant malaria vector is *Anopheles gambiae*.

Keywords: mathematical model; epidemiology; malaria; mosquito; difference equations

1. Introduction

Malaria is an infectious disease caused by *Plasmodium* parasites and transmitted between humans through bites of female *Anopheles* mosquitoes. It is a global public health burden killing over a million people per year, and significant efforts are now being made to control the disease, especially through vector control interventions aimed at reducing disease transmission.

The Roll Back Malaria Partnership (RBM) in its Global Strategic Plan for 2005–2015 [27] announced its intention to protect 80% of the world's population at risk of malaria, through an appropriate vector control strategy involving the use of insecticide-treated nets (ITNs), indoor residual spraying (IRS) and/or where appropriate, some other environmental or biological measures.

Mathematical modelling can play an important role in quantifying the effects of malaria control strategies and determining which strategies are effective in different transmission settings. Here, we present a model of the mosquito feeding cycle that can provide a quantitative understanding of the effects of various vector control strategies.

*Corresponding author. Email: nakul.chitnis@unibas.ch

ISSN 1751-3758 print/ISSN 1751-3766 online

DOI: 10.1080/17513750701769857
http://www.informaworld.com

Mathematical modelling of malaria has primarily consisted of continuous dynamical systems models based on the work of Ross [28] and Macdonald [22], as described by Anderson and May [1], Aron and1 May [4], and Smith and McKenzie [32], including models by Aron [3], Bacaër and Sokhna [5], Chitnis et al. [24], Dietz et al. [9], Koella and Boëte [19], Li et al. [21], Ngwa and Shu [25], Struchiner et al. [34], and Yang [35]. However, mosquitoes do not usually experience a constant mortality rate. The life of a female mosquito consists of a sequence of gonotrophic (or feeding) cycles with discrete phases, each with a different level of risk to the mosquito's survival. Additionally, Anophelines keep to the circadian rhythm and start seeking blood meals about the same time every night. Saul et al. [30] first proposed a cyclical model for the mosquito feeding cycle and malaria transmission. Killeen and Smith [15], Le Menach et al. [23] and Saul [29] extended this model to include the effects of nets and/or animals in diverting and killing mosquitoes, by subdividing the feeding cycle into seeking, feeding and resting phases. However, Le Menach et al. [23] converted the survival probabilities of a feeding cycle, along with the duration of the feeding cycle, into expressions that depend on continuous time.

We extend the previous models, [15] and [29], which had three types of hosts[†] and constant host infectiousness to mosquitoes, to a model with an unrestricted number of types of hosts, each with its own level of availability to mosquitoes and infectiousness to mosquitoes. This allows for a comprehensive modelling of host heterogeneity, including uneven malaria intervention coverage (vector control and chemotherapeutic), body surface area, proximity to breeding sites, housing and host infectivity to mosquitoes. In previous models of the mosquito feeding cycle, all mosquitoes were assumed to take the same amount of time to find a host and the duration of the feeding cycle was fixed. We now assume a geometric distribution for the probability that a mosquito finds a host in a given night and allow the duration of the feeding cycle to vary across mosquitoes. We also further subdivide the feeding cycle into more stages that differentiate between the effects of various vector control interventions.

We use difference equations to model the total population, the infected population and the infective population of host-seeking mosquitoes. Discrete time steps of 1 day better capture the circadian nature of the mosquito's life. We use the term 'day' to represent a 24-hour period and not the hours that are distinct from night. We use the term 'daylight hours' to represent what is usually called day or daylight. We divide the mosquito's gonotrophic cycle into five discrete stages. Each stage has a different survival probability for the mosquito, which may be affected by different interventions.

Applying various vector control interventions to different types of hosts allows us to quantify the effects of these intervention strategies. In the model, we divide the host population into an arbitrary number, n, of categories. These, for example, can be any of, unprotected humans; humans protected by untreated nets; humans protected by ITNs; humans protected by IRS; humans protected by both, ITNs and IRS; humans living in a household with at least one ITN but not sleeping under an ITN; or even livestock and insecticide-treated livestock.

From this model of the dynamics of a single population of mosquitoes feeding on a heterogeneous human (and possibly livestock) population, we evaluate the equilibrium value of several field-measurable quantities, including the sporozoite rate (the proportion of infective mosquitoes) and the entomological inoculation rate (the number of infectious bites each host receives per unit of time). The sporozoite rate and the entomological inoculation rate (EIR) provide measures of transmission levels in a given setting. The difference in these rates for hosts with and without an intervention provides a measure of its effectiveness.

[†] We use the word 'host' here to refer to mammalian blood meal sources for mosquitoes. Since the sexual stage of the *Plasmodium* parasite occurs in the mosquito, the mosquito is biologically defined as the definitive host of malaria and the human is the intermediate host [14]. However, to be consistent with literature in mathematical epidemiology, we use 'hosts' to refer to humans (as hosts for the malaria parasite and as sources of blood meals for mosquitoes) and non-human vertebrates (as blood meal sources for mosquitoes) and 'vectors' to refer to mosquitoes.

Here, we do not model the dynamic effects of infection through humans. Since we consider the infectivity of humans to mosquitoes only as a parameter, and not as a state variable, our model is linear. Smith et al. [33] modelled the process of infection in humans through stochastic simulations. Linking our model to an extension of that in [33] would allow us to implement a model of the full malaria cycle, which we can validate by comparing to field data, and use to provide a comprehensive simulation of the epidemiological effects of vector control interventions. Here, we lay the mathematical foundation of the entomological component of this larger malaria model.

In the following section, we describe the model and derive the equations for the model. Section 3 shows empirical derivations of a number of quantities that can be estimated in the field that would allow direct comparison to the results of our model. We then use a numerical example to show the effectiveness of increasing ITN coverage using parameters from the published literature.

2. Description of model

After emergence from a breeding site, mosquitoes mate and the females search for blood meals, which are necessary for egg development. After encountering and biting a host, the female mosquito finds a resting place, where it digests the blood and evaporates water. The resting time is temperature dependent (shorter at higher temperatures) and is usually 2–3 days in malaria endemic areas. After the eggs are ready, the mosquito flies in search of a water body to lay them, before seeking a host again to repeat the feeding cycle. Figure 1 shows a cartoon of the feeding cycle. In general, mosquitoes begin host-seeking at the same time every night. If they are unsuccessful in biting, they rest through the day and try again the next night. The probability that a mosquito is successful in completing a feeding cycle depends on a variety of factors, including whether or not the human host a mosquito feeds on is protected by an ITN or IRS.

We model each feeding cycle of the mosquito as shown in Figure 2 where an adult female mosquito can be in one of five overall states. Four of these states depend on the type of host that the mosquito feeds on. We label these states with a subscript i with $1 \leq i \leq n$, where i denotes

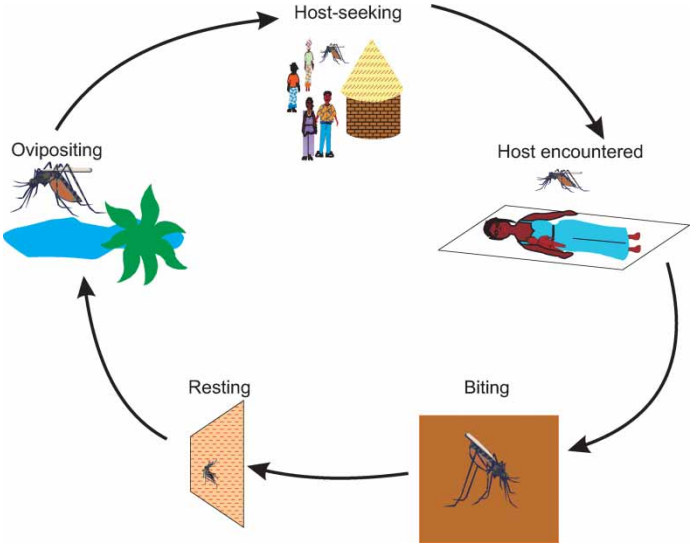

Figure 1. The feeding (or gonotrophic) cycle of the female mosquito. After emergence, mosquitoes seek and bite hosts, rest and lay eggs, before seeking hosts again. The mosquito experiences varying levels of risk in each state.

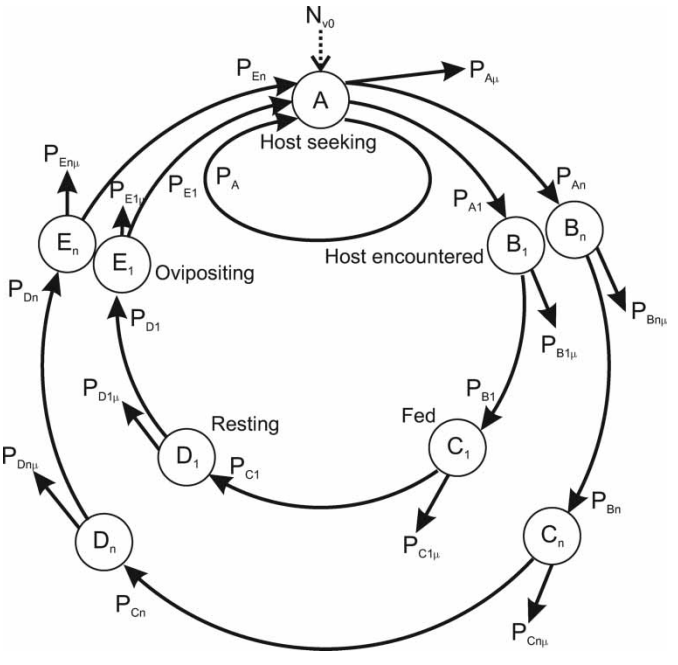

Figure 2. The processes in the feeding cycle of the female mosquito. New mosquitoes emerge from water bodies (and mate) at rate N_{v0} into the host-seeking state A, where they actively search for blood meals. A mosquito may encounter and feed on up to n different types of hosts. Each type of host, represented by subscript i for $1 \leq i \leq n$, is available to mosquitoes at rate α_i. If a mosquito does not encounter a host in a given night, it waits in the host-seeking phase till the next night, with probability, P_A. When a mosquito encounters a host of type i and is committed to biting the host, it moves to state B_i. If the mosquito bites, it moves to state C_i where it searches for a resting place. If it finds a resting place, it moves to state D_i where it rests for a fixed number of days. After resting, the mosquito moves to state E_i where it seeks to lay eggs. If it is successful in laying eggs, it returns to host-seeking state A, where it may then encounter any type of host. At each state, the mosquito may die with some probability, labelled by subscript μ.

the type of host. There are thus a total of $(1 + 4n)$ states. We first describe these states and the processes by which the mosquitoes enter and exit the states. We then list the equations governing these processes.

(i) A**: Host-seeking.** In state A, the mosquito is actively searching for a blood meal. We assume that a fixed number of mosquitoes, N_{v0}, emerge everyday into the total mosquito population and actively seek blood meals. For mosquito species that need to be feeded twice before laying eggs for the first time, we make the simplifying assumption that the emerging mosquitoes have already fed once. The assumption that N_{v0} is constant ignores seasonal variation, which plays a large role in malaria transmission. We plan to extend our model includes seasonality, but we begin our analysis here with an autonomous model. We also assume here that the number of emerging mosquitoes is independent of the number of eggs laid. This assumption is valid, given the large density-dependent death rates in the mosquito larval stages, and only breaks down when the adult population is small.

Although we use a discrete time model for the overall system of malaria in mosquitoes, we embed a continuous time model for the host-seeking phase in mosquitoes. We assume that a mosquito has a constant per-capita death rate of μ_{vA} while host-seeking. N_i is the total population of hosts of type i. Every host of type i is available to mosquitoes at a rate α_i, which depends on the type of host and on the mosquito species. This rate includes any reductions in host availability due to diversionary effects; for example, a host with a diversionary intervention like a net is modelled as having reduced availability to mosquitoes.

A mosquito that appears to 'encounter' a host but is diverted away is modelled as remaining in the host-seeking state. For example, if a mosquito finds a human with an untreated net with no holes and is forced to seek elsewhere, it is modelled as being in the host-seeking state throughout (not encountering a host and entering state B_i), even though it may have been said to be 'diverted'. Mosquitoes encounter hosts of type i at rate $\alpha_i N_i$. Once a mosquito encounters a host of type i, it leaves the host-seeking state and enters state, B_i, and does not re-enter the host-seeing state until it has completed a full gonotrophic cycle. While there is no explicit diversion in the model, it is equivalent to a model with diversion as modelled by Killeen and Smith [15] and Saul [29]. We describe this equivalence in Appendix A.

Mosquitoes only spend a certain amount of time, θ_d, searching for a blood meal per night. During this time, they can either encounter a host of type i and move to state B_i (with probability P_{A^i}), die and leave the population (with probability $P_{A\mu}$), or survive but fail to find a host and remain in state A till the next night (with probability P_A). We assume that if a mosquito is forced to rest till the next night to continue host-seeking, it will not die while resting and will be equally fresh the next night. In reality, some of these mosquitoes may die while resting and may face additional mortality while host-seeking the next day. However, this assumption makes no difference to the results, because it can be relaxed by allowing only a proportion of mosquitoes that wait the night, to survive till the next day and that is equivalent to simply increasing the mosquito mortality rate while host-seeking, μ_{vA}.

(ii) B_i**: Encounters a host of type** i**.** The mosquito encounters and is committed to biting, a host of type i. From state B_i, the mosquito can either bite the host with probability P_{B_i} and move to state C_i or die while attempting to bite and leave the population with probability $P_{B_i\mu}$. Here, we make the simplifying assumption that a mosquito may only bite once in a feeding cycle. We ignore the possibility that a mosquito may bite a second host before resting.

(iii) C_i**: Searching for a resting place.** The mosquito has bitten a host of type i and is searching for a resting place. The mosquito can either find a resting place and move to state D_i with probability P_{C_i} or die after biting with probability $P_{C_i\mu}$.

(iv) D_i**: Resting.** The mosquito is resting after biting a host of type i. We assume that the mosquito rests for a fixed number of days while it digests the blood and develops eggs. It can survive this state with probability P_{D_i} and move to state E_i, or die while resting and leave the population with probability $P_{D_i\mu}$.

(v) E_i**: Oviposition.** The mosquito is seeking to lay eggs after having bitten a host of type i. We assume that the mosquito is able to successfully find an oviposition site, lay eggs and return to the host-seeking state, A, with probability P_{E_i}, or die while trying to do so and leave the population with probability $P_{E_i\mu}$.

We let τ be the time it takes a mosquito to return to host-seeking after it has encountered a host (provided that the mosquito is still alive): it is the time it takes a mosquito to move from state B_i back to state A and is equal to the length of time a fed mosquito requires to produce and lay eggs because all other times are relatively small. We assume that this time does not depend on the type of host (although it would be possible to relax this assumption). Since we assume that mosquitoes begin host-seeking at the same time everyday [18], we use a time step of 1 day for the model equations, and τ when measured in days is a natural number (positive integer).

Humans infected with malaria are infective to mosquitoes if they have gametocytes (sexual stages of the *Plasmodium* parasite) in their blood. If a mosquito feeds on an infective human, there is some probability that the mosquito will ingest both male and female gametocytes, and that they will fuse in the mosquito's stomach to form a zygote, which develops into an oocyst after some temperature-dependent time, θ_o (usually 3–5 days). Based on the assumption that all mosquitoes that develop oocysts are infected (will subsequently develop sporozoites to become infective), the proportion of wild-caught mosquitoes that either already have oocysts, or will

Table 1. Description of the parameters of the model of the mosquito feeding cycle. We assume that time is measured in days.

T:	The length of each time step. For this model, we fix $T = 1$ day. Dimension: Time.
n:	Number of different types of hosts. $n \in \mathbb{N}$.
m:	Number of different types of hosts that are susceptible to malaria. $m \in \mathbb{N}$, $m \leq n$.
N_{v0}:	Number of emerging mosquitoes that survive to the first feeding search per day. Dimension: Animals $\times$ Time^{-1}. $N_{v0} > 0$.
N_i:	Total number of hosts of type i. Dimension: Animals. $N_i > 0$.
α_i:	Availability rate of each host of type i to mosquitoes. This rate includes the reduction in availability of a host due to diversion. Dimension: Animals^{-1} $\times$ Time^{-1}. $\alpha_i > 0$.
μ_{vA}:	Per-capita mosquito death rate while searching for a blood meal. Dimension: Time^{-1}. $\mu_{vA} > 0$.
θ_d:	Maximum length of time that a mosquito searches for a host in 1 day if it is unsuccessful. Dimension: Time. $0 < \theta_d < T$.
P_{B_i}:	Probability that a mosquito bites a host of type i after encountering a host of type i. $0 < P_{B_i} < 1$.
P_{C_i}:	Probability that a mosquito finds a resting place after biting a host of type i. $0 < P_{C_i} < 1$.
P_{D_i}:	Probability that a mosquito survives the resting phase after biting a host of type i. $0 < P_{D_i} < 1$.
P_{E_i}:	Probability that a mosquito lays eggs and returns to host-seeking after biting a host of type i. $0 < P_{E_i} < 1$.
τ:	Time required for a mosquito that has encountered a host to return to host-seeking (provided that the mosquito survives to search again). Dimension: Time. $\tau \in \mathbb{N}$.
P_{iv}:	Probability of parasite transmission from an infective mosquito to a susceptible host of type i per bite. $0 \leq P_{iv} < 1$.
P_{vi}:	Probability of parasite transmission from an infective host of type i to render a susceptible mosquito infective, per bite, provided the mosquito survives long enough. (This term includes the probability that the parasite then survives in the mosquito to produce sporozoites.) $0 \leq P_{vi} < 1$.
I_i:	Proportion of hosts of type i who are infective. $0 \leq I_i < 1$.
θ_s:	Duration of the extrinsic incubation period. This is the time required for sporozoites to develop in the mosquito. Dimension: Time. $\theta_s \in \mathbb{N}$, $\theta_s \geq \tau$.
θ_o:	Oocyst development time. This is the time required for oocysts to develop in the mosquito. Dimension: Time. $\theta_o \in \mathbb{N}$, $\tau \leq \theta_o \leq \theta_s$.

develop oocysts after being kept alive for θ_o days ('the delayed oocyst rate') is approximately equal to the proportion of mosquitoes that were infected when caught [31]. After some more days, the oocysts release sporozoites that travel to the mosquito's salivary glands and the mosquito becomes infective to humans. The temperature-dependent time it takes an infected mosquito to become infective (for sporozoites to travel to the salivary glands after gametocytes enter the mosquito's stomach) is known as the extrinsic incubation period, θ_s (usually 10–12 days in malaria endemic areas). Infective mosquitoes are said to be sporozoite positive because they have sporozoites in their salivary glands. The extrinsic incubation period, θ_s, and the oocyst development time, θ_o, when measured in days, are natural numbers.

We summarize all parameters used in this model in Table 1; derived quantities in Table 2; and field-measurable quantities in Table 3. We define the probabilities of movement from the host-seeking state, P_A, P_{A^i} and $P_{A\mu}$, in terms of the availability of different hosts and of the mosquito death rate. The total rate at which mosquitoes leave the host-seeking state is the sum of the rates at which the mosquitoes encounter each type of host and the death rate: $\sum_{i=1}^{n} \alpha_i N_i + \mu_{vA}$. We assume that they leave the host-seeking state with an exponential distribution so while some mosquitoes will find a host or die on any given night, others will remain in the host-seeking state till the next night. This is an improvement over previous models which assumed that all mosquitoes would leave the host-seeking state after the same amount of time. This allows different mosquitoes to have different lengths of the feeding cycle, depending on how successful they are in host-seeking. As mosquitoes only search for time θ_d in one night, the probability that a mosquito is still host-seeking the following night is the probability that the mosquito is still host-seeking

Table 2. Description of derived parameters for the model of the mosquito feeding cycle.

P_A:	Probability that a mosquito does not find a host and does not die in one night of searching.
P_{A^i}:	Probability that a mosquito finds a host of type i on a given night.
$P_{A\mu}$:	Probability that a mosquito dies while host-seeking on a given night.
$P_{B_i\mu}$:	Probability that a mosquito dies while trying to bite a host of type i.
$P_{C_i\mu}$:	Probability that a mosquito dies while trying to find a resting place after biting a host of type i.
$P_{D_i\mu}$	Probability that a mosquito dies while resting after biting a host of type i.
$P_{E_i\mu}$:	Probability that a mosquito dies while seeking an oviposition site or laying eggs after biting a host of type i.
P_{df}:	Probability that a mosquito finds a host on a given night and then successfully completes the feeding cycle.
P_f:	Probability that a mosquito survives a feeding cycle.
P_{dif}:	Probability that a mosquito finds a host on a given night and then successfully completes the feeding cycle and gets infected.
P_{if}:	Probability that a mosquito survives a feeding cycle and gets infected.
P_{duf}:	Probability that a mosquito finds a host on a given night and then successfully completes the feeding cycle without getting infected.
P_{uf}:	Probability that a mosquito survives a feeding cycle without getting infected.
θ_f:	Average duration of a feeding cycle. Dimension: Time.
Γ:	Vectorial capacity. The expected number of infectious bites on all hosts from mosquitoes infected by one "average" host in one unit of time. Dimension: Time^{-1}.

Table 3. Description of field-measurable quantities for the model of the mosquito feeding cycle. We note here that the terms, parous rate, oocyst rate and sporozoite rate, do not refer to rates (with dimension Time^{-1}), but to proportions. However, the host-biting rate and the entomological inoculation rate are rates with dimension Time^{-1}. Although this may seem inconsistent, it is consistent with commonly used terminology in entomological literature.

K_{vi}:	The infectiousness of hosts of type i to susceptible mosquitoes. This is the proportion of susceptible mosquitoes that become infected after biting any host of type i.
M:	Parous rate. Proportion of host-seeking mosquitoes that have laid eggs at least once.
o_v:	Delayed oocyst rate. Proportion of host-seeking mosquitoes that are infected but not necessarily infective.
$o_v^{(B_i)}$:	Delayed oocyst rate. Proportion of mosquitoes that have encountered a host of type i that are infected but not necessarily infective.
$o_v^{(D_i)}$:	Delayed oocyst rate. Proportion of mosquitoes that are resting after biting a host of type i that are infected but not necessarily infective.
s_v:	Sporozoite rate. Proportion of host-seeking mosquitoes that are infective.
r_v:	Immediate oocyst rate. Proportion of host-seeking mosquitoes with oocysts.
σ_i:	Host-biting rate. Number of mosquito bites that each host of type i receives per unit of time. Dimension: Time^{-1}.
Ξ_i:	Entomological inoculation rate for hosts of type i: the number of infectious bites that one host of type i receives per unit time. Dimension: Time^{-1}.

after time θ_d,

$$P_A = \mathrm{e}^{-\left(\sum_{i=1}^{n} \alpha_i N_i + \mu_{vA}\right)\theta_d}.$$

The probability that a mosquito finds a host of type i in one night is

$$P_{A^i} = \left(1 - \mathrm{e}^{-\left(\sum_{k=1}^{n} \alpha_k N_k + \mu_{vA}\right)\theta_d}\right) \times \frac{\alpha_i N_i}{\sum_{k=1}^{n} \alpha_k N_k + \mu_{vA}},$$

and dies while host-seeking in one night is

$$P_{A\mu} = \left(1 - \mathrm{e}^{-\left(\sum_{i=1}^{n} \alpha_i N_i + \mu_{vA}\right)\theta_d}\right) \times \frac{\mu_{vA}}{\sum_{i=1}^{n} \alpha_i N_i + \mu_{vA}}.$$

The probabilities of leaving each state obey the relationships

$$P_A + \sum_{i=1}^{n} P_{A^i} + P_{A\mu} = 1, \tag{1a}$$

$$P_{B_i} + P_{B_i\mu} = 1 \quad \forall i, \tag{1b}$$

$$P_{C_i} + P_{C_i\mu} = 1 \quad \forall i, \tag{1c}$$

$$P_{D_i} + P_{D_i\mu} = 1 \quad \forall i, \tag{1d}$$

$$P_{E_i} + P_{E_i\mu} = 1 \quad \forall i, \tag{1e}$$

where the symbol $\forall$ means 'for any'.

The probability that a mosquito finds a host on a given night and then survives a complete feeding cycle is

$$P_{df} = \sum_{i=1}^{n} P_{A^i} P_{B_i} P_{C_i} P_{D_i} P_{E_i}.$$

The probability of surviving a feeding cycle is the sum over all the possible nights that a mosquito can successfully bite,

$$\begin{aligned} P_f &= (1 + P_A + P_A^2 + \cdots) P_{df}, \\ &= \frac{P_{df}}{1 - P_A}. \end{aligned} \tag{2}$$

The infectiousness of hosts of type i to mosquitoes, K_{vi}, can be experimentally measured as the proportion of uninfected mosquitoes that become infected (and subsequently infective if they survive long enough) after biting a host of type i. It is defined as

$$K_{vi} = I_i \times P_{vi}.$$

For hosts that cannot contract malaria, such as cattle, $K_{vi} = 0$ because $I_i = 0$, and $P_{iv} = 0$. The probability that a mosquito finds a host on a given night and then survives a complete feeding cycle and gets infected in the process is

$$P_{dif} = \sum_{i=1}^{n} P_{A^i} P_{B_i} P_{C_i} P_{D_i} P_{E_i} K_{vi}.$$

The probability of a mosquito surviving a feeding cycle and getting infected is the sum over all the possible nights that a mosquito can successfully bite,

$$P_{if} = \frac{P_{dif}}{1 - P_A}.$$

For ease of notation, we also introduce P_{duf} and P_{uf}, where P_{duf} is the probability that a mosquito finds a host on a given day, survives a complete feeding cycle and does not get infected:

$$P_{duf} = \sum_{i=1}^{n} P_{A^i} P_{B_i} P_{C_i} P_{D_i} P_{E_i} (1 - K_{vi}),$$

and P_{uf} is the probability a mosquito survives a feeding cycle and does not get infected:

$$P_{uf} = \frac{P_{duf}}{1 - P_A},$$

satisfying

$$P_{df} = P_{dif} + P_{duf},$$
$$P_f = P_{if} + P_{uf}.$$

We have made the simplifying assumption here that mosquito mortality is independent of age, although some studies have shown increasing mortality with age [8]. This assumption is reasonable, because with the high mortality rates that adult mosquitoes are typically subjected to, the probability of a mosquito living a long life is low so the error is low. As mortality rates tend to increase with age, this assumption would overestimate malaria transmission levels. We also ignore the effects of malaria infection on the mortality rates and feeding habits of mosquitoes that some studies have shown [2].

2.1. *Model equations*

The model can be described mathematically as a system of three linear autonomous non-homogeneous difference Equations (3) for the total number of host-seeking mosquitoes, $N_v(t)$, the number of infected (delayed oocyst positive) host-seeking mosquitoes, $O_v(t)$, and the number of infective (sporozoite positive) host-seeking mosquitoes, $S_v(t)$, at time, t. We denote the length of each time step by T. As 1 day (24-hour period) is the most reasonable time step in the mosquito's feeding cycle, we fix $T = 1$ day. We use T to convert between rates and fixed quantities at time t.

$$N_v(t) = N_{v0}T + P_A N_v(t-1) + P_{df} N_v(t-\tau), \tag{3a}$$

$$O_v(t) = P_{dif}(N_v(t-\tau) - O_v(t-\tau)) + P_A O_v(t-1) + P_{df} O_v(t-\tau), \tag{3b}$$

$$\begin{aligned} S_v(t) = {} & P_{dif}\left(\sum_{j=0}^{k_+}\binom{\theta_s - (j+1)\tau + j}{j} P_A^{\theta_s-(j+1)\tau} P_{df}^j\right)(N_v(t-\theta_s) - O_v(t-\theta_s)) \\ & + \left[\sum_{l=1}^{\tau-1} P_{dif}\left(\sum_{j=0}^{k_{l+}}\binom{(\theta_s+l) - (j+2)\tau + j}{j} P_A^{(\theta_s+l)-(j+2)\tau} P_{df}^j\right) P_{df}\right. \\ & \left. \times (N_v(t-(\theta_s+l)) - O_v(t-(\theta_s+l)))\right] + P_A S_v(t-1) + P_{df} S_v(t-\tau), \end{aligned} \tag{3c}$$

with

$$k_+ = \left\lfloor \frac{\theta_s}{\tau} \right\rfloor - 1 \text{ and } k_{l+} = \left\lfloor \frac{\theta_s + l}{\tau} \right\rfloor - 2, \tag{4}$$

where $\lfloor x \rfloor$ is the floor function, that is, the greatest integer less than x, and the binomial coefficient is

$$\binom{a}{b} = \frac{a!}{b!(a-b)!}.$$

The total number of host-seeking mosquitoes, $N_v(t)$, on a given day, t, in Equation (3a) is the sum of newly emerged mosquitoes; mosquitoes from the previous day $(t-1)$ that survived but

were unable to find a blood meal and mosquitoes from τ days earlier $(t-\tau)$ that successfully fed and completed the feeding cycle. The number of infected host-seeking mosquitoes, $O_v(t)$, on a given day, t, in Equation (3b) is the sum of uninfected mosquitoes from τ days earlier $(t-\tau)$ that successfully fed, survived a feeding cycle and got infected; infected mosquitoes from the previous day $(t-1)$ that survived but were unable to find a blood meal, and infected mosquitoes from τ days earlier $(t-\tau)$ that successfully fed and completed the feeding cycle. The number of infective host-seeking mosquitoes, $S_v(t)$, on a given day, t, in Equation (3c) is the sum of uninfected mosquitoes from at least θ_s days ago that got infected, survived and are host-seeking as infective mosquitoes for the first time on day t; infective mosquitoes from the previous day $(t-1)$ that survived but were unable to find a blood meal and infective mosquitoes from τ days earlier $(t-\tau)$ that successfully fed and completed the feeding cycle. The first two terms in the right-hand side of Equation (3c) include all the possible ways in which the mosquitoes could survive at least θ_s days to start their first feeding cycle as an infective mosquito on day t.

We note again that Equation (3) are linear equations because we model the force of infection from humans to mosquitoes as parameters and not as state variables that depend on the force of infection from mosquitoes to humans. We also note that the order of Equation (3), $2\times(\theta_s+\tau-1)+\tau$, is parameter-dependent. The system may be written as

$$x_t = \Upsilon x_{t-1} + \Lambda, \tag{5}$$

where

$$\begin{aligned} x = (&N_v, N_v^{-1}, N_v^{-2}, \ldots, N_v^{-(\theta_s+\tau-2)}, O_v, O_v^{-1}, O_v^{-2}, \ldots, O_v^{-(\theta_s+\tau-2)},\\ &S_v, S_v^{-1}, S_v^{-2}, \ldots, S_v^{-(\tau-1)}), \end{aligned}$$

with $N_v = N_v(t)$, $N_v^{-1} = N_v(t-1)$, $N_v^{-2} = N_v(t-2)$ and so on, for $x = x_t$ and $\Lambda = (N_{v0}, 0, \ldots, 0)$. The matrix Υ is constructed using the definition of x and the right-hand side of Equation (3).

To illustrate the structure of Equation (3) and the construction of Υ, we provide a small example with $\theta_s = 3$ and $\tau = 2$. System (3) reduces to

$$\begin{aligned} N_v(t) &= N_{v0}T + P_A N_v(t-1) + P_{df} N_v(t-2),\\ O_v(t) &= P_{dif}(N_v(t-2) - O_v(t-2)) + P_A O_v(t-1) + P_{df} O_v(t-2),\\ S_v(t) &= P_{dif} P_A (N_v(t-3) - O_v(t-3)) + P_{dif} P_{df} (N_v(t-4) - O_v(t-4))\\ &\quad + P_A S_v(t-1) + P_{df} S_v(t-2). \end{aligned}$$

This can equivalently be written in form (5) with

$$x_t = \begin{pmatrix} N_v(t)\\ N_v^{-1}(t)\\ N_v^{-2}(t)\\ N_v^{-3}(t)\\ O_v(t)\\ O_v^{-1}(t)\\ O_v^{-2}(t)\\ O_v^{-3}(t)\\ S_v(t)\\ S_v^{-1}(t) \end{pmatrix} = \begin{pmatrix} N_v(t)\\ N_v(t-1)\\ N_v(t-2)\\ N_v(t-3)\\ O_v(t)\\ O_v(t-1)\\ O_v(t-2)\\ O_v(t-3)\\ S_v(t)\\ S_v(t-1) \end{pmatrix}, \quad \Lambda = \begin{pmatrix} N_{v0}T\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0 \end{pmatrix},$$

and

$$\Upsilon = \begin{pmatrix} P_A & P_{df} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & P_{dif} & 0 & 0 & P_A & P_{duf} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & P_{dif}P_A & P_{dif}P_{df} & 0 & 0 & -P_{dif}P_A & -P_{dif}P_{df} & P_A & P_{df} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{pmatrix}.$$

The model for the mosquito feeding cycle (3) is mathematically and physically well-posed in the domain

$$\mathcal{D} = \{(N_v, O_v, S_v) \in \mathbb{R}^3 | N_v > O_v \geq S_v > 0\}.$$

The number of infective host-seeking mosquitoes is positive and less than or equal to the number of infected host-seeking mosquitoes, which in turn is less than the total number of host-seeking mosquitoes. $S_v = O_v$ only in the extreme case when the extrinsic incubation period is equal to the resting time of the mosquito, $\theta_s = \tau$.

THEOREM 2.1 *Assuming that initial conditions lie in $\mathcal{D}$, the system of equations for the malaria model in mosquitoes* (3) *has a unique forward orbit that exists and remains in $\mathcal{D}$ for all time* $\{t \in \mathbb{Z} | t \geq 0\}$.

Proof As the system of Equations (3) is linear and autonomous, a unique forward solution exists [12]. For initial conditions in $\mathcal{D}$, the right-hand side of Equation (3) is always positive; the right-hand side of Equation (3a) is greater than the right-hand side of Equation (3b), and the right-hand side of Equation (3b) is greater than or equal to the right-hand side of Equation (3c); so the orbits of Equation (3) are always in $\mathcal{D}$. If $\theta_s > \tau$, then the right-hand side of Equation (3b) is strictly greater than the right-hand side of Equation (3c). ■

System (3) has a unique fixed point,

$$N_v^* = \frac{N_{v0}T}{1 - P_A - P_{df}}, \tag{6a}$$

$$O_v^* = \frac{N_v^* P_{dif}}{1 - P_A - P_{duf}}, \tag{6b}$$

$$S_v^* = \frac{P_{dif}(N_v^* - O_v^*)}{1 - P_A - P_{df}} \times \left[\left(\sum_{j=0}^{k_+} \binom{\theta_s - (j+1)\tau + j}{j} P_A^{\theta_s - (j+1)\tau} P_{df}^j \right) + \sum_{l=1}^{\tau-1} \left(\sum_{j=0}^{k_{l+}} \binom{(\theta_s + l) - (j+2)\tau + j}{j} P_A^{(\theta_s+l)-(j+2)\tau} P_{df}^{j+1} \right) \right], \tag{6c}$$

with k_+ and k_{l+} defined in Equation (4). Linear non-homogeneous difference equations of the form (5) have a unique globally asymptotically stable fixed point if all eigenvalues of Υ, λ_l, have magnitude less than 1. Although we cannot evaluate all eigenvalues, λ_l, in general, the fixed point (6) is unique as it represents the unique solution, $x^* = (\mathbb{I} - \Upsilon)^{-1}\Lambda$ where $\mathbb{I}$ is the $(2\theta_s +$

$3\tau - 2) \times (2\theta_s + 3\tau - 2)$ identity matrix. Additionally, $N_v^* > O_v^* \geq S_v^*$, so the fixed point (6) $\in \mathcal{D}$. From Theorem 2.1, we know that $\mathcal{D}$ is forward invariant so, Equation (6) is not unstable and is thus, at least Lyapunov stable. While we cannot show that the fixed point (6) is globally asymptotically stable in general, in the special cases where $\tau = 1$ and $\tau = 2$, we can show that $|\lambda_l| < 1 \forall \lambda_l$ in the spectrum of Υ, so the fixed point (6) is globally asymptotically stable.

3. Field measurable quantities and derived parameters

We evaluate expressions for the equilibrium states of field-measurable quantities here that can then be compared to field-data. In addition to the expressions derived from the fixed point of the system of difference Equations (6), we empirically derive the field-measurable quantities as a further check. Although we do not use superscript '*', all variables and field-measurable variables in this Section, 3, refer to their equilibrium values and not at a given time, t.

We first empirically evaluate the total number of host-seeking mosquitoes on a given day, N_v as given by Equation (6a). This is the sum of mosquitoes that have never fed, which have fed once, twice and so on. The total number of host-seeking mosquitoes that have never fed is

$$N_v^{(0)} = \frac{N_{v0} T}{1 - P_A}.$$

The total number of host-seeking mosquitoes that have fed once is

$$N_v^{(1)} = \frac{N_{v0} T}{1 - P_A} P_f.$$

The total number of host-seeking mosquitoes is

$$\begin{aligned} N_v &= N_v^{(0)} + N_v^{(1)} + N_v^{(2)} + \cdots, \\ &= \frac{N_{v0} T}{1 - P_A - P_{df}}, \end{aligned} \tag{7}$$

which is exactly N_v^* (6a).

3.1. *Parous rate*

The parous rate, M, is the proportion of host-seeking mosquitoes that have successfully laid eggs. To evaluate the parous rate, we use the total number of mosquitoes that are searching for a blood meal on a given day, N_v, and the number of mosquitoes, searching for a blood meal on a given day, which have never laid eggs, $N_v^{(0)}$.

$$\begin{aligned} M &= \frac{N_v - N_v^{(0)}}{N_v}, \\ &= P_f. \end{aligned} \tag{8}$$

3.2. *Delayed oocyst rates*

The delayed oocyst rate, o_v, is the proportion of host-seeking mosquitoes, that are infected with the malaria parasite, but not necessarily infective, given by $o_v = O_v^*/N_v^*$ (6). We also empirically

calculate the delayed oocyst rate for mosquitoes that have found a host of type i, $o_v^{(B_i)}$, and for mosquitoes that are resting after successfully biting a host of type i, $o_v^{(D_i)}$.

In a similar manner to the derivation of the parous rate in Section 3.1, we first evaluate the total number of host-seeking mosquitoes, N_v, the total number of mosquitoes that have encountered a host of type i, $N_v^{(B_i)}$, and that are resting after feeding on a host of type i, $N_v^{(D_i)}$, on a given day. We also evaluate the number of uninfected host-seeking mosquitoes, $\bar{O}_v$, the uninfected mosquitoes that have encountered a host of type i, $\bar{O}_v^{(B_i)}$, and that are resting after feeding on a host of type i, $\bar{O}_v^{(D_i)}$, on a given day.

$$
\begin{aligned}
N_v &= \frac{N_{v0}T}{(1-P_A)(1-P_f)},\\
N_v^{(B_i)} &= \frac{N_{v0}T}{(1-P_A)(1-P_f)}P_{A^i},\\
N_v^{(D_i)} &= \frac{N_{v0}T}{(1-P_A)(1-P_f)}P_{A^i}P_{B_i}P_{C_i},\\
\bar{O}_v &= \frac{N_{v0}T}{(1-P_A)(1-P_{uf})},\\
\bar{O}_v^{(B_i)} &= \frac{N_{v0}T}{(1-P_A)(1-P_{uf})}P_{A^i},\\
\bar{O}_v^{(D_i)} &= \frac{N_{v0}T}{(1-P_A)(1-P_{uf})}P_{A^i}P_{B_i}P_{C_i}(1-K_{vi}).
\end{aligned}
$$

The delayed oocyst rates are

$$
\begin{aligned}
o_v &= \frac{N_v-\bar{O}_v}{N_v},\\
&= \frac{P_f-P_{uf}}{1-P_{uf}}, \qquad (9)\\
o_v^{(B_i)} &= \frac{N_v^{(B_i)}-\bar{O}_v^{(B_i)}}{N_v^{(B_i)}},\\
&= \frac{P_f-P_{uf}}{1-P_{uf}}, \qquad (10)\\
o_v^{(D_i)} &= \frac{N_v^{(D_i)}-\bar{O}_v^{(D_i)}}{N_v^{(D_i)}},\\
&= \frac{P_f-P_{uf}+K_{vi}(1-P_f)}{1-P_{uf}}. \qquad (11)
\end{aligned}
$$

We note that the proportion of infected mosquitoes that have encountered a host of type i, $o_v^{(B_i)}$, is equal to the proportion of infected host-seeking mosquitoes, o_v. Some algebraic manipulations also confirm that o_v (10) $= O_v^*/N_v^*$ (6).

3.3. *Sporozoite rate*

The sporozoite rate, s_v, is the proportion of host-seeking mosquitoes that are infective, given by S_v^*/N_v^* (6). To empirically calculate s_v, we use N_v and the number of host-seeking mosquitoes

on a given day that are not infective, $\bar{S}_v$. We define k^* as the maximum number of feeding cycles that an infected mosquito can complete before it becomes infective,

$$k^* = \left\lfloor \frac{\theta_s - 1}{\tau} \right\rfloor.$$

For example, if $k^* = 0$, a mosquito will become infective on the first feeding cycle after the one where it became infected. If $k^* = 1$, the mosquito will not be infective on the cycle after it is infected but will be infective two cycles after it is infected.

We can calculate $\bar{S}_v$ as

$$\bar{S}_v = \frac{N_{v0} T}{1 - P_A} \left(\sum_{k=0}^{k^*-1} T_k + \frac{T_{k^*}}{1 - P_{uf}} \right), \tag{12}$$

where

$$\begin{aligned} T_k = {} & P_{duf}^k \left(\frac{1}{1 - P_A} \right)^k \\ & + \sum_{l=1}^{k} \left[\left(\frac{1}{1 - P_A} \right)^{k-l} \left(\sum_{j=0}^{\theta_s - l\tau - 1} \binom{l-1+j}{l-1} P_A^j \right) \left(P_{df}^l P_{duf}^{k-l} - P_{df}^{l-1} P_{duf}^{k-(l-1)} \right) \right] \end{aligned} \tag{13}$$

provides a measure of the probability of surviving k feeding cycles and not getting infected. The sporozoite rate is

$$s_v = \frac{N_v - \bar{S}_v}{N_v}. \tag{14}$$

The complexity of the expressions prevents us from showing s_v (14) $= S_v^*/N_v^*$ (6), in general, but using *Mathematica* we can show that it is true for all integer values of $1 \leq \tau \leq 10$ and $1 \leq \theta_s \leq 50$.

3.4. *Immediate oocyst rate*

The immediate oocyst rate, r_v, is the proportion of mosquitoes that have oocysts in their stomachs. Oocysts develop a certain amount of time (depending on temperature), θ_o, after a mosquito is infected. We calculate r_v exactly as we calculated s_v in Equation (6c), or Equations (12), (13) and (14), replacing the extrinsic incubation period, θ_s, by the oocyst development time, θ_o.

3.5. *Host-biting rate*

The host-biting rate, σ_i, is the number of mosquito bites that each host of type i receives per day. On a given day, there are N_v mosquitoes looking to feed. Out of these, $P_{A^i} \times N_v$ find a host of type i, $P_{A^i} P_{B_i} \times N_v$ bite hosts of type i, and $P_{A^i} P_{B_i} \times N_v / N_i$ bite one host of type i. Dividing by the length of the time step, the number of mosquitoes that successfully bite one host of type i, per day, is

$$\begin{aligned} \sigma_i &= \frac{1}{T} P_{A^i} P_{B_i} \frac{N_v}{N_i}, \\ &= \frac{N_{v0}}{N_i} \frac{P_{A^i} P_{B_i}}{1 - P_A - P_{df}}. \end{aligned} \tag{15}$$

3.6. *Entomological inoculation rate*

The entomological inoculation rate (EIR), Ξ_i, for a host of type i is the number of infectious bites that one host of type i receives per day (sometimes also expressed per year). We evaluate Ξ_i as the product of the number of bites a host of type i receives per day, σ_i, and the proportion of mosquitoes that are infective, s_v,

$$\begin{aligned}\Xi_i &= \sigma_i \times s_v,\\ &= \frac{N_{v0}}{N_i} \times \frac{P_{A^i} P_{B_i}}{1 - P_A - P_{df}} \frac{P_{dif}}{1 - P_A - P_{duf}} \left[\left(\sum_{j=0}^{k_+} \binom{\theta_s - (j+1)\tau + j}{j} P_A^{\theta_s - (j+1)\tau} P_{df}^j \right) \right.\\ &\quad \left. + \sum_{l=1}^{\tau-1} \left(\sum_{j=0}^{k_{l+}} \binom{(\theta_s + l) - (j+2)\tau + j}{j} P_A^{(\theta_s+l)-(j+2)\tau} P_{df}^{j+1} \right) \right].\end{aligned} \tag{16}$$

3.7. *Vectorial capacity*

The vectorial capacity measures the ability of the mosquito population to transmit malaria, originally defined as 'The average number of inoculations with a specified parasite, originating from one case of malaria in unit time, that a vector population would distribute to man if all the vector females biting the case became infected' [11]. Garrett-Jones [10] formulated the vectorial capacity as a product of the man-biting rate, the expectation of infective life and the man-biting habit of the mosquito. Smith and McKenzie [33, (16)] derived the vectorial capacity for the classical Ross-Macdonald model and showed that it could be expressed as the partial derivative of the entomological inoculation rate with respect to the proportion of infective humans at the point where there is no malaria in the population.

We use this formulation by Smith and McKenzie to derive the vectorial capacity for Equation (3) with Ξ_i (16). As the host population is heterogeneous, we need to consider the number of infectious bites on all hosts caused by each host type. We exclude hosts that are immune to malaria (non-humans) from the vectorial capacity calculations. Without loss of generality, we assume that there are m types of hosts capable of contracting and transmitting malaria, with $m \leq n$, and order the types of host so that the first m types are malaria-susceptible ($P_{iv} \neq 0$ for $i \leq m$).

For hosts that can contract malaria, we define Π_{ij} as the limit of the rate of change of the number of infectious bites on one host of type i per day resulting from mosquitoes infected from all hosts of type j, with respect to K_{vj} as K_v approaches zero,

$$\Pi_{ij} = \left. \frac{\partial \Xi_i}{\partial K_{vj}} \right|_{K_v = 0}, \text{ for } i \text{ and } j, \text{ such that } P_{iv} \neq 0 \text{ and } P_{jv} \neq 0, \tag{17}$$

where $K_v = (K_{v1}, \ldots, K_{vj}, \ldots, K_{vn})$. Taking the limit $K_v \to 0$ ignores the effects of superinfection, that is, one mosquito that is infected twice counts as two infected mosquitoes. Evaluating Equation (17),

$$\begin{aligned}\Pi_{ij} &= \frac{N_{v0}}{N_i} \times \frac{P_{A^i} P_{B_i} P_{A^j} P_{B_j} P_{C_j} P_{D_j} P_{E_j}}{(1 - P_A - P_{df})^2} \times \left[\left(\sum_{h=0}^{k_+} \binom{\theta_s - (h+1)\tau + h}{h} P_A^{\theta_s - (h+1)\tau} P_{df}^h \right) \right.\\ &\quad \left. + \sum_{l=1}^{\tau-1} \left(\sum_{h=0}^{k_{l+}} \binom{(\theta_s + l) - (h+2)\tau + h}{h} P_A^{(\theta_s+l)-(h+2)\tau} P_{df}^{h+1} \right) \right].\end{aligned} \tag{18}$$

We define Ξ_{ij} as the number of infectious bites on 1 host of type i in 1 day caused by mosquitoes infected from hosts of type j. At low values of K_{vj},

$$\Xi_{ij} \approx \Pi_{ij} K_{vj}. \tag{19}$$

We use the assumption that every mosquito gets infected when it bites ($K_{vj} = 1$) to estimate the number of infectious bites that one host of type i receives in 1 day from mosquitoes infected by all hosts of type j as Π_{ij}. Then, $N_i \Pi_{ij}$ is the number of infectious bites that all hosts of type i receive in 1 day from mosquitoes infected from all hosts of type j. The sum $\sum_{i=1}^{m} N_i \Pi_{ij}$ is the total number of infectious bites that all hosts receive in 1 day from mosquitoes infected by all hosts of type j. The double sum $\sum_{j=1}^{m} \sum_{i=1}^{m} N_i \Pi_{ij}$ is the total number of infectious bites that all hosts receive in 1 day from mosquitoes infected by any host. As we calculate the vectorial capacity at equilibrium, all days are the same and the double sum $\sum_{j=1}^{m} \sum_{i=1}^{m} N_i \Pi_{ij}$ also represents the total number of infectious bites on all hosts from mosquitoes infected by all hosts in 1 day. The vectorial capacity is then this double sum divided by the total population size,

$$\Gamma = \frac{\sum_{j=1}^{m} \sum_{i=1}^{m} N_i \Pi_{ij}}{\sum_{k=1}^{m} N_k}, \tag{20}$$

which may equivalently be expressed as a matrix product,

$$\Gamma = (N_1 \dots N_m) \begin{pmatrix} \Pi_{11} & \dots & \Pi_{1m} \\ \vdots & \ddots & \vdots \\ \Pi_{m1} & \dots & \Pi_{mm} \end{pmatrix} \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix} \frac{1}{\sum_{k=1}^{m} N_k}.$$

Evaluating Equation (20),

$$\begin{aligned} \Gamma = \frac{N_{v0}}{\sum_{k=1}^{m} N_k} \times \frac{\left(\sum_{i=1}^{m} P_{A^i} P_{B_i}\right)\left(\sum_{j=1}^{m} P_{A^j} P_{B_j} P_{C_j} P_{D_j} P_{E_j}\right)}{(1 - P_A - P_{df})^2} \\ \times \left[\left(\sum_{h=0}^{k_+} \binom{\theta_s - (h+1)\tau + h}{h} P_A^{\theta_s - (h+1)\tau} P_{df}^h\right)\right. \\ \left. + \sum_{l=1}^{\tau-1} \left(\sum_{h=0}^{k_{l+}} \binom{(\theta_s + l) - (h+2)\tau + h}{h} P_A^{(\theta_s+l)-(h+2)\tau} P_{df}^{h+1}\right)\right]. \end{aligned} \tag{21}$$

In the special case where $m = n$ (all types of hosts are susceptible to malaria), the vectorial capacity simplifies to

$$\begin{aligned} \Gamma = \frac{N_{v0}}{\sum_{k=1}^{n} N_k} \times \frac{\left(\sum_{i=1}^{n} P_{A^i} P_{B_i}\right) P_{df}}{(1 - P_A - P_{df})^2} \times \left[\left(\sum_{h=0}^{k_+} \binom{\theta_s - (h+1)\tau + h}{h} P_A^{\theta_s - (h+1)\tau} P_{df}^h\right)\right. \\ \left. + \sum_{l=1}^{\tau-1} \left(\sum_{h=0}^{k_{l+}} \binom{(\theta_s + l) - (h+2)\tau + h}{h} P_A^{(\theta_s+l)-(h+2)\tau} P_{df}^{h+1}\right)\right]. \end{aligned} \tag{22}$$

We now show that the empirical derivation of the vectorial capacity (from first principles, as was derived in [29] and [30]) is equal to Equation (21), confirming our derivation, and the use of Equation (16) from [32]. We first define Ψ_{ij} as the number of new inoculations received by all hosts of type i from mosquitoes infected by one host of type j in 1 day (assuming all mosquitoes that bite get infected),

$$\Psi_{ij} = \overbrace{\frac{N_{v0}}{1-P_A-P_{df}}}^{\Psi_{ij}^{(A)}} \times \overbrace{\frac{P_{A^j}P_{B_j}P_{C_j}P_{D_j}P_{E_j}}{N_j}}^{\Psi_{ij}^{(B)}} \times \overbrace{\underbrace{\left[\left(\sum_{h=0}^{k_+}\binom{\theta_s-(h+1)\tau+h}{h}P_A^{\theta_s-(h+1)\tau}P_{df}^h\right) + \sum_{l=1}^{\tau-1}\left(\sum_{h=0}^{k_{l+}}\binom{(\theta_s+l)-(h+2)\tau+h}{h}P_A^{(\theta_s+l)-(h+2)\tau}P_{df}^{h+1}\right)\right]}_{\Psi_{ij}^{(C)}} \times \underbrace{\frac{P_{A^i}P_{B_i}}{1-P_A-P_{df}}}_{\Psi_{ij}^{(D)}}}^{\Psi_{ij}^{(C)}},$$

where $\Psi_{ij}^{(A)}$ is the number of mosquitoes who are host-seeking in 1 day, $\Psi_{ij}^{(B)}$ is the proportion of mosquitoes that bite one host of type j on that day and then survive the feeding cycle, $\Psi_{ij}^{(C)}$ is the proportion that then survive long enough to be infective, and $\Psi_{ij}^{(D)}$ is the total of all possible bites on hosts of type i. In a similar manner to Equation (20), we evaluate the vectorial capacity as

$$\Gamma = \frac{\sum_{j=1}^{m}\sum_{i=1}^{m}N_j\Psi_{ij}}{\sum_{k=1}^{m}N_k},$$

which is equal to our first derivation of vectorial capacity (21).

It is important to note that vectorial capacity overestimates the transmission potential of the mosquito population because this definition is based on the two assumptions that superinfection is ignored and that a mosquito gets infected every time it bites. Note also that these two assumptions, ignoring superinfection and mosquitoes getting infected every time they bite, are only made for the vectorial capacity calculations and not for the other entomological quantities.

3.8. *Average duration of a feeding cycle*

The average duration of a feeding cycle, θ_f, is the weighted average of each possible feeding cycle duration for mosquitoes that complete a feeding cycle,

$$\begin{aligned}\theta_f &= \frac{P_{df}\sum_{i=0}^{\infty}(\tau+iT)P_A^i}{P_f},\\ &= \tau + \frac{P_A T}{1-P_A}.\end{aligned} \tag{23}$$

Although θ_f cannot be explicitly measured, it is useful in comparing the results of this model (3) to those of previous models.

4. Numerical simulation

As described earlier, there is a concerted effort to cover large proportions of at-risk populations with at least one malaria control intervention. We use this model to simulate the effects of increasing

ITN coverage, on malaria transmission. We divide the host population into two groups, humans with ITNs and humans without ITNs. We vary the proportion of humans in each group and evaluate the equilibrium value of selected field-measurable quantities and derived parameters. We denote the human population with ITNs by $i = 1$ and the human population without ITNs by $i = 2$. The baseline parameter values used in the numerical simulation are in Table 4. Parameters are accurate to two significant figures, except for τ and θ_s, which are natural numbers. The total human population, $N_1 + N_2$, is fixed at 1,000, while the population in each group is varied from 1 to 999. Increasing N_1 from 1 to 999 simulates increasing ITN coverage.

We plot the field-measurable and derived parameters described in Section 3 (except for the immediate oocyst rate) at equilibrium against increasing ITN coverage. For all parameter values in Table 4, and in all plots shown, the magnitudes of all eigenvalues of Υ are less than 1. Thus, the fixed point (6) is globally asymptotically stable and all orbits converge to the equilibrium values that we plot here.

In addition to the parameter values shown in Table 4, since we do not model infection in humans, we use three different values of the infectiousness of humans with ITNs to mosquitoes, K_{vi}, to estimate the effects of this simplifying assumption. In one set of simulations, we assume that ITN users have the same infectiousness as unprotected humans, $K_{v1} = 0.030$. This assumption is valid in high transmission areas [16]. In a second set of simulations, we make the crude approximation that infectivity reduces linearly with prevalence, which showed a 13% reduction in ITN users [20], $K_{v1} = 0.026$ as in Table 4. Finally, for comparison, we look at the effects of a 50% reduction in infectivity of ITN users, $K_{v1} = 0.015$. We also run simulations where we allow the partial duration of the feeding cycle, τ, to vary between 2 and 4, and extrinsic incubation period, θ_s, to vary between 10 and 12.

Figure 3 plots the parous rate, M (8), against human ITN coverage, for parameter values shown in Table 4, showing the decreasing survival probability of a mosquito through one feeding cycle

Table 4. Parameter values used to simulate the effects of increasing ITN coverage. Humans with ITNs are represented by the subscript $i = 1$ and unprotected humans are represented by $i = 2$. Details of the derivation of these parameter values are in Appendix B. Here, 'TP' stands for 'this paper' and 'an' stands for 'animals'. Detailed parameter descriptions are in Table 1.

Parameter	Short description	Value	Reference
T	Time step	1 day	TP
n	No. of types of hosts	2	TP
m	No. of types of susc. hosts	2	TP
N_{v0}	Mosq. emergence rate	25,000 an/days	[15]
$N_1 + N_2$	Host population	1, 000 an	[15], TP
α_1	Host availability	0.0040 (an $\times$ days)$^{-1}$	[15]
α_2	Host availability	0.0072 (an $\times$ days)$^{-1}$	[15]
μ_{vA}	Mosq. death rate	1.6 days^{-1}	[15]
θ_d	Host-seeking time	0.33 days	[29]
P_{B_1}	Prob. of biting	0.70	[15]
P_{B_2}	Prob. of biting	0.95	[15]
P_{C_1}	Prob. of finding rest. site	0.70	[15]
P_{C_2}	Prob. of finding rest. site	0.95	[15]
P_{D_1}	Prob. of resting	0.94	TP
P_{D_2}	Prob. of resting	0.94	TP
P_{E_1}	Prob. of laying eggs	0.93	[17]
P_{E_2}	Prob. of laying eggs	0.93	[17]
τ	Resting time	3 days	[7]
θ_s	Ext. incubation period	11 days	[6]
K_{v1}	Host infectiousness	0.026	[20]
K_{v2}	Host infectiousness	0.030	[15]

as more humans are covered by ITNs. Figure 4 plots the proportion of infected host-seeking mosquitoes, o_v, against increasing ITN coverage for parameter values in Table 4 and three values of K_{v1}.

Figure 5 shows the decrease in the proportion of infective host-seeking mosquitoes, s_v, with increasing ITN coverage. Figure 5(a) with parameter values from Table 4 but three values of K_{vi} show that the infectiousness of ITN users to mosquitoes, K_{v1}, makes little difference to s_v. Figure 5(b) with parameter values from Table 4 but three values of τ shows that the partial duration of the feeding cycle has a large effect on the sporozoite rate. Figure 5(c) with parameter values

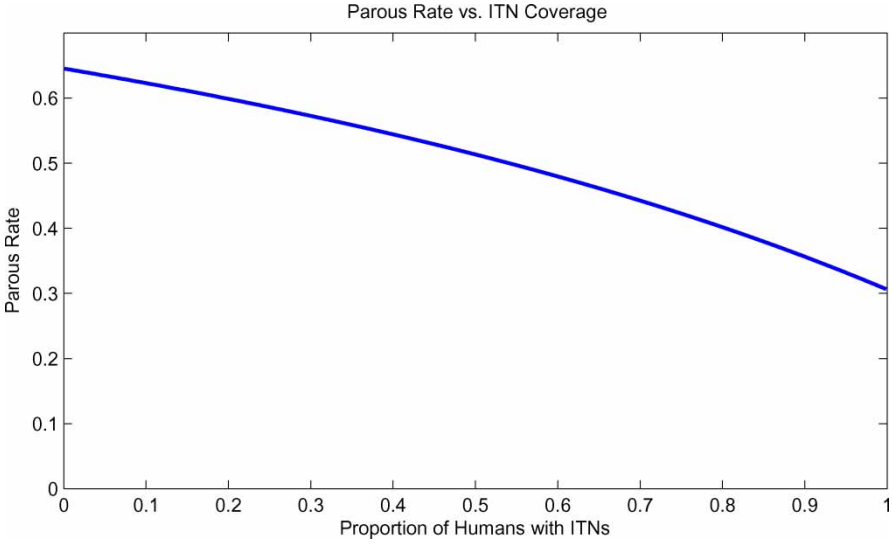

Figure 3. The parous rate, M, is equal to probability that a mosquito survives an entire feeding cycle, P_f. For parameter values in Table 4, covering 80% of the human population with ITNs would reduce P_f from 65% to 40%.

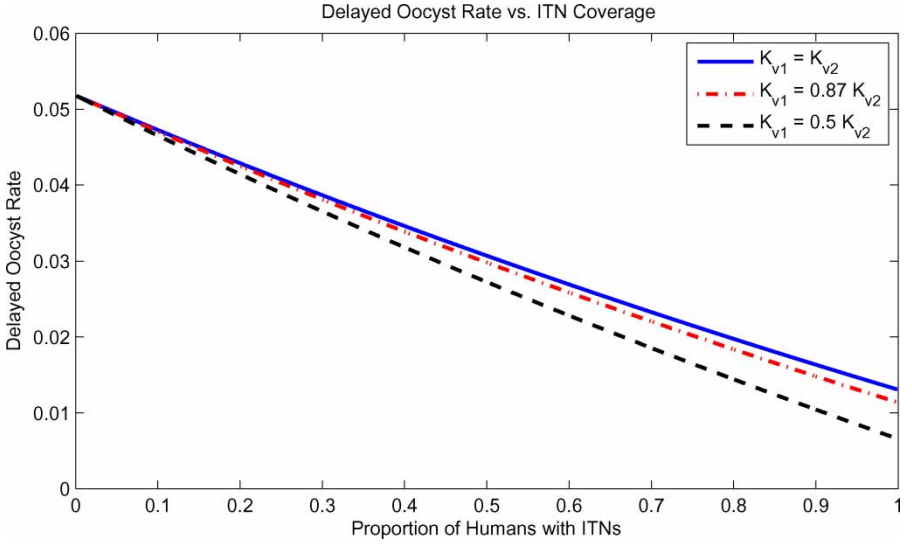

Figure 4. The delayed oocyst rate, o_v, is the proportion of host-seeking mosquitoes that are infected. As ITN coverage increases to 80%, o_v reduces from 5.2% to 2.0%, 1.8%, and 1.4% for the three values of human infectiousness to mosquitoes.

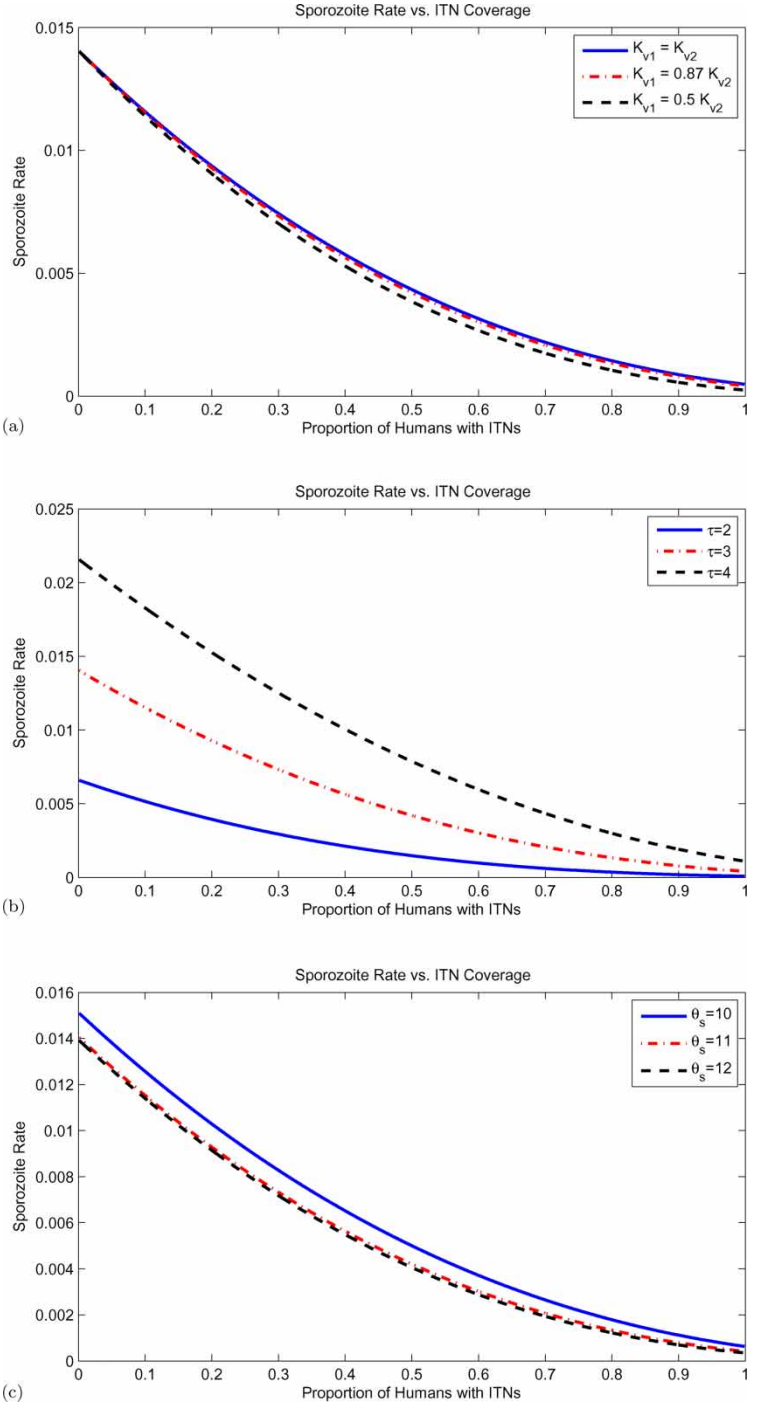

Figure 5. The sporozoite rate, s_v, is an important measure of malaria transmission levels because it is the proportion of host-seeking mosquitoes that are infective. (a) With parameter values in Table 4 for the three values of human infectivity of ITN users, K_{v1}, s_v decreases from 1.4% at zero ITN coverage to 0.14%, 0.13% and 0.10% at 80% ITN coverage. s_v is not sensitive to K_{v1}. (b) With parameter values in Table 4, for three different values of the partial duration of the feeding cycle ($\tau = 2$, $\tau = 3$ and $\tau = 4$), s_v decreases from 0.66%, 1.4% and 2.2% at zero ITN coverage to 0.036%, 0.13% and 0.30% at 80% ITN coverage, respectively. s_v is sensitive to τ. (c) With parameter values in Table 4, for three different values of the extrinsic incubation period ($\theta_s = 10$, $\theta_s = 11$ and $\theta_s = 12$), s_v decreases from 1.5%, 1.4% and 1.4% at zero ITN coverage to 0.18%, 0.13% and 0.12% at 80% ITN coverage, respectively. s_v is somewhat sensitive to θ_s.

Table 5. Values of the sporozoite rate, s_v, the vectorial capacity, Γ, and EIR, Ξ_1 and Ξ_2, for different values of the partial duration of the feeding cycle, τ, and the extrinsic incubation period, θ_s, with other parameter values given in Table 4. The human population is fixed at $N_1 = 600$ and $N_2 = 400$, that is, 60% of the human population is protected by ITNs. All four entomological measures are sensitive to τ and are sensitive to θ_s only when τ is small.

	$\tau = 2$	$\tau = 3$	$\tau = 4$
$\theta_s = 10$	$s_v = 0.0015$	$s_v = 0.0037$	$s_v = 0.0061$
$\theta_s = 11$	$s_v = 0.00098$	$s_v = 0.0030$	$s_v = 0.0060$
$\theta_s = 12$	$s_v = 0.00075$	$s_v = 0.0029$	$s_v = 0.0059$
$\theta_s = 10$	$\Xi_1 = 0.029$	$\Xi_1 = 0.073$	$\Xi_1 = 0.12$
$\theta_s = 11$	$\Xi_1 = 0.019$	$\Xi_1 = 0.059$	$\Xi_1 = 0.12$
$\theta_s = 12$	$\Xi_1 = 0.015$	$\Xi_1 = 0.056$	$\Xi_1 = 0.12$
$\theta_s = 10$	$\Gamma = 1.7$	$\Gamma = 4.1$	$\Gamma = 6.8$
$\theta_s = 11$	$\Gamma = 1.1$	$\Gamma = 3.3$	$\Gamma = 6.6$
$\theta_s = 12$	$\Gamma = 0.82$	$\Gamma = 3.2$	$\Gamma = 6.5$
$\theta_s = 10$	$\Xi_2 = 0.072$	$\Xi_2 = 0.18$	$\Xi_2 = 0.29$
$\theta_s = 11$	$\Xi_2 = 0.047$	$\Xi_2 = 0.14$	$\Xi_2 = 0.29$
$\theta_s = 12$	$\Xi_2 = 0.036$	$\Xi_2 = 0.14$	$\Xi_2 = 0.28$

from Table 4 but three values of θ_s shows that while $\theta_s = 11$ and $\theta_s = 12$ are similar, $\theta_s = 10$ results in a higher sporozoite rate. Table 5 shows s_v with different combinations of τ and θ_s. We see here that s_v is sensitive to changes in τ and the sensitivity of s_v to θ_s depends on the value of τ and this sensitivity decreases as τ increases.

Figure 6 shows the host-biting rate, σ_i (15), for both humans with ITNs and unprotected humans against increasing ITN coverage. It also shows the host-biting rate for an 'average' human, taking the weighted average of the two human subgroups. The host-biting rate does not depend on K_{vi}, τ or θ_s. Figure 7 shows EIR, Ξ_i, for protected and unprotected humans, and their weighted average, for three different values of K_{v1}. As in the plot for s_v, the value of K_{v1} makes little difference to the EIR. Table 5 shows a high sensitivity of EIR to τ and some sensitivity to θ_s. Although not shown here, plots of Ξ_i against ITN coverage with varying τ and θ_s show similar variance to the plots for s_v against ITN coverage. Figure 8 shows the decrease in vectorial capacity, Γ,

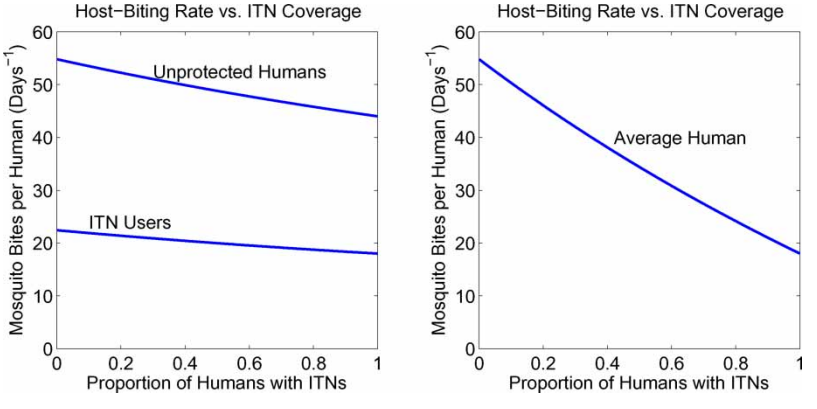

Figure 6. The host-biting rate, σ_i, is the total number of mosquito bites that a host of type i receives per day. We show σ_i for both unprotected humans and humans with ITNs, and for their weighted average. While ITN users receive significantly fewer bites than their unprotected counterparts at any coverage level of ITNs, the unprotected humans also see a small decrease in mosquito bites as ITN coverage increases.

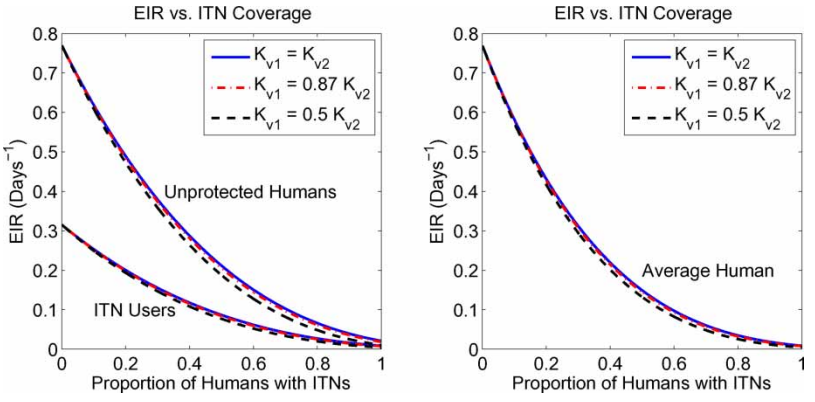

Figure 7. The entomological inoculation rate (EIR), Ξ_i, is the key measure of malaria transmission levels as it is the number of infectious mosquito bites received per host per day. At any level of coverage, ITN users receive fewer infectious bites per day than unprotected humans, although this difference reduces as ITN coverage increases. As ITN coverage reaches 80%, unprotected humans have only a slightly higher EIR than ITN users. For the three values of K_{v1}, EIR for unprotected humans decreases from 0.77 infectious bites per day at zero ITN coverage to 0.066, 0.061 and 0.048 infectious bites per day at an ITN coverage level of 80%, showing the community effects of ITNs. The decrease for an 'average' human is even greater. For the three values of K_{v1}, EIR for ITN users reduces from 0.31 infectious bites per host per day at zero coverage to 0.027, 0.025 and 0.020 infectious bites per host per day at 80% coverage.

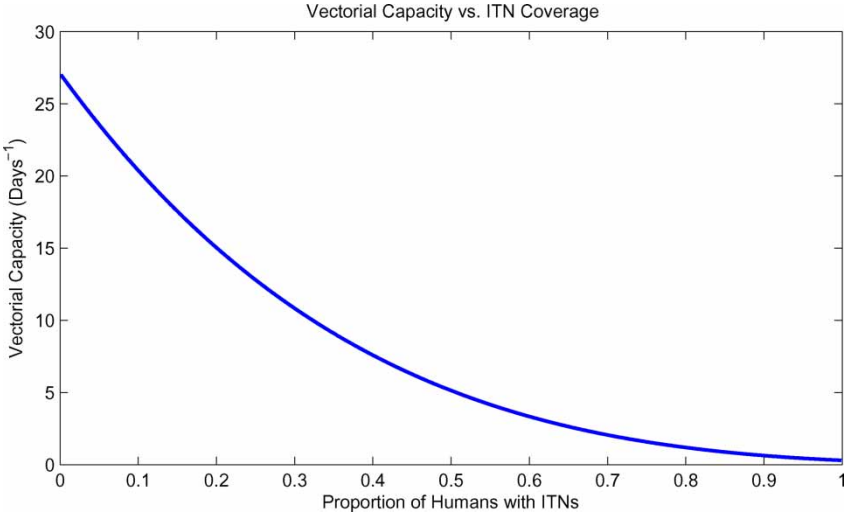

Figure 8. The vectorial capacity, Γ, is a measure of the potential of the vector population to transmit malaria in the absence of malaria. It is defined as the expected number of infectious bites on all hosts, in the absence of superinfection, originating from mosquitoes infected from one host in 1 day. Increasing ITN coverage to 80% decreases the vectorial capacity from 27 infectious bites per day to 1.9 infectious bites per day.

against increasing ITN coverage. Similar to s_v and Ξ_i, Table 5 shows that Γ is sensitive to τ and somewhat sensitive to θ_s at low values of τ. Finally, Figure 9 shows the increase in the average duration of the feeding cycle, θ_f versus increasing ITN coverage.

For parameters where the entomological quantities depend smoothly on the parameter (all parameters in Table 1 except T, n, m, τ, θ_o and θ_s), we can also calculate the sensitivity index of the entomological quantity to the parameter. The sensitivity index, ζ_p^u, of a variable u that depends

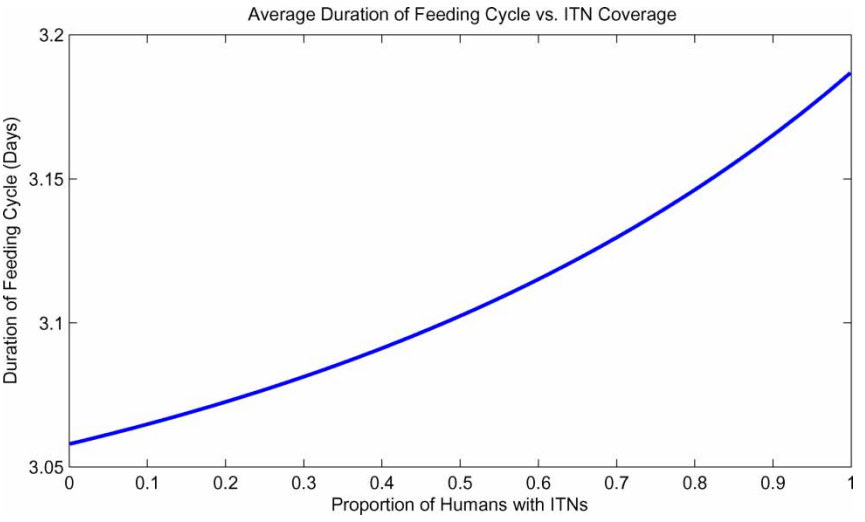

Figure 9. The average duration of a feeding cycle, θ_f, provides a measure of how likely a female mosquito is to encounter a host on its first day of host-seeking. This shows a small increase in the proportion of mosquitoes that are unable to feed and do not die while host-seeking as ITN coverage increases. Note that the labels of the y-axis begin at 3.05 and not at 0.

smoothly on parameter, p is defined as,

$$\zeta_p^u = \frac{\partial u}{\partial p} \times \frac{p}{u}. \tag{24}$$

Sensitivity indices for important entomological quantities to the parameters of the model, at baseline values in Table 4 with $N_1 = 600$ and $N_2 = 400$, are shown in Table 6. We see that the entomological quantities are more sensitive to the mosquito's probability of surviving each stage of the feeding cycle, especially to P_{B_i}, and more so for the unprotected humans.

Table 6. Sensitivity indices for entomological quantities to parameters at values in Table 4, with $N_1 = 600$ and $N_2 = 400$, that is, 60% of the human population is protected by ITNs.

	M	o_v	s_v	σ_1	σ_2	Ξ_1	Ξ_2	Γ	θ_f
N_{v0}	0	0	0	+1	+1	+1	+1	+1	0
N_1	−0.037	−0.099	−0.29	−0.38	−0.38	−0.67	−0.67	−0.87	−0.033
N_2	+0.27	+0.53	+1.2	−0.17	−0.17	+1.0	+1.0	+1.2	−0.039
α_1	−0.037	−0.099	−0.29	+0.62	−0.38	+0.33	−0.67	−0.27	−0.033
α_2	+0.27	+0.53	+1.2	−0.17	+0.83	+1.0	+2.0	+1.6	−0.039
μ_{vA}	−0.23	−0.44	−1.2	−0.45	−0.45	−1.6	−1.6	−1.6	−0.022
θ_d	-3.8×10^{-17}	$+4.4 \times 10^{-17}$	−0.24	0.00	0.00	−0.24	−0.24	−0.24	−0.094
P_{B_1}	+0.31	+0.55	+1.5	+1.3	+0.29	+2.7	+1.7	+2.2	0
P_{B_2}	+0.69	+1.3	+3.3	+0.63	+1.6	+3.9	+4.9	+4.6	0
P_{C_1}	+0.31	+0.55	+1.5	+0.29	+0.29	+1.7	+1.7	+1.8	0
P_{C_2}	+0.69	+1.3	+3.3	+0.63	+0.63	+3.9	+3.9	+3.9	0
P_{D_1}	+0.31	+0.55	+1.5	+0.29	+0.29	+1.7	+1.7	+1.8	0
P_{D_2}	+0.69	+1.3	+3.3	+0.63	+0.63	+3.9	+3.9	+3.9	0
P_{E_1}	+0.31	+0.55	+1.5	+0.29	+0.29	+1.7	+1.7	+1.8	0
P_{E_2}	+0.69	+1.3	+3.3	+0.63	+0.63	+3.9	+3.9	+3.9	0
K_{v1}	0	+0.27	+0.27	0	0	+0.27	+0.27	0	0
K_{v1}	0	+0.70	+0.70	0	0	+0.70	+0.70	0	0

5. Discussion and concluding remarks

We developed and analysed a linear difference equation model for the survival of female mosquitoes and their malaria infection status. This model is an improvement over previous models in that it allows for an arbitrary number of types of hosts, each with different properties, such as availability to mosquitoes infectiousness to mosquitoes, and mortality probabilities for mosquitoes. This provides greater flexibility in modelling heterogeneity in human populations and malaria intervention coverage. At the finest simulation level, each host type could even correspond to an individual, with parameter values selected from appropriate probability distributions. The model also further subdivides the feeding cycle into more stages, allowing it to capture the different mortality effects of various vector control interventions. Finally, the model allows the duration of the feeding cycle to vary across mosquitoes. In previous cyclical models, the duration of the feeding cycle was fixed for all mosquitoes so the models ignored time. Our goal in this paper is to build a rigorous foundation for a mathematical model of malaria infection in mosquitoes, which can then be extended to include seasonal effects, and linked to a model of malaria dynamics in humans, to compare the efficacy and effectiveness of different, single and combined, sets of interventions.

The focus of global malaria vector control interventions today is on ITNs and IRS [27]. ITNs, with insecticidal and diversionary properties, would reduce the availability of hosts, and kill mosquitoes that are attempting to feed. This would reduce α_i, P_{B_i} and P_{C_i}. We distinguish between death, before and after feeding (P_{B_i} and P_{C_i}), because although it makes little difference to mosquito survival, it makes a substantial difference to malaria transmission. IRS has mostly insecticidal effects on resting mosquitoes, but can have diversionary effects, depending on the insecticide used. For example, DDT has been shown to have repellency effects when sprayed inside houses [26]. IRS, thus, reduces α_i and P_{D_i}. The magnitude of the effects of ITNs and IRS on these parameters will depend on the predominant mosquito species, the type of insecticide used, the type of net used, host behaviour and mosquito resistance to insecticide. Other vector control interventions in use today, include larval control, insecticide-treated livestock and diversionary measures such as house-screening and personal repellents. Larval control, by source reduction or larviciding, would reduce the emergence rate of new mosquitoes, N_{v0}. The addition of insecticide-treated livestock would add a new host type to the population that would reduce the mosquito life span and the human biting rate. Its effect on malaria transmission would depend on how zoophilic the predominant malaria vector is. House-screening and personal repellents would reduce host availability, α_i.

The model can also incorporate natural heterogeneity when each human is considered as a separate host type. Host availability, α_i, can be chosen from a probability distribution to account for natural variations in human attractiveness to mosquitoes, including body size and proximity to breeding sites. The mosquito's probability of successfully laying eggs, P_{E_i}, would also depend on its host's proximity to a breeding site.

Here, we used our model to simulate increasing ITN coverage, using parameters from published data (largely from Killeen and Smith (2007) [15]) to model a population of *Anopheles gambiae* feeding on a human population, with no cattle, that is representative of areas like Ifakara, Tanzania. As demonstrated in field trials in western Kenya [13], our results showed ITNs to be effective in reducing malaria transmission. Our model shows a similar reduction in the parous rate, M, with increasing ITN coverage to that shown in [15]. The reduction in the sporozoite rate, s_v, and EIR, Ξ_i, for unprotected humans also appear similar in our model to that in [15], but in our model s_v and Ξ_2 reach lower levels as ITN coverage approaches 100%. Similar to Killeen and Smith (2007) [15], our model (3) shows beneficial effects to unprotected humans at both, low and high, ITN coverage levels. This means that the entire population benefits from increasing

ITN coverage, although, as expected, humans with ITNs benefit more, especially at low coverage levels. Similar to [15], the incremental benefit of ITNs seems higher at low coverage levels. There is no threshold value below which there is no protection. As a further check, test cases at 0% and 100% ITN coverage with appropriate parameter values in our model also reproduce results in Saul (2003) [29]. Our analysis also shows that the key measures of malaria transmission, s_v, Ξ_i and Γ, are most sensitive to the partial duration of the feeding cycle, τ.

Although we only show results for a single mosquito population, it is possible to model more than one mosquito species feeding on the same human population, by replicating the system of Equations (3) with the same value for the human infectivity, K_{vi}. Since the infectivity of humans to mosquitoes is considered as an independent parameter, the systems of equations, for each mosquito species, will be decoupled. When the force of infection from humans to mosquitoes is linked to the force of infection from mosquitoes to humans, the equations for the different species will no longer be decoupled and the order of the system will increase (and the equations will be non-linear). We can also select parameters for additional mosquito species to simulate populations of insecticide-resistant mosquitoes.

Our next step is to allow the emergence rate of mosquitoes, N_{v0}, to vary periodically as a function of time to capture the important effects of seasonality. We can then link this periodic model to a stochastic simulation model for malaria transmission and dynamics in humans based on that of Smith et al. (2006) [33] to model the full malaria transmission cycle in humans and mosquitoes. This will make it possible to evaluate the effectiveness of vector control and other malaria control interventions, allowing for the non-linear dynamics of infectiousness.

Acknowledgements

NC is supported by a postdoctoral fellowship from PATH-MACEPA. TS is supported by a grant from the Bill and Melinda Gates Foundation. RS is supported through PATH by a grant from the Bill and Melinda Gates Foundation. The authors thank Paul Libiszowski for providing the cartoon of the mosquito feeding cycle (Figure 1). The authors also thank Jim Cushing, Klaus Dietz, Yvonne Geissbühler, Gerry Killeen, Christian Lengeler, Steve Lindsay, Louis Molineaux, Melissa Penny, Allan Saul, Allan Schapira and David Smith, for valuable discussions and comments. The authors also thank two anonymous referees for their helpful comments and suggestions.

References

[1] R.M. Anderson and R.M. May, *Infectious Diseases of Humans: Dynamics and Control*, Oxford Unversity Press, Oxford, 1991.
[2] R.A. Anderson, B.G.J. Knols, and J.C. Koella, *Plasmodium falciparum sporozoites increase feeding-associated mortality of their mosquito hosts Anopheles gambiae s.l*, Parasitology 120 (2000), pp. 329–333.
[3] J.L. Aron, *Mathematical modeling of immunity to malaria*, Math. Biosci. 90 (1988), pp. 385–396.
[4] J.L. Aron and R.M. May, *The population dynamics of malaria.* in *The Population Dynamics of Infectious Disease: Theory and Applications*, R.M. Anderson, ed, Chapman and Hall, London, 1982, pp. 139–179.
[5] N. Bacaër and C. Sokhna. *A reaction-diffusion system modeling the spread of resistance to an antimalarial drug*, Math. Biosc. Eng. 2(2) (2005), pp. 227–238.
[6] M.F. Boyd, *Epidemiology: Factors related to the definitive host*, in *Malariology*, M.F. Boyd, ed., Vol. 1, W.B. Saunders, Philadelphia, 1949, pp. 608–697.
[7] P.A. Buxton and H.S. Leeson, *Anopheline mosquitoes: Life history*, in *Malariology*, M.F. Boyd, ed., Vol. 1, W.B. Saunders, Philadelphia, 1949, pp. 257–283.
[8] A.N. Clements and G.D. Paterson, *The analysis of mortality and survival rates in wild populations of mosquitoes*, J. Appl. Ecol. 18 (1981), pp. 373–399.
[9] K. Dietz, L. Molineaux, and A. Thomas, *A malaria model tested in the African savannah*, Bull. WHO 50 (1974), pp. 347–357.
[10] C. Garrett-Jones, *Prognosis for interruption of malaria transmission through assessment of the mosquito's vectorial capacity*, Nature 204(4964) (1969), pp. 1173–1175.
[11] C. Garrett-Jones and B. Grab, *The assessment of insecticidal impact on the malaria mosquito's vectorial capacity, from data on the population of parous females*, Bull. WHO 31 (1964), pp. 71–86.
[12] J. Guckenheimer and P. Holmes, *Nonlinear Oscillations, Dynamical Systems, and Bifurcations of Vector Fields, Applied Mathematical Sciences*, 7ed., vol. 42, Springer, New York, 2002.

[13] W.A. Hawley, et al., *Implications of the western Kenya permethrin-treated bed net study for policy, program implementation, and future research*, Am. J. Tropical Med. Hygiene 68 (Suppl. 4) (2003), pp. 168–173.
[14] C.G. Huff, *Life cycles of malaria parasites with special reference to the newer knowledge of pre-erythrocytic stages*, in *Malariology*, M.F. Boyd, ed., Vol. 1, W.B. Saunders, Philadelphia, 1949, pp. 54–64.
[15] G.F. Killeen and T.A. Smith, *Exploring the contributions of bed nets, cattle, insecticides and excitorepellency in malaria control: a deterministic model of mosquito host-seeking behaviour and mortality*, Trans. Roy. Soc. Tropical Medicine Hygiene 101 (2007), pp. 867–880.
[16] G.F. Killeen, A. Ross, and T. Smith, *Infectiousness of malaria-endemic human populations to vectors*, Am. J. Tropical Med. Hygiene 75 (Suppl. 2) (2006), pp. 38–45.
[17] G.F. Killeen, A. Seyoum, and B.G. J, Knols, *Rationalizing historical successes of malaria control in Africa in terms of mosquito resource availablity management*, Am. J. Tropical Med. Hygiene 71 Suppl. 2 (2004), pp. 87–93.
[18] G.F. Killeen, et al., *Quantifying behavioural interactions between humans and mosquitoes: evaluating the protective efficacy of insecticidal nets against malaria transmission in rural Tanzania*, BMC Infec. Diseases 6(161) (2006).
[19] J.C. Koella and C. Boëte, *A model for the coevolution of immunity and immune evasion in vector-borne disease with implications for the epidemiology of malaria*, Am. Nat. 161(5) (2003), pp. 698–707.
[20] C. Lengeler, *Insecticide-treated bed nets and curtains for preventing malaria, The Cochrane Database of Systematic Reviews*, 2, January 2007.
[21] J. Li, et al., *Dynamic malaria models with environmental changes*, in *Proceedings – Thirty-Fourth Southeastern Symposium on System Theory*, Huntsville, AL, USA, 2002, pp. 396–400.
[22] G. Macdonald, *The Epidemiology and Control of Malaria*, Oxford University Press, London, 1957.
[23] A. Le Menach, et al., *An elaborated feeding cycle model for reductions in vectorial capacity of night-biting mosquitoes by insecticide-treated nets*, Malaria J. 6(10) (2007).
[24] N. Chitnis, J.M. Cushing, and J.M. Hyman, *Bifurcation analysis of a mathematical model for malaria transmission*, SIAM J. Appl. Math. 67(1) (2006), pp. 24–45.
[25] G.A. Ngwa and W.S. Shu, *A mathematical model for endemic malaria with variable human and mosquito populations*, Math. Comput. Model. 32 (2000), pp. 747–763.
[26] D.R. Roberts, et al., *A probability model of vector behaviour: effects of DDT repellency, irritancy, and toxicity in malaria control*, J. Vector Ecol. 25(1) (2000), pp. 48–61.
[27] Roll Back Malaria Partnership. RBM Global Strategic Plan 2005–2015. http://www.rollbackmalaria.org /forumV/docs/gsp_en.pdf, November 2005.
[28] R. Ross, *The prevention of malaria*, 2 ed., John Murray, London, 1911.
[29] A. Saul, *Zooprophylaxis or zoopotentiation: the outcome of introducing animals on vector transmission is highly dependent on the mosquito mortality while searching*, Malaria J. 2(32) (2003).
[30] A.J. Saul, P.M. Graves, and B.H. Kay, *A cyclical feeding model for pathogen transmission and its application to determine vector capacity from vector infection rates*, J. Appl. Ecol. 27 (1990), pp. 123–133.
[31] M.W. Service, *Mosquito Ecology, Field Sampling Methods*, Elsevier, London, 2 ed., 1993.
[32] D.L. Smith and F.E. McKenzie, *Statics and dynamics of malaria infection in Anopheles mosquitoes*, Malaria J. 3(13) (2004).
[33] T. Smith, et al., *Mathematical modeling of the impact of malaria vaccines on the clinical epidemiology and natural history of Plasmodium falciparum malaria: Overview*, Am. J. Tropical Med. Hygiene 75 (Suppl. 2) (2006), pp. 1–10.
[34] C.J. Struchiner, M.E. Halloram, and A. Spielman, *Modeling malaria vaccines I: New uses for old ideas*, Math. Biosci. 94(1) (1989), pp. 87–113.
[35] H.M. Yang, *Malaria transmission model for different levels of acquired immunity and temperature-dependent parameters (vector), Revista de Saúde Pública*, 34(3) (2000), pp. 223–231.

Appendix A. Effects of diversion

Although model (3) does not explicitly contain diversion, it is equivalent to a model with explicit diversion. We describe such a model here and then show that with a change of variables, the new model reduces to the original model.

We first define a new model with explicit diversion, as described in Killeen and Smith [15], where when mosquitoes have encountered a host, they can either bite, die or be diverted to host-seeking again. We denote parameters of the model with diversion with the superscript '(div)' to distinguish them from the parameters of the original model. In the new model, the definition of state B_i changes to a mosquito encountering a host and not being committed to biting. The mosquito can then bite the host with probability $P_{B_i}^{(div)}$ and move to state C_i, die while attempting to bite with probability $P_{B_i\mu}^{(\mathrm{div})}$, or be diverted back to the host-seeking state, A, with probability $P_{B_i\Delta}^{(\mathrm{div})}$. These probabilities obey the relationship

$$P_{B_i}^{(\mathrm{div})} + P_{B_i\mu}^{(\mathrm{div})} + P_{B_i\Delta}^{(\mathrm{div})} = 1 \quad \forall\, i, \tag{A1}$$

whereas in the original model,

$$P_{B_i} + P_{B_i\mu} = 1 \quad \forall\, i. \tag{1b}$$

In the original model, we separate the diversion process so that the mosquito can 'encounter' a host and be diverted while still in the host-seeking state, A. The mosquito truly encounters a host of type i and enters state B_i only when it has

overcome diversion and is fully committed to biting a host. From B_i, the mosquito can then either bite host i or die while trying to bite, but cannot directly go back to host-seeking.

The relationships between the probabilities in the original model and the model with explicit diversion are

$$P_{B_i} = \frac{P_{B_i}^{(\mathrm{div})}}{P_{B_i}^{(\mathrm{div})} + P_{B_i\mu}^{(\mathrm{div})}} = \frac{P_{B_i}^{(\mathrm{div})}}{1 - P_{B_i\Delta}^{(\mathrm{div})}}, \tag{A2}$$

$$P_{B_i\mu} = \frac{P_{B_i\mu}^{(\mathrm{div})}}{P_{B_i}^{(\mathrm{div})} + P_{B_i\mu}^{(\mathrm{div})}} = \frac{P_{B_i\mu}^{(\mathrm{div})}}{1 - P_{B_i\Delta}^{(\mathrm{div})}}. \tag{A3}$$

The effects of diversion for each kind of host are incorporated into the availability of that type of host

$$\alpha_i = \alpha_i^{(\mathrm{div})}(1 - P_{B_i\Delta}^{(\mathrm{div})}). \tag{A4}$$

All other parameters in the model with explicit diversion are the same as in the original model. Using these change of variables, (A2), (A3) and (A4), the expressions for all derived parameters and field-measurable quantities are the same for both models.

Appendix B. Derivation of parameter values for numerical simulation

We derive values for most parameters in Table 4 from values of parameters in Killeen and Smith (2007) [15] to compare the results of the two models for increasing coverage of ITNs. The parameters are for *Anopheles gambiae* in the absence of livestock. We use a time step of $T = 1$ day. The emergence rate of new mosquitoes, N_{v0}, is the same as that in [15]. We keep the total human population at 1,000, while varying the subpopulation in each group from 1 to 999 to model increasing net coverage. We use an estimate of the mosquito searching time per day of $\theta_d = 8$ hours from Saul (2003) [29] and Killeen et al. (2006) [18].

We use death and diversion rates, with and without nets, from [15] to calculate values of $\alpha_1, \alpha_2, \mu_{vA}$ and the probabilities of a mosquito biting humans with and without nets. In modelling mosquito deaths while feeding, Killeen and Smith (2007) [15] do not distinguish between deaths before and after the proboscis enters the human. For this numerical example, we assume that the probability of dying immediately before biting, is equal to the probability of dying immediately after biting, so $P_{B_i} = P_{C_i}$. Then, $P_{B_1} P_{C_1}$ is the probability (in [15]) that a mosquito survives feeding on a human with an ITN, and $P_{B_2} P_{C_2}$ is the probability (in [15]) that a mosquito survives feeding on an unprotected human. We assume that ITNs do not affect the oviposition probability so $P_{E_1} = P_{E_2}$. We calculate P_{E_1} by assuming that a mosquito has a survival probability of 0.8 per day while seeking an oviposition site and that it seeks for 0.33 days [17]. We assume that ITNs do not affect the probability of surviving the resting phase, so $P_{D_1} = P_{D_2}$. We pick P_{D_1} such that, at minimum ITN coverage, P_f Equation (2) matches P_f in Killeen and Smith (2007) [15].

Both, τ and θ_s, depend on environmental conditions and vary with temperature and relative humidity. We use reasonable values of $\tau = 3$ [7] and $\theta_s = 11$ [6], which are consistent with parameter values used in [15] and [29]. We assume that the probability of disease transmission from unprotected humans to susceptible mosquitoes, $K_{v2} = 0.030$, from [15]. We assume that the reduction of the infectiousness of ITN users to mosquitoes when compared to unprotected humans is equal to the reduction in malaria prevalence in ITN users. Lengeler [20] showed a prevalence reduction of 13% so we use $K_{v1} = 0.026$. In the numerical simulations, we also vary τ from 2 to 4, θ_s from 10 to 12 and use three different values for K_{v1}.

Although values for some of the parameters are not available from field studies, we hope the new model will help focus experiments aiming to estimate these quantities.