On a three-stage structured model for the dynamics of malaria transmission with human treatment, adult vector demographics and one aquatic stage

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Abstract

A modelling framework that describes the dynamics of populations of the female *Anopheles sp* mosquitoes is used to develop and analyse a deterministic ordinary differential equation model for dynamics and transmission of malaria amongst humans and varying mosquito populations. The framework includes a characterization of the gonotrophic cycle of the female mosquito. The epidemiological model also captures a novel feature whereby treated human's blood can become mosquitocidal to the questing mosquitoes upon the successful ingestion of the treated human's blood. Analysis of the disease free system, that is the model in the absence of infection in the human and mosquito populations, reveals the presence of a basic offspring number, $\mathcal{N}$, whose size determines the existence and stability of a thriving mosquito population in the sense that when $\mathcal{N} \leq 1$ we have only the mosquito extinction steady state which is globally asymptotically stable, while for $N > 1$ we have the persistent mosquito population steady state which is also globally asymptotically stable for these range of values of $\mathcal{N}$. In the presence of disease, $\mathcal{N}$ still strongly affects the properties of the epidemiological model in the sense that for $\mathcal{N} \leq 1$ the only steady state for the system is the mosquito extinction steady state, which is globally and asymptotically stable. As $\mathcal{N}$ increases beyond unity in the epidemiological model, we obtained the epidemiological basic reproduction number, R_0. For $R_0 < 1$, the disease free equilibrium, with both healthy thriving susceptible human and mosquito populations, is globally asymptotically stable. Both $\mathcal{N}$ and R_0 are studied for control purposes and our study highlights that multiple control schemes would have a stronger impact on reducing both $\mathcal{N}$ and R_0 to values small enough for a possible disease vector control and disease eradication. Our model further illustrates that newly emerged mosquitoes that are infected with the malaria parasite during their first blood meal play an important and strong role in the malaria disease dynamics. Additionally, mosquitoes at later gonotrophic cycle stages also impact the dynamics but their contributions to the total mosquito population size decreases with increasing number of gonotrophic cycles. The size of the contribution into the young mosquito population is also dependent on the length of the gonotrophic cycles, an important bionomic parameter, as well as on how the mosquitoes at the final gonotrophic cycles are incorporated into the modelling scheme.

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Highlights

- Gonotrophic cycles are essential in mosquito size and malaria disease burden estimation.
- Basic offspring number, which depends on number of gonotrophic cycles, determines existence, stability and size of a mosquito population.
- For , a disease threshold parameter exists; for, a globally asymptotically stable human and mosquito steady-state co-exists.
- Newly emerged mosquitoes exposed to malaria parasites during first blood meal strongly influence malaria disease burden/dynamics.
- Gonotrophic cycle length affects and size of the contribution into the aquatic/young mosquito population.

1 Introduction

Malaria, a parasite-caused disease, remains one of the most highly prevalent and deadly human diseases, with significant impact in the tropics, especially, sub-saharan Africa. Although, between 2000 and 2015 malaria mortality rates fell among all age groups, including children under five, [30], there were about 216 million cases of malaria in 91 countries in 2016 (an increase of five million compared with 2015) and, in fact, the number of malaria cases has been increasing in some parts of the Americas, South-East Asia, Western Pacific and Africa. Thus, although in many other regions infections are stable or going down, the severity of the malaria problem is still a cause for concern.

There has been an appreciable effort at the world stage level to fight malaria infestation as a disease within human populations. Some of these efforts have been successful at the local level, where some WHO areas have recorded zero new cases of malaria over an appreciable period of time [30]. Most of the large scale efforts, starting with the UN sponsored Garki project [14], through the Roll Back Malaria initiative or the partnership towards a world free of malaria together with the Bill and Melinda Gates foundation as well as some private research initiatives towards the development of an effective vaccine against malaria disease [9], are still to yield fruits. Measuring the level of success of the control efforts at the local and global scale requires the use of indices that are robust enough to serve as indicators of progress or failure. Some approaches that have been used as measurable indices of control include, but are not limited to, the computation of the *incidence rate* (the number of new infections from susceptible individuals per unit time), the *prevalence rate* (the proportion of infections in the entire population) and others. Each of the aforementioned indices, though very useful as an immediate indicator of disease presence, is static and may not be very useful if one was to begin to study the disease dynamics over longer periods of time. In this case, one may wish to examine dynamic indices of transmissibility such as the *secondary attack rate* (the proportion of infected individuals in a country or region amongst the susceptible population that are in contact with each primary infected person in the population) or the *reproduction number* (the average number of successful transmissions attributable to each infected person). The secondary attack rate measures the risk of transmission and carries limited information as it can only indicate the risk as a range from low to high, while the reproduction number would offer a more accurate and dynamic index to quantify the actual number of possible new cases. The reproduction number is largest when the single infectious person is introduced into a completely susceptible population; this would be the case of the introduction of a new infectious malaria carrier into a malaria free zone where conditions of transmission are favourable. When the reproduction number is calculated for a situation where we have a new infection introduced into a completely susceptible population, we talk of *the basic reproduction number*. The theory asserts that the infection can spread into the population if the basic reproduction number is greater than one.

Calculating the basic reproduction number for a disease requires that one understands all features of the particular infectious disease such as effective contacts rates, incubation periods, recovery rates, etc, that will be different for different infectious diseases. For the case of malaria, the computation of the reproduction number is complicated by the fact that the malaria parasite has adapted its life cycle so that it needs to grow both in the human and the mosquito population and by the fact that the parasite is naturally passed from one human to the other only because of the human biting habit of the *Anopheles sp* mosquito. That is, each single mosquito must bite two different humans at two different times to be able to serve as a vector for the malaria transmission rom one human to another. Within the framework of the mosquito's life style, we assume that these two different effective bites will take place at two distinct gonotrophic cycles. This requirement for the mosquito to have an effective biting contact involving two different humans means that we must study the characteristics of the disease within both the mosquito and human populations. From the mathematical perspective, we need to develop mathematical models that capture the dynamics of both the mosquito and the human populations in a more accurate manner. One important byproduct of a good mathematical model for the dynamics of malaria transmission is the formula for the basic reproduction number. Several models for dynamics of malaria transmission and the population dynamics of malaria vector have been studied. These include [18, 19, 17, 15, 16, 21] among many others. However, in the current

literature we have not come across mathematical models that take into consideration the fact that for the malaria disease to be transmitted from one human to the next by the *Anopheles sp* mosquito, the vector must bite the two persons involved at different times. The purpose of the current manuscript is to derive and study a mathematical model for the dynamics of malaria transmission that takes into consideration the multiple biting habit of the mosquito and, in the process, to derive a more realistic estimate for the basic reproduction number for malaria. We exploit the fact that the mosquito's reproductive life cycle can be divided into *gonotrophic cycles*[1] and, while counting the number of such gonotrophic cycles, we use the time lapse required to complete each gonotrophic cycle as a means to indirectly include the mosquito's age structure into the mosquito-human interactive framework. So, only the mosquitoes in the transmission chain that are old enough and were infected early enough would contribute to the process of transferring the malaria infection from human to human. We continue to build our model within the earlier framework proposed by Ngwa [18] and used before in Ngonghala et al. [15, 16, 17] and Nourridine et al. [21]. In the following subsection, we briefly describe this framework and also indicate the objectives of this paper.

1.1 The mosquito reproductive stages and demographic framework

Each mosquito can be in one of three physiological states: (i) at the breeding site (these are adult female vectors at the breeding site that are either newly emerged or are older but have laid eggs at least once before), (ii) questing for blood meals (these are the questing vectors: fertilized and searching for blood meals), and (iii) resting after a blood meal in preparation for reproducing (these are mosquitoes resting after a blood meal and that will eventually move to a breeding site to lay eggs, if they arrive there successfully). Each vector can also have different infection status: infected, infectious or susceptible. It is understood that for a single mosquito to transfer an infection from one human host to another, three conditions must be satisfied: first, it must bite two hosts at different sufficiently distinct points in time, second, the mosquito must survive during the infection's development; that is, between the time the mosquito is infected and the time when it has become infectious and thus in the position to transfer the infection to the next human host and, third, a physiological reproductive need must be triggered so that the mosquito starts seeking for another blood meal. The meeting of these requirements play an important role in the malaria transmission problem and also has a direct bearing on the size of the mosquito population since each successful gonotrophic cycle leads to an increase in the mosquito's population as more offspring may arise. Now, for the *Anopheles sp* mosquito and the malaria parasite for example, it takes about 10 days from the time the mosquito ingests the malaria gametocytes from an infectious human to the time when the mosquito is able to transfer the infection to another human if, and when, it has a *successful* contact with that human, [22]. During the adult female mosquito's terrestrial life period, the reproductive centred activities of blood feeding and egg laying continue and it is assumed that at some point in its quest for blood meals from the human population, the mosquito can become infected with the malaria parasite. However, because of the 10 days time lapse between being infected and being infectious, any active mosquito that successfully picks up a malaria infection will become infectious after at least two gonotrophic cycles. From this reasoning, an adult mosquito that got infected with the malaria parasite within the first few days of eclosion can be come infectious to humans only approximately from its second week of existence after hatching from the pupa. To mathematically capture the disease dynamics, the incubation period as well as the period of infectivity for the disease within the mosquito population can be built directly into the number of gonotrophic cycles that the mosquito could have had during its entire life history as we now present below

Reproductive success of mosquitoes requires that a newly emerged adult female mosquito locates a mating partner followed by proper mating. For the *Anopheles sp* mosquito, the mating takes place within the first $3-5$ days of the adult's life. There is a controversy over which event comes first:

[1]The cyclic path of blood feeding $\longrightarrow$ resting for egg maturation $\longrightarrow$ oviposition $\longrightarrow$ blood feeding that is repeated several times during the mosquitos entire reproductive life is referred to as the gonotrophic cycle. The length of the gonotrophic cycle is the interval between successive batches of eggs.

mating before the first blood feeding episode or taking the first blood meal before mating and whether the female mosquito re-mates at all, [31, 29]. Here, we assume that the female *Anopheles sp* mosquito mates once and, after mating she stores the spermatozoa in spermatheca after copulation, so that during each subsequent oviposition, the eggs can be fertilized during their transit through the oviduct [25, 4, 6, 10, 3, 7]. When the fertilized female mosquito ingests blood, she rests while the blood is digested and the eggs are developed. Afterwards she migrates to a suitable place, the *vector breeding site,* where she lays her eggs and then resumes seeking a host for the next blood meal. The cycle of blood feeding and egg laying, also known as the *gonotrophic cycle* [11], repeats itself until the female dies. In the current paper, we explicitly count the gonotrophic cycles that a reproducing mosquito can undergo in its entire reproductive life, as in [20], but for the sake of mathematical tractability, after cycle two, we lump all subsequent gonotrophic cycles into the third gonotrophic cycle through a feedback looping mechanism to ensure that we capture all the questing population, as shown in Figure 1 below. This assumption introduces long lived mosquitoes, in contrast to [20] where it was assumed that in the last cycle, the mosquito lays its last batch of eggs and dies. Though the later is more realistic, we continue to use the former for mathematical tractability. So, all mosquitoes that are still alive and active after the third gonotrophic cycle are re-classed into the third cycle. What is sought, and captured, in the modelling here is the fact that each reproductive episode is preceded by a successful blood meal ingestion from a human host; an activity that may result in the transmission of the malaria infection between the human and the mosquito hosts. However, only mosquitoes that have gone through two or more gonotrophic reproductive cycles, and that were infected at least two cycles earlier, can transmit the infection to the human.

The identification of a mosquito at different stages of the gonotrophic cycle, its vital demographic parameters as well as its physiological and disease status, places it into easily identifiable compartments that can be useful for the purposes of mathematical modelling. We note that many of these compartments will overlap. For example, while the physiological compartments are mutually exclusive with each other, the disease and physiological compartments can overlap. The compartmentalization so constructed allows us to follow the progression of each vector through the different classes, as they proceed with survival strategies. So, a newly emerged adult female mosquito must mate, seek and receive a blood meal, rests, lays eggs to complete its first reproductive cycle, and then the pattern of blood feeding, resting and egg laying is repeated in each cycle as many times as it is possible during ts entire adult life period. In the process of taking a blood meal from an infected human, it can get nfected and can also pass on the infection to the next human as soon as the parasite has matured in the mosquito. So the disease dynamic processes can be coupled to the life style of the mosquito by exploiting the fact that the *mosquito has a human blood feeding habit.* A rather remarkable complement, and a completion of the coupling process, is the ability, through this modelling framework, to quantify the reproductive gains that accrue to the mosquito consequent on its interaction and successful acquisition of a blood meal from humans.

Ingestion of a vertebrate's blood is an integral part of the female *Anopheles sp* mosquito's reproductive life and each egg laying episode is preceded by a vertebrate blood meal. The blood feeding habit of the mosquito is also influenced by its blood preference factor in the sense that some mosquitoes prefer human blood (anthropophilic mosquitoes), while the others prefer non-human blood (zoophilic mosquitoes). We do not explicitly consider mosquitoes which prefer to feed on non-human blood in this paper since we can safely assume that such mosquitoes will not contribute to human malaria transmission; even though they may contribute to the mosquito population size. Omitting these class of mosquitoes does not adversely affect the analysis presented here since only those mosquitoes that repeatedly feed on humans, and thus are most likely to be responsible for the human malaria transmission are of interest in this study. It is not well understood whether mosquitoes can change their blood preference subject to availability of vertebrate host, however we shall use the fact that there is a possibility of alternative blood meals (from non-human host) for the mosquito, when we derive the expression for the flow rate of the breeding site mosquitoes to human habitats, to emphasize the fact that we have not considered the conservation of all breeding site mosquitoes in the modelling process.

Within the human population we only consider a compartmentalization according to the disease status and divide the human population into three classes: the susceptible (S_h), infectious (I_h) and treated (T_h). So progression from the susceptible to infectious class occurs after a successful encounter with an infectious questing mosquito, while progression from the infectious to the treated compartment occurs only after treatment. Treatment provides recovery from the infection with partial immunity so that members from the treated class eventually become susceptible after some time. An added feature of the treated class is that its members' blood become toxic to mosquitoes so that a questing mosquito that feeds on this class may die due to the fact that the treatment renders the treated human's blood mosquitocidal because it contains engineered deadly antigens, [23]. It is assumed that, because of the cost, only those that are infected with malaria and present with symptoms receive the treatment. So one objective of this paper is to measure the impact of this feature of the treated malaria patients on the overall dynamics of the malaria transmission problem. However, the primary objective of this paper is to asses the impact of the additional compartments modelling the fact that we allow only aged mosquitoes in the transmission chain to be infectious to humans, particularly from the points of view of the mosquito population size, malaria disease control and the measurable index of transmissibility. The outcome is an improved formula for the basic reproduction number for malaria.

The remaining part of the paper is organised in the following way: in Section 2 we present in detail the model formulation and show how the different compartments link up together into a coherent framework for mosquito-human-mosquito-malaria interactions. We show how we can scale the system to reduce the relevant parameters at the end of Section 2. In Section 3 we begin the analysis of the model with the disease free, or mosquito only dynamics model, and continue the analysis with the full epidemiological model in Section 4. We conclude the paper with a discussion in Section 5, where we also present possible areas of control and an overall conclusion.

2 Model formulation

We now give a detailed derivation of the model equations to be studied in this paper. We consider, for a start, an SITS (Susceptible-Infectious-Treated-Susceptible) model for the malaria transmission dynamics in the human population and an SI epidemiological model for the malaria dynamics in the mosquito population. As we shall see, though we consider an SI epidemiological model for the dynamics in the mosquito population, what we get is in fact an SEI epidemiological model because the recognition of the different gonotrophic cycles introduces an age structure in the model.

2.1 Notation

The notation for the different types of state variables, that captures the different compartments discussed above, is explained and shown in Table 1. Since all mosquito and human state variables can either be in an infected or susceptible state, we identify susceptible variables with the letter S and infected variables with the letter I, followed by subscript that will further identify the type of the variable being used. For example, $I_{u_{k,j}}$ is used to represent an infected mosquito of type U that is in its k-th reproductive stage and picked up the infection at its j-reproductive stage, and S_{u_k} is used to represent a susceptible mosquito of type U at the reproductive stage k. Thus aging is factored into the modelling framework by counting and identifying the reproductive stages of each mosquito through the subscripts k and j, as explained in Table 2. The double subscript notation employed here allows us to track each active mosquito through its reproductive stages and so indirectly captures an age structure[2] of the population in the sense that at the same reproductive stage, mosquitoes of type V are always younger that mosquitoes of type U. In fact, all adult mosquito of type V at the reproductive stage k are always considered far younger than mosquitoes of type U at the reproductive stages $k+1$, $k = 1, 2, \ldots,$. The parameters of the system are detailed in Table 3 where, we display each parameter of the system stating clearly its physical meaning and quasi dimensional unit.

[2]We ignore all those adult mosquitoes that do not succeed to enter the reproductive cycle chain for any reasons.

Type of variable	Description	Quasi-dimension
V	These are vectors at the breeding site that are either newly emerged or have returned to the breeding site to lay eggs. We call these **the breeding site** vectors.	M
W	These are vectors that have left the breeding site (perhaps to the human habitat) to search of a blood meal. We call these **questing vectors.**	M
U	These are vectors that have succeeded in acquiring a blood meal and are now resting in view of returning to the breeding site to lay eggs. We generally refer to these type of vectors as **reproducing vectors.**	M
N_h	Host of human type from which the mosquito can draw needed blood as needed for its survival as a species	H
A	Aquatic stages of the vector: these include eggs, larvae and pupae	A

Table 1: Types of state variables and their quasi dimensional unit which is either H for humans, A for aquatic life stage, and M for adult mosquitoes or terrestrial forms of the mosquito

State variable	Description	Quasi-dimension
S_h, I_h, T_h	Density of susceptible, infectious and treated humans	H
S_{l_k}	Density of susceptible vectors of type l in the k-th reproductive stage of their life, $k \geq 1$ and $l \in \{u, v, w\}$.	M
$I_{l_{k,j}}$	Infected vector of type l at the reproductive stage k, that was first exposed and picked up the malaria infection at the reproductive stage j, $k, j \geq 1$ and $l \in \{u, v, w\}$.	M

Table 2: Detailed description of state variables showing the disease status and their quasi-dimension. The human and mosquito populations are both divided into classes representing disease status; that is, susceptible and infectious classes. The mosquito population is further divided into classes representing physiological status as well as the stage of their life in terms of the gonotrophic cycle count.

As indicated earlier, the human population is divided into three classes linked to their disease status: the susceptible (S_h), infectious (I_h) and treated (T_h). The new feature here, based on the recent 2018 study, [23], is that the treated class T is completely protected against further infection for the time when the medication is active, while at the same time the blood from humans T has a mosquitocidal effect on the questing mosquitoes. Interactions between questing mosquitoes and humans from the treated class therefore can serve as an additional cause of death for the questing mosquitoes. Births occur in all human compartments at rate λ_h, while natural deaths occur at rate μ_h. Infected humans can recover without treatment at rate r_h to join the susceptible class, while the infected humans receive treatment at rate δ_h to enter the treated class, where they eventually loose their protection at the rate γ_h to join the susceptible class. Disease related deaths have not been considered in the present formulation.

The mosquito population is divided into two broad classes: the aquatic class representing juvenile forms of the mosquito and the terrestrial class representing the adult forms of the mosquito. The terrestrial class is further divided into compartments representing the physiological status so that at any time t we have:

(i) **type** V mosquitoes, which are the mosquitoes at the breeding site, that are either newly emerging

from the aquatic stage, or have returned to the breeding site after their resting period to lay eggs;

(ii) **type** W mosquitoes that have left the breeding site and are questing for blood meals within the human population;

(iii) **type** U mosquitoes that have successfully acquired a blood meal from a human and are now resting before returning to the breeding site to lay eggs.

The transition from type V to type W is triggered by the reproductive need that requires that a female mosquito ingests vertebrate blood for the maturation of her eggs, while the transition from type W to type U is made possible by a successful acquisition of a blood meal from a human and, finally, the transition from type U to type V is possible only if the mosquito survives the resting period required for the maturation of her eggs. It is assumed that in each of these states, the mosquito can be killed. For example, it is assumed that if a mosquito fails to acquire a blood meal during an interaction with a human, then it has been killed. Each of the U, V and W types of mosquitoes are further divided into sub classes representing its reproductive stage as determined by the number of gonotrophic cycles it has undergone. With this compartmentalization, if N_u is the total size of the population of type U, then N_u is obtained as the sum of all U type mosquitoes in different gonotrophic stages. Similar definitions apply for the total size of breeding site mosquitoes, N_v, and the total size of questing mosquitoes, N_w. So, from the adopted compartmentalization, in addition to the aquatic stage density A, the total active adult mosquito populations N_m and the human population N_h at time t are given, respectively, by

$$N_h = S_h + I_h + T_h, \quad N_m = N_u + N_v + N_w, \tag{1}$$

where N_u is total size of the reproducing vectors, N_v is total size of the breeding site vectors and N_w is the total size of the questing vectors. These are computed using the expressions

$$\begin{aligned} N_u &= \sum_{k=1}^{3} S_{u_k} + \sum_{j=1}^{3}\sum_{k=j}^{3} I_{u_{k,j}}, \quad N_v = \sum_{k=1}^{3} S_{v_k} + \sum_{j=1}^{2}\sum_{k=j+1}^{3} I_{v_{k,j}}, \\ N_w &= \sum_{k=1}^{3} S_{w_k} + \sum_{j=1}^{2}\sum_{k=j+1}^{3} I_{w_{k,j}}. \end{aligned}$$

Natural deaths in all mosquito compartments are denoted by μ_*, where the subscript is the label of the variable whose death rate we wish to describe. For example, μ_{Sv_1} is the death rate of susceptible vectors of type V at the gonotrophic cycle 1 and $\mu_{Iw_{3,1}}$ is the death rate of infected questing mosquitoes at the gonotrophic cycle 3 that were infected at gonotrophic cycle 1.

In Table 4, we show the transitions that take place within the mosquito populations. The full human-mosquito interactive framework in the presence of malaria disease is shown in Figures 1 and 2. Basically, Figure 1 shows the flow and the progression of the mosquitoes from a lower gonotrophic cycle count to higher ones. The points in the chain, where mosquitoes can interact with humans are clearly indicated with the shaded H-box attached to relevant w mosquito compartment. All mosquitoes that fail to take a blood meal at any H-interactive location are assumed to have been killed during the interaction, and each mosquito that succeeds at this point transforms with probability q_w to a mosquito of type U, which later contributes to the aquatic stages of the mosquito population through simple oviposition of eggs at the rate $\lambda_v(U)$ per reproducing mosquito of type U. Type U mosquitoes can either be infected, indicated by the I label, or susceptible (indicated with the S label). Mosquitoes at gonotrophic cycle 3 (and above) that survive, re-enter the chain through a pull back term at a reduced rate indexed with the proportion θ_k or $\theta_{k,j}$. In Figure 2 we show the human-mosquito interactive scenarios at the different gonotrophic cycles. Successful human-mosquito interactions at all the gonotrophic cycles contribute to an increase in the mosquito population size

and, if infection is successful, it is with probability p_{hw} and then, we also have the introduction of new infections in the mosquito population. Successful mosquito-human interactions at gonotrophic cycles 3, in addition to leading to an increase of the mosquito population size, may also lead to the introduction of new infections into the human population with probability p_{wh}. It is understood that p_{hw} is, in general, different from p_{wh}. The human-mosquito interactive points only show mosquitoes of type W interacting with humans H. As in [17, 15, 16], we consider the following types of successful transitions and possible outcomes:

(i) Successful interactions between mosquitoes and humans that do not lead to the transfer of infection between the two species but lead to an increase in the mosquito population size;

(ii) Successful interactions between humans and mosquitoes that lead to the transfer of new infections between the two species as well as to an increase in the mosquito population size;

(iii) Unsuccessful interactions between humans and mosquitoes are assumed to result in the death of the latter.

In the present framework, we have not considered the possibility of unsuccessful interactions between humans and mosquitoes after which the mosquito lives to try and bite a human again.

The epidemiological model studied in this paper is an SITS (Susceptible-Infectious-Treated-Susceptible) model for the flow of the disease within the human population, as shown in Figure 2, and an SEI (Susceptible-Exposed-Infectious) model for the flow of the disease within the mosquito population. As mentioned earlier, one important novelty of the introduced model is the idea that blood from the treated humans can have a mosquitocidal effect on the mosquitos upon ingestion, [23]. On the other hand, a simplification here is that we assume an instantaneous infectiousness within the human population while, in the mosquito population we allow for a development (incubation) of the disease, that is captured through the aging process of the adult parasite carrying female mosquitos. More precisely, the incubation period is described implicitly by considering the gonotrophic and life stage cycles. It is illustrated in detail in Figure 1. There we see that any new infection that enters the mosquito compartment comes as a result of a successful interaction between a type W susceptible mosquito and an infectious human and, if this is the case, we allow at least six stages (representing a considerable delay) from the moment of the first infection to the compartment labelled $I_{w_{3,1}}$, through which the infection can pass into the human population. In the case of mosquitoes becoming infected in their first gonotrophic cycle that, due to the mosquito's life span, accounts for the majority of human infections, it means that at least two gonotrophic cycles must pass before they become infectious. If a mosquito gets infected at a later cycle, it still must pass through at least six life stages which are lumped into 2 or 1 gonotrophic cycles but, due to the mosquito life span, the chances of it living long enough to be able to pass the infection to humans are small. Therefore, lumping the higher gonotrophic cycles does not distort the overall picture of the spread of malaria.

On the other hand, we observe that a mosquito infected during its first gonotrophic cycle also must live through six stages to become infectious in its third gonotrophic cycle hence, from the modelling perspective, we can interpret the model as requiring the delay of two gonotrophic cycles between becoming infected and becoming infectious also for the mosquitoes infected during the second and third cycles. To make the notation consistent with this interpretation, we will treat the mosquitoes that were infected in the third gonotrophic cycle, reproduced and begun the next gonotrophic cycle, as if they were infected in the second cycle. In a similar way, to become infectious, the mosquitoes that were infected during the second cycle, must live through one more cycle and, if they survive, they reproduce and begin the next cycle, but then they are treated as if they were infected during the first cycle. In this way, the infectious mosquitoes can be considered as having survived two gonotrophic cycles after becoming infected and thus they are grouped in one class, labelled $I_{w_{3,1}}$, as if all of them were infected in the first cycle.

We believe that our framework captures the fact that only older mosquitoes that were infected early enough can be infectious to humans and thus there is a large portion of the mosquito population that do not contribute to the transfer of the infection between humans.

Parameter	Description	Quasi-dimension
L	Bio-transition factor or rate of oviposition per reproducing vector. A measure of successful contribution into the aquatic stages.	AM^{-1}
ν_A	Rate of transition from aquatic to adult stage.	T^{-1}
ξ_v	Bio-transition factor to measure successful transition from aquatic to adult stage.	MA^{-1}
$\mu_{A,1}$	Natural death rate of aquatic stage organisms.	T^{-1}
$\mu_{A,2}$	Additional death rate at the aquatic stage due to limitation of aquatic resources.	$A^{-1}T^{1}$
ρ_k	Rate of flow of reproductive stage k susceptible resting vectors to the breeding site.	T^{-1}
$\rho_{k,j}$	Rate of flow of resting vectors at reproductive stage k that was first infected at reproductive stage j to the breeding site.	T^{-1}
a_k	Rate of flow of breeding site vectors at reproductive stage k to human habitat sites. This is weighted by the proportion of anthropophilic mosquitoes to zoophilic mosquitoes to give $b_k(H)$.	T^{-1}
r_h	Rate of recovery of infectious humans.	T^{-1}
δ_h	Rate of treatment of infectious humans.	T^{-1}
γ_h	Rate of loss of protection from treatment.	T^{-1}
λ_*	Natural birth rate. In the human population it has the subscript h, and in the vector population, it has the subscript v. In general λ_* is a density dependent function of the population size.	H (or M) T^{-1}
μ_*	Natural death rate. In the human population, it is has the subscript h while in the vector population the subscript is the label for the class of vector under consideration. For example, μ_{Sv_1} is the natural death rate for susceptible vectors of type v in their first stage of life. In general, μ_* could be a function of the given population size.	H (or M) T^{-1}
b_w	Human biting rate of the mosquitoes. The density of bites placed on humans by each questing mosquito per unit time.	$BM^{-1}T^{-1}$
p_{hw}	Infectivity of the humans to mosquitoes. It is the probability that a successful bite placed by a susceptible mosquito on an infectious human will transfer the infection to the mosquito.	1
p_{wh}	Infectivity of the mosquitoes to humans. This is the probability that a successful bite placed by an infectious mosquito on a susceptible human will transfer the infection to the human.	1
q_w	Probability of successfully acquiring a blood meal from a human.	1
θ_{s_k}	Fraction of susceptible reproducing vectors at reproductive stage k that eventually survive to re-enter the chain.	1
$\theta_{i_{k,j}}$	Fraction of stage k reproducing vectors that first picked up infection at stage j and that eventually survive to re-enter the chain.	1
α	Fraction of vectors that survive to enter the reproducing class after successfully harvesting blood from treated humans.	1

Table 3: Description of parameters and their quasi-dimension: H(Humans), M(Mosquitoes at adult stage), T(Time), B(Bites), A (Aquatic stage mosquitoes).

Transition schema	**Description**	**Rate and Outcome**
$S_{v_k} \rightarrow S_{w_k}$ (or $I_{v_{k,j}} \rightarrow I_{w_{k,j}}$).	Type V susceptible vector (or infectious vector at reproductive stage k that first picked up infection at stage j) is attracted to humans.	$b_k(H)$. Vector moves to human habitat to become a reproductive stage k questing vector.
$S_{u_k} \rightarrow S_{v_k}$ (or $I_{u_{k,j}} \rightarrow I_{v_{k+1,j}}$)	Type U susceptible vector (or infectious vector at reproductive stage k that first picked up infection at reproductive stage j) is attracted to breeding sites. $k \rightarrow k+1$.	ρ_k, $\rho_{k,j}$. Vector moves to breeding site to lay eggs as a breeding site vector at reproductive stage $k+1$.
$S_{w_k} + S_h \rightarrow S_{u_k} + S_h$	Type W susceptible vector in its k-th stage in life interacts to feed on a susceptible human.	$q_w\beta_k(S_{w_k}, S_H)$. Successful acquisition of a blood meal $\rightarrow$ reproducing vectors of type U; no new infections.
$S_{w_k} + I_h \rightarrow I_{u_{k,k}} + I_h$	Type W susceptible vector at reproductive stage k feeds on an infectious human. Transfer of infection may occur with probability p_{hw} to produce an infected k-stage vector of type U.	$p_{hw}q_w\beta_k(S_{w_k}, I_H)$. Successful acquisition of a blood meal $\rightarrow$ reproducing infectious vector of type U. New infections enter the system through human to mosquito transmission.
$S_{w_k} + T_h \rightarrow S_{w_k} + T_h$	Susceptible mosquito of type W in its $k-$th stage in life interacts to bite a treated human.	$q_w\beta_k(S_{w_k}, T_h)$. Successful acquisition of a blood. A fraction α survives to become susceptible reproducing vectors of type U; no new infections.
$I_{w_{k,j}} + S_h \rightarrow I_{u_{k,j}} + I_h$	Infectious vector of type W at reproductive stage k that was first infected with the malaria parasite at reproductive stage j interacts to bite a susceptible human.	$p_{wh}q_w\beta_k(I_{w_{k,}}, S_H)$. Successful acquisition of a blood meal $\rightarrow$ reproducing infectious vectors of type U and an infectious human. New infections enter the system through mosquito to human transmission.
$I_{w_{k,j}} + I_h \rightarrow I_{u_{k,j}} + I_h$	Infectious vector of type W at reproductive stage k that first became infected at reproductive stage j interacts to bite an infectious human.	$q_w\beta_k(I_{w_{k,j}}, I_H)$. Successful acquisition of a blood meal $\rightarrow$ reproducing infectious vectors of type U; no new infections.
$I_{w_{k,j}} + T_h \rightarrow I_{u_{k,j}} + T_h$	Infectious vector of type W at reproductive stage k that first became infected at reproductive stage j bites a treated human.	$q_w\beta_k(I_{w_{k,j}}, T_H)$. Successful acquisition of a blood. A fraction α survives to become susceptible reproducing vectors of type U; no new infections.

Table 4: Description of the different transitions and their outcomes. $b_k(H) = a_k\frac{H}{H+\kappa}$, and the exposure rate $\beta_m(X_m, Y_h) = b_w\frac{X_m Y_h}{N_h}$ where N_h is the total size of the human population, X_m is a fraction of the component of the vector population and Y_h is a component of the human population. Whenever there is a successful mosquito-human interactions, there is at least production of new mosquitoes.

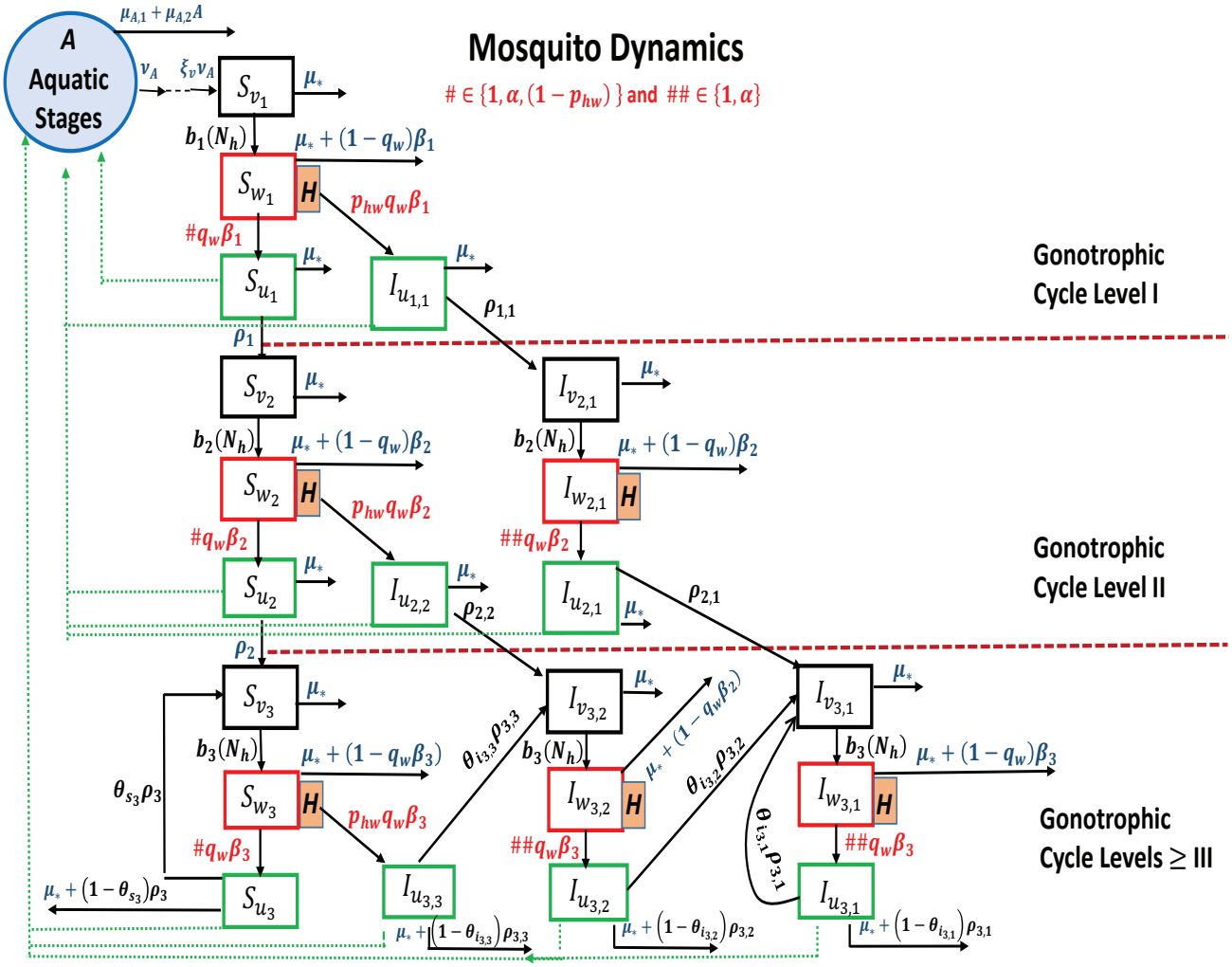

Figure 1: Figure showing the flow in the mosquito dynamics. The different gonotrophic cycle levels are clearly shown and each lower level feeds into the higher level. The points where human interactions with mosquitoes are possible are H-shaded, and the contributions to the aquatic stages are shown with the dotted lines leading to the circular block labelled aquatic stages. Only mosquitoes of type W can interact with humans and only mosquitoes that have successfully interacted with humans can change status to mosquitoes of type U and enter the next gonotrophic cycle. Mosquitoes in gonotrophic cycles greater than or equal to three are allowed to reenter the chain in the backward loop at the reduced rate with the proportion θ_{s_k} or $\theta_{i_{k,j}}$, depending on the disease status of the mosquito. Reentering infected mosquitoes are relabelled to indicate the number of gonotrophic cycles since infection so that the infective mosquitoes are always treated as if they were infected during the first cycle. We read this from this figure by observing that whenever a new infection enters the mosquito population through a successful infection of a susceptible mosquito, we must wait at least 2 gonotrophic cycles (or count six arrows from the point of first infection) before entering the class labelled $I_{w_{3,1}}$ through which the infection must pass to enter the human population. In this figure, $\#q$ (respectively, $\#\#q$) is the probability that type S_{w_k} mosquitoes, for $k = 1, 2, 3$ (respectively, type $I_{w_{k,j}}$ mosquitoes for $k, j = 1, 2, 3$), successfully acquire blood from a human, changing status to a corresponding type S_{u_i} (respectively, $I_{u_{k,j}}$) mosquito. For $\# = 1$, S_{w_k} successfully acquired the blood meal from a susceptible human; for $\# = \alpha$, it was acquired from a human treated with the modelled mosquitocidal drug, however, the mosquito survived the mosquitocidal effects of the drug; for $\# = 1 - p_{hw}$, it was acquired from an infectious human, however, the mosquito failed to pick-up the parasite from the infectious human with probability $1 - p_{hw}$. For $\#\#q$, when $\#\# = 1$, $I_{w_{k,j}}$ successfully acquired the blood meal from either a susceptible human or an infectious human, meanwhile when $\#\# = \alpha$, the successful meal was from a treated human, with the mosquito surviving the mosquitocidal effects of the drug.

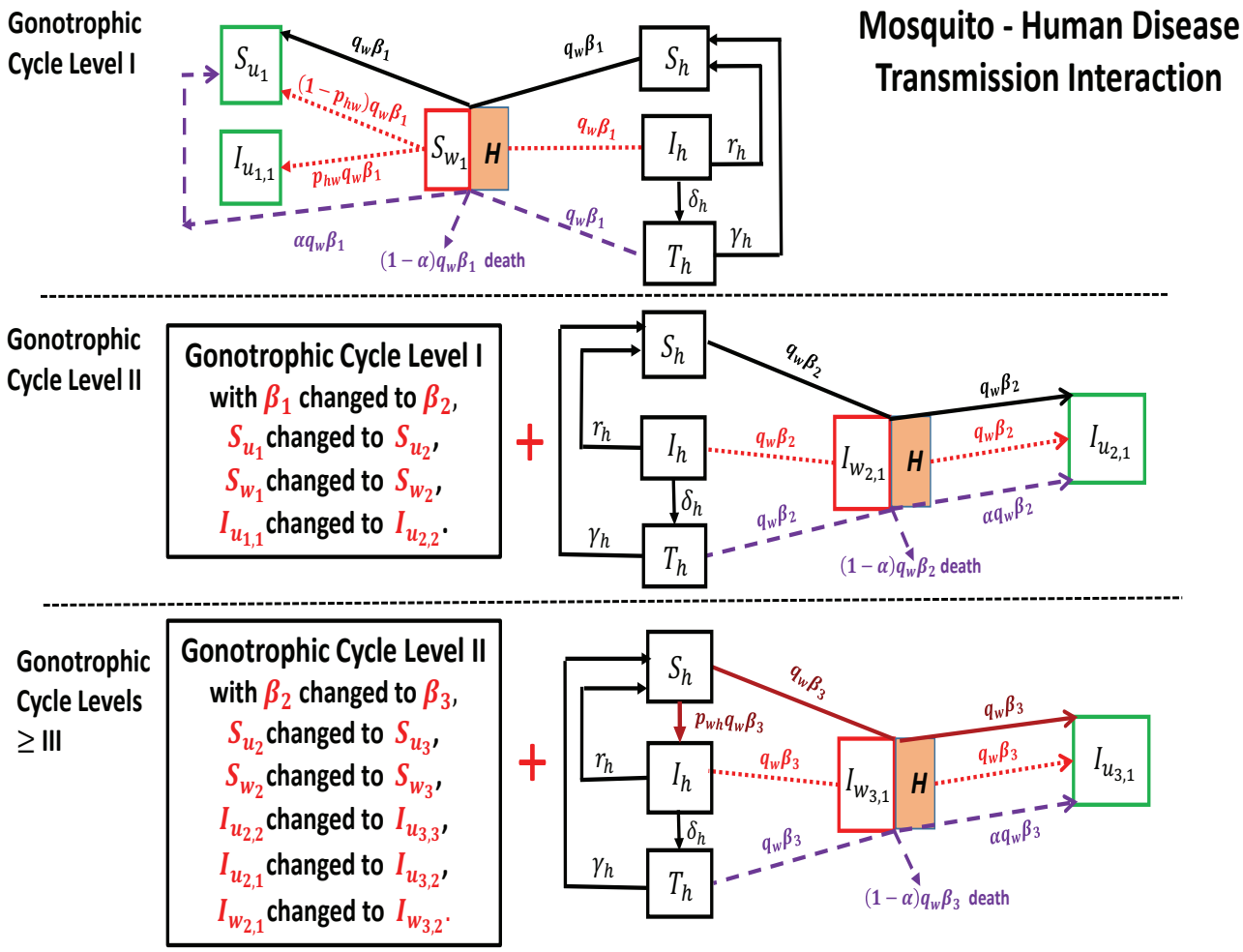

Figure 2: Figure showing the flow in the mosquito-human epidemiological model dynamics. The points where the mosquito interacts with humans are possible are indicated with the H-shaded block and the possible outcomes in the mosquito population and the flow of disease dynamics in the human populations are indicated at each gonotrophic cycle. At the gonotrophic cycles 1 and 2, no new infections are possible within the human population since the gonotrophic time period is shorter than the sporogonic within-vector parasite cycle [27, 26]. However, at gonotrophic cycles 3 or more, new infections are possible in the human population due to interactions between humans and infectious mosquitoes and, as a result, there is a flow depicting new infections from the susceptible to the infectious class in the human population. Demographic flows such as births and deaths are not shown in this figure, but it is understood that natural death and births occur in each compartment, as explained in the text.

2.2 The flow and exposure rates

Here we briefly describe how we model the different flow and contact rates within and between the mosquito and human populations.

(i) *The flow rate from the breeding site to human habitat:* We start with the premise that various adult mosquitoes have different blood preferences in the sense that some mosquitoes prefer non-human, or animal, blood over human blood (zoophilic mosquitoes), while others prefer human blood meals over the animal ones (anthropophilic mosquitoes). However, the decision to target a particular type of blood depends on a number of factors including, say, the proximity to the blood source, and others, which we do not consider here. To proceed, we introduce parameters that allow for quantifying the preferences of female *Anopheles sp* mosquitoes that seek, or quest, for the vertebrate blood meals prior to the initiation of a gonotrophic cycle. We define two blood preference factors, or zoophilic indices, B_h (the number of mosquitoes per human that prefer human blood) and B_v (the number of mosquitoes per animal, or non-human host, that prefer animal or non-human blood). So, if the density of humans and non-humans present are, respectively, H and $\tilde{V}$, then from the just assumed definition of B_h and B_v, we have that B_hH and $B_v\tilde{V}$ mosquitoes get attracted to humans and non-humans, respectively[3]. Of the $B_hH + B_v\tilde{V}$ mosquitoes that leave the breeding site to become questing vectors, a proportion $\frac{B_hH}{B_hH+B_v\tilde{V}} = \frac{H}{H+\kappa}$ quest in the human population, while the remainder $1 - \frac{H}{H+\kappa}$ will quest in the animal population. We note that if either $B_h = 0$ or $H = 0$, then all female adult mosquitoes will quest for blood within the animal population and we have a situation, where there are no interactions with humans. Though in the mosquito only model we could still model the mosquito population dynamics from an animal-mosquito perspective, this case is not very interesting from the human-malaria-mosquito modelling perspective and so we do not pursue this angle here. On the other hand, if either $B_v = 0$ or $\tilde{V} = 0$, then all female adult mosquitoes quest only for human blood and we have solely anthropophilic mosquitoes to deal with. In what follows, we shall assume that $B_h > 0$, $B_v > 0$, $H > 0$ and $\tilde{V} \geq 0$ to capture the possibility of having both zoophilic and anthropophilic mosquitoes. We then interpret $\kappa = \frac{B_v}{B_h}\tilde{V}$ as a parameter that measures the presence of alternative blood source for mosquitoes. Here, as in [20], it is reasonable to assume that each fertilized vector at each reproductive stage will have its blood preference, but for simplicity, we have assumed that the blood preference will be the same for all mosquitoes of the same species, and account only for anthropophilic mosquitoes. Therefore the flow rate to humans by the breeding site mosquitoes is $b_k(H) = a_k\frac{H}{H+\kappa}$, and a_k is as defined in Table 3.

(ii) *The rate of exposure of humans to mosquitoes:* The exposure rate of mosquitoes at the reproductive stage k to humans $\beta_k(\star, \star)$ is modelled using a restricted form of homogeneous mixing based on the idea that the mosquito has a human biting habit. We start by defining the human biting rate b_w of questing mosquitoes at reproductive stage k as the number of bites placed by each mosquito on humans per unit time so that if there are N_{w_k} questing mosquitoes at the reproductive stage k and N_h humans, we have a total of $b_w\frac{N_{w_k}}{N_h}$ bites per human per unit time. If we have a total of S_h susceptible humans in the population, this leads to $b_w\frac{N_{w_k}}{N_h}S_h$ bites placed on susceptible humans and the proportion $\frac{I_{w_k}}{N_{w_k}}b_w\frac{N_{w_k}}{N_h}S_h = b_w\frac{I_{w_k}S_h}{N_h}$ is a measure of the exposure of susceptible humans to potentially infectious mosquitoes at the reproductive stage k. Therefore, the exposure rate between susceptible humans and infectious mosquitoes at the reproductive stage k is $\beta_k(I_{w_k}, S_h) = b_w\frac{I_{w_k}S_h}{N_h}$. In general, the exposure rate between any fraction of the human population $\frac{Y_h}{N_h}$, where the total human population is N_h, and the questing mosquitoes of density X_{w_k} at the reproductive stage k, is $\beta_k(X_{w_k}, Y_h) = b_w\frac{X_{w_k}Y_h}{N_h}$. There are two levels of having a successful exposure and/or effective contact: at the first level, the mosquito

[3]We do not insist on a conservation of the total mosquito population from the breeding site in this flow argument

can successfully take a blood meal with probability q_w and then live to reproduce, or this contact fails with probability $1 - q_w$ and the mosquito is assumed killed, while at the second level the successful feeding can lead to the transfer of the infection, either from human to mosquito with probability p_{hw}, or from mosquito to human with probability p_{wh}. It is then understood that where the transfer of infection was possible but did not take place, the chance is $1 - p_{hw}$ or $1 - p_{wh}$, as the case may be.

(iii) *The rate of recruitment into the aquatic stages:* The rate of recruitment into the aquatic stages will eventually determine the rate of adult mosquito eclosion (emergence of new adult mosquitoes). We model this by assuming that the female reproducing mosquitoes have a birth rate, that is, the density of offspring produced by one reproducing mosquito per unit time, and define a real valued function $\lambda_v : [0, \infty) \to \mathbb{R}$ whose output is a measure of the birth rate per reproducing vector of type $U \in [0, \infty)$ per unit time. We argue as follows: If each mosquito u of type U eventually produces $\lambda_v(u)$ aquatic organisms per unit time, then, in the presence of u vectors of type U, $\lambda_v(u)$ is the density dependent (only on mosquitoes of type U) per capita birth rate. Therefore, u vectors (of type U) will lead to $u\lambda_v(u)$ new aquatic type vectors per unit time. The function λ_v must have some desired properties. When we consider all sources of births in the mosquito population, the rate of contribution into the aquatic stages, for a given recruitment function of our choice, is then an expression of the form

$$\text{Rate of recruitment into aquatic stages} = \sum_k \rho_k \lambda_v(S_{u_k}) S_{u_k} + \sum_{(k,j)} \rho_{k,j} \lambda_v(I_{u_{k,j}}) I_{u_{k,j}}, \tag{2}$$

if it is assumed that each of these mosquitoes live separate and independent life style. On the other hand we can assume that λ_v is a function of the total reproducing mosquito population, $N_u = \sum_k S_{u_k} + \sum_{(k,j)} I_{u_{k,j}}$, and hence we have an expression of the form

$$\text{Rate of recruitment into aquatic stages} = \sum_k \rho_k \lambda_v(N_u) S_{u_k} + \sum_{(k,j)} \rho_{k,j} \lambda_v(N_u) I_{u_{k,j}}, \tag{3}$$

where there is a strong dependence on the total size of the reproducing mosquitoes. The actual existence of mosquitoes to continue to the next generations depends on the fact that the reproducing mosquitoes must find suitable breeding sites to lay their eggs. It may be that a mosquito will choose a particular breeding site over another depending on several factors that could include the absence of predators, presence of other larvae at that breeding site and even the proximity from the resting place. Thus, the relationship between the reproducing mosquitoes and the newly emerging adults cannot simply be assumed to be a linear response. This justifies our assumption that the adult mosquito eclosion rate is density dependent. Some sources, for example [5], use a delay modelling argument (after assuming the existence of a birth rate function satisfying some biologically meaningful properties), to derive a formula for the rate of emergence of new adults in a delayed differential equation framework. Others, see for example [1, 12], approach the problem of modelling the rate of new adult mosquito eclosion by including at least one (or more) state variable to represent the aquatic stages of the mosquito and then evoke the idea that the limitation of the carrying capacity of the breeding site will introduce a competition in the aquatic stages of the mosquito population's eggs or larvae as a source of nonlinearity and density dependence on the dynamics. Here, we simply assume that the net effect of the activities of the reproducing mosquitoes contribute to the density of adult mosquito vectors in the next generation through the birth term at a rate dependent on the birth rate function $\lambda_v : [0, \infty) \to \mathbb{R}$, to write down the expressions given by (2) and (3). The function λ_v, so described and fixed in general, is assumed to depend in a nonlinear way on the size of the reproducing mosquitoes, the mosquitoes that eventually survive the questing processes and then are in a position to lay eggs. Therefore the form of λ_v should therefore not be interpreted as modelling the competition between the adult mosquitoes.

(iv) *The flow rate of resting vectors to the breeding site.* Vectors of type U return to the breeding site at the rate ρ_*, where the subscript is linked to the variable whose flow rate is described. Since each mosquito only can be in one of two disease states (susceptible or infected), we distinguish flow rates with either a single subscript notation for susceptible vectors or a double subscript notation for infected vectors. For example, we write ρ_k to represent the rate of flow of susceptible vectors of type U at the reproductive stage k, S_{u_k}, to the breeding site and $\rho_{k,j}$ to represent the flow rate of infected vectors of type U at the reproductive stage k that were first infected at the reproductive stage j, $I_{u_{k,j}}$, to the breeding site. We conjecture that that older vectors, perhaps because of experience and memory effects [13], may have a faster flow rate to the breeding site than younger ones that may need more time to search and locate it. However, in a simplistic calculation, we can assume the flow rates to the breeding site to be the same for all ages.

(v) All other flow rates from one compartment to the other are simply assumed to be inversely proportional to residence time within the given compartment.

2.3 The model equations

We now write down the equations for each state variable, based on the description given above. The flow diagrams in Figures 1 and 2 show the links between the different compartments. By counting the different state variables, following the compartmentalization shown in Figure 1, we can work out the number of equations to formulate. In all we have: (i) The susceptible mosquito variables $(S_{v_k}, S_{w_k}, S_{u_k})$, $k = 1, 2, 3$, leading to 9 equations in total, (ii) the infected mosquito variables $(I_{v_{k,j}}, I_{w_{k,j}}, I_{u_{k,j}})$, $k, j \in \{1, 2, 3\}$–12 equations, the human variables (S_h, I_h, T_h)- 3 equations. In total, we have 24 equations. Thus, the equations governing the rate of change of the different state variables, including one aquatic stage, can be written down as we now present below.

For the dynamics within the mosquito population we have the 21 equations

$$
\begin{aligned}
\frac{dA}{dt} &= \text{Rate of recruitment into aquatic stages} - (\nu_A + \mu_{A,1} + \mu_{A,2}A)A,\\
\frac{dS_{v_1}}{dt} &= \xi_v \nu_A A - (\mu_{Sv_1} + b_1(N_h))S_{v_1},\\
\frac{dS_{w_1}}{dt} &= b_1(N_h)S_{v_1} - (\beta_1(S_{w_1}, S_h) + \beta_1(S_{w_1}, I_h) + \beta_1(S_{w_1}, T_h)) - \mu_{Sw_1}S_{w_1},\\
\frac{dS_{u_1}}{dt} &= q_w\beta_1(S_{w_1}, S_h) + (1 - p_{hw})q_w\beta_1(S_{w_1}, I_h) + \alpha q_w\beta_1(S_{w_1}, T_h) - (\rho_1 + \mu_{Su_1})S_{u_1},\\
\frac{dI_{u_{1,1}}}{dt} &= p_{hw}q_w\beta_1(S_{w_1}, I_h) - (\rho_{1,1} + \mu_{Iu_{1,1}})I_{u_{1,1}},\\
\frac{dS_{v_2}}{dt} &= \rho_1 S_{u_1} - (b_2(N_h) + \mu_{Sv_2})S_{v_2},\\
\frac{dI_{v_{2,1}}}{dt} &= \rho_{1,1}I_{u_{1,1}} - (b_2(N_h) + \mu_{Iv_{2,1}})I_{v_{2,1}},\\
\frac{dS_{w_2}}{dt} &= b_2(N_h)S_{v_2} - (\beta_2(S_{w_2}, S_h) + \beta_2(S_{w_2}, I_h) + \beta_2(S_{w_2}, T_h)) - \mu_{Sw_2}S_{w_2},\\
\frac{dI_{w_{2,1}}}{dt} &= b_2(N_h)I_{v_{2,1}} - \big(\beta_2(I_{w_{2,1}}, S_h) + \beta_2(I_{w_{2,1}}, I_h) + \beta_2(I_{w_{2,1}}, T_h)\big) - \mu_{Iw_{2,1}}I_{w_{2,1}},\\
\frac{dS_{u_2}}{dt} &= q_w\beta_2(S_{w_2}, S_h) + (1 - p_{hw})q_w\beta_2(S_{w_2}, I_h) + \alpha q_w\beta_2(S_{w_2}, T_h) - (\rho_2 + \mu_{Su_2})S_{u_2},\\
\frac{dI_{u_{2,2}}}{dt} &= p_{hw}q_w\beta_2(S_{w_2}, I_h) - (\rho_{2,2} + \mu_{Iu_{2,2}})I_{u_{2,2}},\\
\frac{dI_{u_{2,1}}}{dt} &= q_w\beta_2(I_{w_{2,1}}, S_h) + q_w\beta_2(I_{w_{2,1}}, I_h) + \alpha q_w\beta_2(I_{w_{2,1}}, T_h) - (\rho_{2,1} + \mu_{Iu_{2,1}})I_{u_{2,1}},\\
\frac{dS_{v_3}}{dt} &= \rho_2 S_{u_2} + \theta_{s_3}\rho_3 S_{u_3} - (b_3(N_h) + \mu_{Sv_3})S_{v_3},
\end{aligned}
$$

$$
\begin{aligned}
\frac{dI_{v_{3,2}}}{dt} &= \rho_{2,2}I_{u_{2,2}} + \theta_{i_{3,3}}\rho_{3,3}I_{u_{3,3}} - (b_3(N_h) + \mu_{Iv_{3,2}})I_{v_{3,2}}, \\
\frac{dI_{v_{3,1}}}{dt} &= \rho_{2,1}I_{u_{2,1}} + \theta_{i_{3,2}}\rho_{3,2}I_{u_{3,2}} + \theta_{i_{3,1}}\rho_{3,1}I_{u_{3,1}} - (b_3(N_h) + \mu_{Iv_{3,1}})I_{v_{3,1}}, \\
\frac{dS_{w_3}}{dt} &= b_3(N_h)S_{v_3} - (\beta_3(S_{w_3}, S_h) + \beta_3(S_{w_3}, I_h) + \beta_3(S_{w_3}, T_h)) - \mu_{Sw_3}S_{w_3}, \\
\frac{dI_{w_{3,2}}}{dt} &= b_3(N_h)I_{v_{3,2}} - \big(\beta_3(I_{w_{3,2}}, S_h) + \beta_3(I_{w_{3,2}}, I_h) + \beta_3(I_{w_{3,2}}, T_h)\big) - \mu_{Iw_{3,2}}I_{w_{3,2}}, \\
\frac{dI_{w_{3,1}}}{dt} &= b_3(N_h)I_{v_{3,1}} - \big(\beta_3(I_{w_{3,1}}, S_h) + \beta_3(I_{w_{3,1}}, I_h) + \beta_3(I_{w_{3,1}}, T_h)\big) - \mu_{Iw_{3,1}}I_{w_{3,1}}, \\
\frac{dS_{u_3}}{dt} &= q_w\beta_3(S_{w_3}, S_h) + (1 - p_{hw})q_w\beta_3(S_{w_3}, I_h) + \alpha q_w\beta_3(S_{w_3}, T_h) - (\rho_3 + \mu_{Su_3})S_{u_3}, \\
\frac{dI_{u_{3,3}}}{dt} &= p_{hw}q_w\beta_3(S_{w_3}, I_h) - (\rho_{3,3} + \mu_{Iu_{3,3}})I_{u_{3,3}}, \\
\frac{dI_{u_{3,2}}}{dt} &= q_w\beta_3(I_{w_{3,2}}, S_h) + q_w\beta_3(I_{w_{3,2}}, I_h) + \alpha q_w\beta_3(I_{w_{3,2}}, T_h) - (\rho_{3,2} + \mu_{Iu_{3,2}})I_{u_{3,2}}, \\
\frac{dI_{u_{3,1}}}{dt} &= q_w\beta_3(I_{w_{3,1}}, S_h) + q_w\beta_3(I_{w_{3,1}}, I_h) + \alpha q_w\beta_3(I_{w_{3,1}}, T_h) - (\rho_{3,1} + \mu_{Iu_{3,1}})I_{u_{3,1}}.
\end{aligned} \tag{4}
$$

For the dynamics within the human population we have three equations

$$
\begin{aligned}
\frac{dS_h}{dt} &= \lambda_h N_h + r_h I_h + \gamma_h T_h - p_{wh}q_w\beta_3(I_{w_{3,1}}, S_h) - \mu_h S_h, \\
\frac{dI_h}{dt} &= p_{wh}q_w\beta_3(I_{w_{3,1}}, S_h) - (r_h + \delta_h + \mu_h)I_h, \\
\frac{dT_h}{dt} &= \delta_h I_h - (\gamma_h + \mu_h)T_h.
\end{aligned} \tag{5}
$$

The novelty in the current modelling exercise lies in the fact that, in the absence of infection, $I_h = I_{u_{*,*}} = I_{w_{*,*}} = T_h = 0$, we have the mosquito population only dynamic model. In this case, the disease free system is a three-stage reproductive system for the mosquito populations with one aquatic stage A, given by the system of equations:

$$
\begin{aligned}
\frac{dA}{dt} &= \text{Rate of recruitment into aquatic stages} - (\nu_A + \mu_{A,1} + \mu_{A,2}A)A, \\
\frac{dS_{v_1}}{dt} &= \xi_v\nu_A A - (\mu_{Sv_1} + b_1(N_h))S_{v_1}, \\
\frac{dS_{w_1}}{dt} &= b_1(N_h)S_{v_1} - \beta_1(S_{w_1}, S_h) - \mu_{Sw_1}S_{w_1}, \\
\frac{dS_{u_1}}{dt} &= q_w\beta_1(S_{w_1}, S_h) - (\rho_1 + \mu_{Su_1})S_{u_1}, \\
\frac{dS_{v_2}}{dt} &= \rho_1 S_{u_1} - (b_2(N_h) + \mu_{Sv_2})S_{v_2}, \\
\frac{dS_{w_2}}{dt} &= b_2(N_h)S_{v_2} - \beta_2(S_{w_2}, S_h) - \mu_{Sw_2}S_{w_2}, \\
\frac{dS_{u_2}}{dt} &= q_w\beta_2(S_{w_2}, S_h) - (\rho_2 + \mu_{Su_2})S_{u_2}, \\
\frac{dS_{v_3}}{dt} &= \rho_2 S_{u_2} + \theta_{s_3}\rho_3 S_{u_3} - (b_3(N_h) + \mu_{Sv_3})S_{v_3}, \\
\frac{dS_{w_3}}{dt} &= b_3(N_h)S_{v_3} - \beta_3(S_{w_3}, S_h) - \mu_{Sw_3}S_{w_3}, \\
\frac{dS_{u_3}}{dt} &= q_w\beta_3(S_{w_3}, S_h) - (\rho_3 + \mu_{Su_3})S_{u_3},
\end{aligned} \tag{6}
$$

with the associated equation

$$
\frac{dS_h}{dt} = (\lambda_h - \mu_h)S_h. \tag{7}
$$

Given that in the absence of infection $N_h = S_h$, this is also the equation for the total human population. Since the interaction between the mosquitoes and the humans does not have an effect on the human population except in the presence of the disease, equation (7) shows that if $\lambda_h > \mu_h$ we have growth in the human population and decay when $\lambda_h < \mu_h$. For simplicity, we can assume that $\lambda_h = \mu_h$ leading to a constant human population model. The disease free model is therefore capable of displaying more complex behaviour from the point of view of the mosquito than is the case with conventional malaria models.

For the total mosquito population under consideration, we separate the aquatic stages from the adult stages and denote the total sum of the active adult mosquitoes of type U, V and W, respectively, by N_u, N_v and N_w, as shown in (1), and from linearity we have,

$$\begin{aligned}
\frac{dA}{dt} &= \text{Rate of recruitment into aquatic stages} - (\nu_A + \mu_{A,1} + \mu_{A,2}A)A, \\
\frac{dN_v}{dt} &= \sum_{k=1}^{3} \frac{dS_{v_k}}{dt} + \sum_{j=1}^{2} \sum_{k=j+1}^{3} \left(\frac{dI_{v_{k,j}}}{dt} \right), \\
\frac{dN_w}{dt} &= \sum_{k=1}^{3} \frac{dS_{w_k}}{dt} + \sum_{j=1}^{2} \sum_{k=j+1}^{3} \left(\frac{dI_{w_{k,j}}}{dt} \right), \\
\frac{dN_u}{dt} &= \sum_{k=1}^{3} \frac{dS_{u_k}}{dt} + \sum_{j=1}^{3} \sum_{k=j}^{3} \frac{dI_{u_{k,j}}}{dt},
\end{aligned} \tag{8}$$

so that adding up all the relevant equations from (4) we have the system

$$\frac{dA}{dt} = \text{Rate of recruitment into aquatic stages} - (\nu_A + \mu_{A,1} + \mu_{A,2}A)A, \tag{9}$$

$$\frac{dN_m}{dt} = \xi_v \nu_A A - b_w(1 - q_w)N_w - (1 - \alpha)\frac{T_h N_w}{N_h} - \text{natural deaths}, \tag{10}$$

where

$$\begin{aligned}
\text{natural deaths} &= \sum_{k=1}^{3} (\mu_{Sv_k} S_{v_k} + \mu_{Su_k} S_{u_k} + \mu_{Sw_k} S_{w_k}) + \sum_{j=1}^{2} \sum_{k=j+1}^{3} \left(\mu_{Iv_{k,j}} I_{v_{k,j}} + \mu_{Iw_{k,j}} I_{w_{k,j}} \right) \\
&\quad + \sum_{j=1}^{3} \sum_{k=j}^{3} \left(\mu_{Iu_{k,j}} I_{u_{k,j}}. \right)
\end{aligned} \tag{11}$$

For simplicity, we assume a constant rate of oviposition, so that the function $\lambda_v : [0, \infty) \to \mathbb{R}$ is the constant function, $\lambda_v(x) = L,\ \forall x \in \mathbb{R}^+$, in which case models (2) and (3) will lead to the same rate of oviposition given by

$$\text{Rate of recruitment into aquatic stages} = L \left(\sum_k \rho_k S_{u_k} + \sum_{(k,j)} \rho_{k,j} I_{u_{k,j}} \right). \tag{12}$$

Then, the equations governing the total population take the form

$$\frac{dA}{dt} = L \left(\sum_k \rho_k S_{u_k} + \sum_{j=1}^{3} \sum_{k=j}^{3} \rho_{k,j} I_{u_{k,j}} \right) - (\nu_A + \mu_{A,1} + \mu_{A,2}A)A, \tag{13}$$

$$\frac{dN_m}{dt} = \xi_v \nu_A A - b_w(1 - q_w)N_w - (1 - \alpha)\frac{T_h N_w}{N_h} - \text{natural deaths}, \tag{14}$$

where the expression for natural deaths is given by (11). Equation (13) shows that each reproducing vector supplies the aquatic stages at the constant rate L and that the rate of removal of organisms

from the aquatic stage comprises the transitions into the adult stage at the rate ν_A, the deaths from natural causes at the rate $\mu_{A,1}$ and additional deaths due to overcrowding at occur at the rate $\mu_{A,2}A$. Equation (14) shows that the rate of increases of the total adult population is determined by the quantity of new adults emerging from the aquatic stages at the rate $\xi_v\nu_A$ and the deaths or removals due to three reasons (1) deaths due to natural causes, (2) deaths due to unsuccessful interaction with the human population with probability $(1-q_w)$ and (3) deaths with probability $(1-\alpha)$ due to the mosquitocidal effect of the drugs used in the treatment of infected persons, [23]. Equation (14) clearly shows the dependence of the size of the total population on the size of the questing mosquito population. The natural death for mosquitoes at each reproductive stage is assumed to be inversely proportional to their life span, which in turn is determined by how much time is left for the mosquito to live as captured by the gonotrophic cycle counter at that time. Now, since all the death rates are constant, the total death rate for the adult mosquito population is μN_m for some constant μ. A proposal on how to calculate these residence times, and hence the natural death rates was given in [20]. Essentially it is assumed that the youngest vectors are the susceptible mosquitoes of type V just emerging from the aquatic stage, represented here by S_{v_1}, while the oldest vectors are the reproducing vectors of type U at the last reproductive stage. We use the following argument to derive a system of equations whose solution will contain the solution of the system (13)-(14). From the continuity and positivity of the variables and parameters, there exist a positive constant c such that $\left(\sum_k \rho_k S_{u_k} + \sum_{j=1}^{3}\sum_{k=j}^{3}\rho_{k,j}I_{u_{k,j}}\right) \leq cN_m$ since each $S_* \leq N_m$. So, ignoring all the other sources of death for the adults mosquito population, we can argue that from continuity and positivity, there exist $\mu > 0$ such that the sum over all natural death rates is bounded above μN_m. So, we can use the equivalent system

$$\left.\begin{array}{rcl} \frac{dA}{dt} & \leq & LcN_m - (\nu_A + \mu_{A,1} + \mu_{A,2}A)A, \\ \frac{dN_m}{dt} & \leq & \xi_v\nu_A A - \mu N_m, \end{array}\right\} \tag{15}$$

from which using standard results on differential inequalities and the solutions of the corresponding system, we can establish boundedness of solutions (13)-(14). System (15), with equality is monotone competitive and clearly has bounded solutions. In fact, we can easily show that there exists a parameter $\tilde{\mathcal{N}} = \frac{Lc\xi_v\nu_A}{\mu(\nu_A+\mu A,1)}$ such that for $\tilde{\mathcal{N}} < 1$ the only steady state of the system is the trivial steady state $(N_m, A) = (0, 0)$ which is globally and asymptotically stable, while for $\tilde{\mathcal{N}} > 1$, there is a unique non-trivial steady state $(N_m, A) = (N_m^*, A^*)$ which is globally also globally and asymptotically stable. That is, a transcritical bifurcation occurs at $\tilde{\mathcal{N}} = 1$ where a stable non-trivial steady state solution emerges as the trivial steady state solution looses stability as $\tilde{N}$ increases through $\tilde{N} = 1$. So the solutions of the (15) always exist and are bounded. And so by extension, the solutions of the full system are bounded.

Now, using the formula for β_k, we have the epidemiological system

$$\frac{dA}{dt} = L\left(\sum_k \rho_k S_{u_k} + \sum_{(k,j)} \rho_{k,j} I_{u_{k,j}}\right) - (\nu_A + \mu_{A,1} + \mu_{A,2}A)A, \tag{16}$$

$$\frac{dS_{v_1}}{dt} = \xi_v\nu_A A - (\mu_{Sv_1} + b_1(N_h))S_{v_1}, \tag{17}$$

$$\frac{dS_{w_1}}{dt} = b_1(N_h)S_{v_1} - (b_w + \mu_{Sw_1})S_{w_1}, \tag{18}$$

$$\frac{dS_{u_1}}{dt} = q_w b_w \left(\frac{S_h}{N_h} + (1-p_{hw})\frac{I_h}{N_h} + \alpha\frac{T_h}{N_h}\right) S_{w_1} - (\rho_1 + \mu_{Su_1})S_{u_1}, \tag{19}$$

$$\frac{dI_{u_{1,1}}}{dt} = p_{hw}q_w b_w \frac{I_h}{N_h} S_{w_1} - (\rho_{1,1} + \mu_{Iu_{1,1}})I_{u_{1,1}}, \tag{20}$$

$$\frac{dS_{v_2}}{dt} = \rho_1 S_{u_1} - (b_2(N_h) + \mu_{Sv_2})S_{v_2}, \tag{21}$$

$$\frac{dI_{v_{2,1}}}{dt} = \rho_{1,1}I_{u_{1,1}} - (b_2(N_h) + \mu_{Iv_{2,1}})I_{v_{2,1}}, \tag{22}$$

$$\frac{dS_{w_2}}{dt} = b_2(N_h)S_{v_2} - (b_w + \mu_{Sw_2})\,S_{w_2}, \tag{23}$$

$$\frac{dI_{w_{2,1}}}{dt} = b_2(N_h)I_{v_{2,1}} - \left(b_w + \mu_{Iw_{2,1}}\right) I_{w_{2,1}}, \tag{24}$$

$$\frac{dS_{u_2}}{dt} = q_w b_w \left(\frac{S_h}{N_h} + (1-p_{hw})\frac{I_h}{N_h} + \alpha\frac{T_h}{N_h}\right) S_{w_2} - (\rho_2 + \mu_{Su_2})S_{u_2}, \tag{25}$$

$$\frac{dI_{u_{2,2}}}{dt} = p_{hw}q_w b_w \frac{I_h}{N_h} S_{w_2} - (\rho_{2,2} + \mu_{Iu_{2,2}})I_{u_{2,2}}, \tag{26}$$

$$\frac{dI_{u_{2,1}}}{dt} = q_w b_w \left(\frac{S_h}{N_h} + \frac{I_h}{N_h} + \alpha\frac{T_h}{N_h}\right) I_{w_{2,1}} - (\rho_{2,1} + \mu_{Iu_{2,1}})I_{u_{2,1}}, \tag{27}$$

$$\frac{dS_{v_3}}{dt} = \rho_2 S_{u_2} + \theta_{s_3}\rho_3 S_{u_3} - (b_3(N_h) + \mu_{Sv_3})S_{v_3}, \tag{28}$$

$$\frac{dI_{v_{3,2}}}{dt} = \rho_{2,2}I_{u_{2,2}} + \theta_{i_{3,3}}\rho_{3,3}I_{u_{3,3}} - (b_3(N_h) + \mu_{Iv_{3,2}})I_{v_{3,2}}, \tag{29}$$

$$\frac{dI_{v_{3,1}}}{dt} = \rho_{2,1}I_{u_{2,1}} + \theta_{i_{3,3}}\rho_{3,2}I_{u_{3,2}} + \theta_{i_{3,1}}\rho_{3,1}I_{u_{3,1}} - (b_3(N_h) + \mu_{Iv_{3,1}})I_{v_{3,1}}, \tag{30}$$

$$\frac{dS_{w_3}}{dt} = b_3(N_h)S_{v_3} - (b_w + \mu_{Sw_3})\,S_{w_3}, \tag{31}$$

$$\frac{dI_{w_{3,2}}}{dt} = b_3(N_h)I_{v_{3,2}} - \left(b_w + \mu_{Iw_{3,2}}\right) I_{w_{3,2}}, \tag{32}$$

$$\frac{dI_{w_{3,1}}}{dt} = b_3(N_h)I_{v_{3,1}} - \left(b_w + \mu_{Iw_{3,1}}\right) I_{w_{3,1}}, \tag{33}$$

$$\frac{dS_{u_3}}{dt} = q_w b_w \left(\frac{S_h}{N_h} + (1-p_{hw})\frac{I_h}{N_h} + \alpha\frac{T_h}{N_h}\right) S_{w_3} - (\rho_3 + \mu_{Su_3})S_{u_3}, \tag{34}$$

$$\frac{dI_{u_{3,3}}}{dt} = p_{hw}q_w b_w \frac{I_h}{N_h} S_{w_3} - (\rho_{3,3} + \mu_{Iu_{3,3}})I_{u_{3,3}}, \tag{35}$$

$$\frac{dI_{u_{3,2}}}{dt} = q_w b_w \left(\frac{S_h}{N_h} + \frac{I_h}{N_h} + \alpha\frac{T_h}{N_h}\right) I_{w_{3,2}} - (\rho_{3,2} + \mu_{Iu_{3,2}})I_{u_{3,2}}, \tag{36}$$

$$\frac{dI_{u_{3,1}}}{dt} = q_w b_w \left(\frac{S_h}{N_h} + \frac{I_h}{N_h} + \alpha\frac{T_h}{N_h}\right) I_{w_{3,1}} - (\rho_{3,1} + \mu_{Iu_{3,1}})I_{u_{3,1}}, \tag{37}$$

$$\frac{dS_h}{dt} = \lambda_h N_h + r_h I_h + \gamma_h T_h - p_{wh}q_w b_w \frac{S_h}{N_h} I_{w_{3,1}} - \mu_h S_h, \tag{38}$$

$$\frac{dI_h}{dt} = p_{wh}q_w b_w \frac{S_h}{N_h} I_{w_{3,1}} - (r_h + \delta_h + \mu_h)I_h, \tag{39}$$

$$\frac{dT_h}{dt} = \delta_h I_h - (\gamma_h + \mu_h)T_h. \tag{40}$$

Simplifications: If we set $\lambda_h = \mu_h$, then N_h is constant and one of the equations for the human compartments becomes redundant. Thus we can work only with two equations since then we can determine the third variable from $S_h + I_h + T_h = N_h = N_h(0)$, a constant.

2.4 Scaling and non-dimensionalisation

We scale the system by setting, for $k, j \in \{1, 2, 3\}$,

$$\tau = \frac{t}{T^0},\ s_{u_k} = \frac{S_{U_k}}{S^0_{U_k}},\ s_{w_k} = \frac{S_{W_k}}{S^0_{W_k}},\ s_{v_k} = \frac{S_{V_k}}{S^0_{V_k}},\ i_{u_{k,j}} = \frac{I_{U_{k,j}}}{I^0_{U_{k,j}}},\ i_{v_{k,j}} = \frac{I_{V_{k,j}}}{I^0_{V_{k,j}}}, \tag{41}$$

$$i_{w_{k,j}} = \frac{I_{W_{k,j}}}{I^0_{W_{k,j}}},\ a = \frac{A}{A^0},\ s_h = \frac{S_h}{N_h},\quad i_h = \frac{I_h}{N_h},\ t_h = \frac{T_h}{N_h}, \tag{42}$$

where the terms with zero superscript are reference variables for each of terms in the system. Given that we do not have a clear idea on the actual bounds for the sizes of each of the variables for the vector equation at each reproductive stage, we select these representative variables so that we have a system with a tractable number of parameters as follows:

$$A^0 = \frac{\nu_A+\mu_{A,1}}{\mu_{A,2}},\ S^0_{v_1}=\frac{\xi_v\nu_A A^0}{\mu_{Sv_1}+b_1(N_h)},\ S^0_{w_1}=\frac{b_1(N_h)S^0_{v_1}}{b_w+\mu_{Sw_1}},\ S^0_{u_1}=\frac{q_w b_w S^0_{w_1}}{\rho_1+\mu_{Su_1}}, \tag{43}$$

$$I^0_{u_{1,1}} = \frac{p_{hw}q_w b_w S^0_{w_1}}{\rho_{1,1}+\mu_{Iu_{1,1}}},\ S^0_{v_2}=\frac{\rho_1 S^0_{u_1}}{\mu_{Sv_2}+b_2(N_h)},\ I^0_{v_{2,1}}=\frac{\rho_{1,1}I^0_{u_{1,1}}}{b_2(N_h)+\mu_{Iv_{2,1}}}, \tag{44}$$

$$S^0_{w_2} = \frac{b_2(N_h)S^0_{v_2}}{b_w+\mu_{Sw_2}},\ I^0_{w_{2,1}}=\frac{b_2(N_h)I^0_{v_{2,1}}}{b_w+\mu_{Iw_{2,1}}},\ S^0_{u_2}=\frac{q_w b_w S^0_{w_2}}{\rho_2+\mu_{Su_2}},\ I^0_{u_{2,2}}=\frac{p_{hw}q_w b_w S^0_{w_2}}{\rho_{2,2}+\mu_{Iu_{2,2}}}, \tag{45}$$

$$I^0_{u_{2,1}} = \frac{q_w b_w I^0_{w_{2,1}}}{\rho_{2,1}+\mu_{Iu_{2,1}}},\ S^0_{v_3}=\frac{\rho_2 S^0_{u_2}}{\mu_{Sv_3}+b_3(N_h)},\ I^0_{v_{3,2}}=\frac{\rho_{2,2}I^0_{u_{2,2}}}{b_3(N_h)+\mu_{Iv_{3,2}}}, \tag{46}$$

$$I^0_{v_{3,1}} = \frac{\rho_{2,1}I^0_{u_{2,1}}}{b_3(N_h)+\mu_{Iv_{3,1}}},\ S^0_{w_3}=\frac{b_3(N_h)S^0_{v_3}}{b_w+\mu_{Sw_3}},\ I^0_{w_{3,2}}=\frac{b_3(N_h)I^0_{v_{3,2}}}{b_w+\mu_{Iw_{3,2}}}, \tag{47}$$

$$I^0_{w_{3,1}} = \frac{b_3(N_h)I^0_{v_{3,1}}}{b_w+\mu_{Iw_{3,1}}},\ S^0_{u_3}=\frac{q_w b_w S^0_{w_3}}{\rho_3+\mu_{Su_3}},\ I^0_{u_{3,3}}=\frac{p_{hw}q_w b_w S^0_{w_3}}{\rho_{3,3}+\mu_{Iu_{3,3}}}, \tag{48}$$

$$I^0_{u_{3,2}} = \frac{q_w b_w I^0_{w_{3,2}}}{\rho_{3,2}+\mu_{Iu_{3,2}}},\ I^0_{u_{3,1}}=\frac{q_w b_w I^0_{w_{3,1}}}{\rho_{3,1}+\mu_{Iu_{3,1}}},\ T^0=\frac{1}{\mu_h}. \tag{49}$$

Then, we define the dimensionless parameter groupings for $k,j\in\{1,2,3\}$

$$\left.\begin{array}{rcl}
b_{s_k} &=& (b_k(N_h)+\mu_{Sv_k})T^0,\ b_{i_{k,j}}=(b_k(N_h)+\mu_{Iv_{k,j}})T^0\\
\tau_{s_k} &=& (b_w+\mu_{Sw_k})T^0,\ \tau_{i_{k,j}}=(b_w+\mu_{Iw_{k,j}})T^0\\
\rho_{s_k} &=& (\rho_k+\mu_{Su_k})T^0,\ \rho_{i_{k,j}}=(\rho_{k,j}+\mu_{Iu_{k,j}})T^0\\
a_s &=& \mu_h T^0,\ a_i=(r_h+\mu_h+\delta_h)T^0,\ a_t=(\gamma_h+\mu_h)T^0,\ \lambda_h=\mu_h\\
\beta_s &=& \frac{p_{wh}q_w b_w I^0_{w_{3,1}}}{\mu_h N_h},\ \beta_i=\frac{p_{wh}q_w b_w I^0_{w_{3,1}}}{(r_h+\mu_h+\delta_h)N_h}\ \delta=\frac{\delta_h}{r_h+\mu_h},\ \gamma=\frac{\gamma_h}{\mu_h},\ r=\frac{r_h}{\mu_h}\\
\gamma_{s_3} &=& \frac{\theta_{s_3}\rho_3 S^0_{u_3}}{(b_3(N_h)+\mu_{Sv_3})S^0_{v_3}},\ \gamma_{i_{3,3}}=\frac{\theta_{i_{3,3}}\rho_{3,3}I^0_{u3,3}}{(b_3(N_h)+\mu_{Iv_{3,2}})I^0_{v_{3,2}}}\\
\gamma_{i_{3,2}} &=& \frac{\theta_{i_{3,2}}\rho_{3,2}I^0_{u_{3,2}}}{(b_3(N_h)+\mu_{Iv_{3,1}})I^0_{v_{3,1}}},\ \gamma_{i_{3,1}}=\frac{\theta_{i_{3,1}}\rho_{3,1}I^0_{u3,1}}{(b_3(N_h)+\mu_{Iv_{3,1}})I^0_{v_{3,1}}}\\
c_k &=& \frac{L\rho_k S^0_{u_k}}{A^0(\nu_A+\mu_{A,1})},\ c_{k,j}=\frac{L\rho_{k,j}I^0_{u_{k,j}}}{A^0(\nu_A+\mu_{A,1})},\ c_0=(\nu_A+\mu_{A,1})T^0
\end{array}\right\}, \tag{50}$$

leading to the scaled system

$$\frac{da}{d\tau} = c_0\left(\sum_{k=1}^{3}c_k s_{u_k}+\sum_{j=1}^{3}\sum_{k=j}^{3}c_{k,j}i_{u_{k,j}}-(1+a)a\right), \tag{51}$$

$$\frac{ds_{v_1}}{d\tau} = b_{s_1}(a-s_{v_1}), \tag{52}$$

$$\frac{ds_{w_1}}{d\tau} = \tau_{s_1}(s_{v_1}-s_{w_1}), \tag{53}$$

$$\frac{ds_{u_1}}{d\tau} = \rho_{s_1}((s_h+(1-p_{hw})i_h+\alpha t_h)s_{w_1}-s_{u_1}), \tag{54}$$

$$\frac{di_{u_{1,1}}}{d\tau} = \rho_{i_{1,1}}(s_{w_1}i_h-i_{u_{1,1}}), \tag{55}$$

$$\frac{ds_{v_2}}{d\tau} = b_{s_2}(s_{u_1}-s_{v_2}), \tag{56}$$

$$\frac{di_{v_{2,1}}}{d\tau} = b_{i_{2,1}}(i_{u_{1,1}}-i_{v_{2,1}}), \tag{57}$$

$$\frac{ds_{w_2}}{d\tau} = \tau_{s_2}(s_{v_2} - s_{w_2}), \tag{58}$$
$$\frac{di_{w_{2,1}}}{d\tau} = \tau_{i_{2,1}}(i_{v_{2,1}} - i_{w_{2,1}}), \tag{59}$$
$$\frac{ds_{u_2}}{d\tau} = \rho_{s_2}((s_h + (1-p_{hw})i_h + \alpha t_h)s_{w_2} - s_{u_2}), \tag{60}$$
$$\frac{di_{u_{2,2}}}{d\tau} = \rho_{i_{2,2}}(s_{w_2} i_h - i_{u_{2,2}}), \tag{61}$$
$$\frac{di_{u_{2,1}}}{d\tau} = \rho_{i_{2,1}}((s_h + i_h + \alpha t_h)i_{w_{2,1}} - i_{u_{2,1}}), \tag{62}$$
$$\frac{ds_{v_3}}{d\tau} = b_{s_3}(s_{u_2} + \gamma_{s_3} s_{u_3} - s_{v_3}), \tag{63}$$
$$\frac{di_{v_{3,2}}}{d\tau} = b_{i_{3,2}}(i_{u_{2,2}} + \gamma_{i_{3,3}} i_{u_{3,3}} - i_{v_{3,2}}), \tag{64}$$
$$\frac{di_{v_{3,1}}}{d\tau} = b_{i_{3,1}}(i_{u_{2,1}} + \gamma_{i_{3,2}} i_{u_{3,2}} + \gamma_{i_{3,1}} i_{u_{3,1}} - i_{v_{3,1}}), \tag{65}$$
$$\frac{ds_{w_3}}{d\tau} = \tau_{s_3}(s_{v_3} - s_{w_3}), \tag{66}$$
$$\frac{di_{w_{3,2}}}{d\tau} = \tau_{i_{3,2}}(i_{v_{3,2}} - i_{w_{3,2}}), \tag{67}$$
$$\frac{di_{w_{3,1}}}{d\tau} = \tau_{i_{3,1}}(i_{v_{3,1}} - i_{w_{3,1}}), \tag{68}$$
$$\frac{ds_{u_3}}{d\tau} = \rho_{s_3}((s_h + (1-p_{hw})i_h + \alpha t_h)s_{w_3} - s_{u_3}), \tag{69}$$
$$\frac{di_{u_{3,3}}}{d\tau} = \rho_{i_{3,3}}(s_{w_3} i_h - i_{u_{3,3}}), \tag{70}$$
$$\frac{di_{u_{3,2}}}{d\tau} = \rho_{i_{3,2}}((s_h + i_h + \alpha t_h)i_{w_{3,2}} - i_{u_{3,2}}), \tag{71}$$
$$\frac{di_{u_{3,1}}}{d\tau} = \rho_{i_{3,1}}((s_h + i_h + \alpha t_h)i_{w_{3,1}} - i_{u_{3,1}}), \tag{72}$$
$$\frac{ds_h}{d\tau} = a_s(1 + r i_h + \gamma t_h - \beta_s i_{w_{3,1}} s_h - s_h), \tag{73}$$
$$\frac{di_h}{d\tau} = a_i(\beta_i s_h i_{w_{3,1}} - i_h), \tag{74}$$
$$\frac{dt_h}{d\tau} = a_t(\delta i_h - \gamma t_h). \tag{75}$$

From a mathematical and Physical stand point, all we wish to establish is whether for a given set of initial conditions, the system defined by equations (51)-(75) has a bounded and biologically meaningful solution. Let $\boldsymbol{x} \in \mathbb{R}^{24}$ be a vector of state variables as represented by system (51)-(75). Then, we situate the type of solutions that are of biological interest to us with the following definition.

Definition 1 (Realistic solution.) *Let $\boldsymbol{x} \in \mathbb{R}^{24}$ be a solution of system* (51)-(75)*. The solution $\boldsymbol{x}$ is called realistic if each component of $\boldsymbol{x}$ is bounded and non-negative. That is, if each $x_i \in [0, \infty), i = 1, 2, \cdots, 24$*

3 Analyzing the model's equations: the disease free model

In the absence of infection, the disease free system for humans reduces to $N_h =$ constant, while the mosquito subsystem turns into

$$\frac{da}{d\tau} = c_0 \left(\sum_{k=1}^{3} c_k s_{u_k} - (1+a)a \right), \tag{76}$$

$$\frac{ds_{v_1}}{d\tau} = b_{s_1}(a - s_{v_1}),\ \frac{ds_{w_1}}{d\tau} = \tau_{s_1}(s_{v_1} - s_{w_1}),\ \frac{ds_{u_1}}{d\tau} = \rho_{s_1}(s_{w_1} - s_{u_1}), \tag{77}$$

$$\frac{ds_{v_2}}{d\tau} = b_{s_2}(s_{u_1} - s_{v_2}),\ \frac{ds_{w_2}}{d\tau} = \tau_{s_2}(s_{v_2} - s_{w_2}),\ \frac{ds_{u_2}}{d\tau} = \rho_{s_2}(s_{w_2} - s_{u_2}), \tag{78}$$

$$\frac{ds_{v_3}}{d\tau} = b_{s_3}(s_{u_2} + \gamma_{s_3}s_{u_3} - s_{v_3}),\ \frac{ds_{w_3}}{d\tau} = \tau_{s_3}(s_{v_3} - s_{w_3}),\ \frac{ds_{u_3}}{d\tau} = \rho_{s_3}(s_{w_3} - s_{u_3}). \tag{79}$$

Now, let $\boldsymbol{x} = (a, s_{v_1}, s_{w_1}, s_{u_1}, \cdots, s_{v_3}, s_{w_3}, s_{u_3})^T$ be a column vector in R_+^{10}. Then the disease free system may be written in the form

$$\frac{d\boldsymbol{x}}{d\tau} := \boldsymbol{f}(\boldsymbol{x}) = A(\boldsymbol{x})\boldsymbol{x}, \quad \boldsymbol{x}(0) = \boldsymbol{x}_0, \tag{80}$$

where A is a 10×10 matrix that may be written in the block form

$$A(\boldsymbol{x}) = \begin{pmatrix} -c_0(1+a) & \boldsymbol{c}_1 & \boldsymbol{c}_2 & \boldsymbol{c}_3 \\ \boldsymbol{b}_1 & \boldsymbol{B}_1 & \boldsymbol{O} & \boldsymbol{O} \\ \boldsymbol{0} & \boldsymbol{s}_2 & \boldsymbol{B}_2 & \boldsymbol{O} \\ \boldsymbol{0} & \boldsymbol{O} & \boldsymbol{s}_3 & \boldsymbol{B}_3 \end{pmatrix}, \tag{81}$$

where $\boldsymbol{B}_k, k = 1, 2, 3$ are 3×3 matrices , $\boldsymbol{b}_1$ is a 3×1 column vector and $\boldsymbol{c}_k,\ k = 1, 2, 3$ are 1×3 row vectors given by

$$\boldsymbol{b}_1 = (b_{s_1}, 0, 0)^T,\ \ \boldsymbol{c}_k = (0, 0, c_0c_k),\ k = 1, 2, 3, \tag{82}$$

$$\boldsymbol{B}_k = \begin{pmatrix} -b_{s_k} & 0 & 0 \\ \tau_{s_k} & -\tau_{s_k} & 0 \\ 0 & \rho_{s_k} & -\rho_{s_k} \end{pmatrix},\ k = 1, 2, \quad \boldsymbol{B}_3 = \begin{pmatrix} -b_{s_3} & 0 & b_{s_3}\gamma_{s_3} \\ \tau_{s_3} & -\tau_{s_3} & 0 \\ 0 & \rho_{s_3} & -\rho_{s_3} \end{pmatrix}, \tag{83}$$

$$\boldsymbol{s}_k = \begin{pmatrix} 0 & 0 & b_{s_k} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},\ k = 2, 3 \text{ are } 3 \times 3 \text{ matrices }, \tag{84}$$

$$\boldsymbol{0} = (0, 0, 0)^T \text{ and } \boldsymbol{O} \text{ are respectively } 1 \times 3 \text{ and } 3 \times 3 \text{ zero matrices.} \tag{85}$$

Clearly $A(\boldsymbol{x})$ is a Metzler matrix and since the right hand side is Lipschitz continuous, there exists a maximally defined solution whenever the initial condition $\boldsymbol{x}(0)$ is chosen non-negative. That is, for non-negative initial conditions, $\boldsymbol{x}(t)$ exists and is non-negative, for all $t > 0$, from the Picard-Lindelöf (or Cauchy-Lipschitz) Theorem, [8]. Furthermore, since $A(\boldsymbol{x})$ is a Metzler matrix the maximal solution so identified is also bounded as demonstrated above. Such a solution is also realistic in the sense of Definition 1.

The scaled version of system (80) shows clearly the possibility of two steady state solutions: the trivial equilibrium solution $s_{v_k}^* = s_{u_k}^* = s_{w_k}^* = a^* = 0$ and the nontrivial equilibrium solution $s_{v_k} = s_{u_k} = s_{w_k} = a^*$, for each $k = 1, 2$ and $s_{v_3}^* = s_{u_3}^* = s_{w_3}^* = \frac{1}{1-\gamma_{s_3}}a^*$. Thus, the non-trivial steady state, when it exists, must satisfy the equation:

$$c_0\left(\left(c_1 + c_2 + c_3\frac{1}{1-\gamma_{s_3}}\right)a^* - (1+a^*)a^*\right) = 0 \Rightarrow a^* = 0 \text{ or } a^* = c_1 + c_2 + \frac{c_3}{1-\gamma_{s_3}} - 1. \tag{86}$$

The non-zero solution for a^* in (86) is realistic, that is, non-negative, only if $\gamma_{s_3} < 1$ and $c_1 + c_2 + \frac{c_3}{1-\gamma_{s_3}} > 1$. To see that γ_{s_3} is indeed less than unity, we return to the definition of this quantity in terms of the original variables to see that

$$\gamma_{s_3} = \frac{\theta_{s_3}\rho_3 S_{u_3}^0}{(b_3(N_h) + \mu_{Sv_3})S_{v_3}^0} = \frac{b_3\rho_3 b_w q_w \theta_{s_3}}{(\rho_3 + \mu_{Su_3})(\mu_{Sv_3} + b_3)(b_w + \mu_{Sw_3})} < 1$$

since $q_w, \theta_{s_3} \in [0, 1]$. Now set $\mathcal{N} = c_1 + c_2 + \frac{c_3}{1-\gamma_{s_3}}$ to see that if $\mathcal{N} < 1$, we have only the trivial steady state and that when $\mathcal{N} > 1$, a new non-trivial steady state appears. A transcritical bifurcation, where

a non-trivial steady state comes into existence as $\mathcal{N}$ increases through unity, occurs at $\mathcal{N}=1$. Hence, from now, we interpret the quantity $\mathcal{N}$ as the *basic offspring number* and write, in terms of this basic offspring number, the disease free equilibrium (DFE) state in the form:

$$\begin{array}{rcl} s_{v_k}^{DFE} & = & s_{u_k}^{DFE} = s_{w_k}^{DFE} = \mathcal{N}-1, \\ s_{v3}^{DFE} & = & s_{u3}^{DFE} = s_{w3}^{DFE} = \frac{1}{1-\gamma_{s_3}}(\mathcal{N}-1), \end{array} \quad \mathcal{N} = c_1 + c_2 + \frac{c_3}{1-\gamma_{s_3}}. \tag{87}$$

Thus, whenever we shall refer to the disease free equilibrium solution, $\boldsymbol{x}^{DFE}$, we shall mean the solution $\boldsymbol{x} \in \mathbb{R}^{10}$ where

$$\boldsymbol{x}^* = \boldsymbol{x}^{DFE} = \left(a^{DFE}, s_{v_1}^{DFE}, s_{w_1}^{DFE}, s_{u_1}^{DFE}, s_{v_2}^{DFE}, s_{w_2}^{DFE}, s_{u_2}^{DFE}, s_{v_3}^{DFE}, s_{w_3}^{DFE}, s_{u_3}^{DFE}\right) \tag{88}$$

together with $s_h = 1$, where the system is in equilibrium with values given by (87) and all disease related variable are zero. We have proved the following result.

Theorem 1 *System (80) always admits* $\mathbf{0}$ *as an equilibrium solution for all values of its parameters. If* $\mathcal{N} > 1$*, then it also admits a positive equilibrium,* $\boldsymbol{x}^*$ *whose size and existence is completely determined by the threshold parameter* $\mathcal{N}$

The trivial equilibrium solution identified by Theorem 1 always exists for all parameter values of the system and represent the extinction state, where the system postulates the fact that the mosquito population has died out. The non-zero equilibrium state predicted by the same theorem only exist, as a realistic solution of the system in the sense of Definition 1, when $\mathcal{N} > 1$. The threshold parameter $\mathcal{N}$, identified with the offspring number for the system has ecological and biological importance.

The basic offspring number has properties analogous to the basic reproduction number in epidemiological models in that if this number is bigger than unity, the mosquito population can establish itself in the environment and if the number is less than or equal to unity, the mosquito population will die out. This interpretation allows us to define the basic offspring number as *the average number of new adult mosquitoes that can arise from one reproducing adult mosquito during the entire period of that reproducing mosquito's reproductive life in the absence of density dependence.* The basic offspring number is a measurable index of mosquito abundance through which we can discuss mosquito control strategies.

Remark 1 *We can state the following remarks*

1. *Given the fact that we count the reproductive age of the mosquito in terms of the gonotrophic cycles, we expect that the identified basic offspring number will have contributions from each gonotrophic cycle. To see this, using the parameter groupings from* (43)-(49) *and* (50)*, we easily establish that, in the original parameters of the model, we have*

$$\mathcal{N} = L\xi_v \frac{\nu_A}{\nu_A + \mu_{A,1}} w_{s_1}(1 + w_{s_2} + w_{s_2}\frac{w_{s_3}}{1-\gamma_{s_3}}), \quad \gamma_{s_3} = \theta_{s_3} w_{s_3}, \tag{89}$$

where,

$$\begin{array}{rcl} w_{s_1} & = & \dfrac{\rho_1}{\rho_1 + \mu_{Su_1}} \dfrac{b_w}{b_w + \mu_{Sw_1}} \dfrac{b_1(N_h)}{b_1(N_h) + \mu_{Sv_1}} q_w, \\ w_{s_2} & = & \dfrac{\rho_2}{\rho_2 + \mu_{Su_2}} \dfrac{b_w}{b_w + \mu_{Sw_2}} \dfrac{b_2(N_h)}{b_2(N_h) + \mu_{Sv_2}} q_w, \\ w_{s_3} & = & \dfrac{\rho_3}{\rho_3 + \mu_{Su_3}} \dfrac{b_w}{b_w + \mu_{Sw_3}} \dfrac{b_3(N_h)}{b_3(N_h) + \mu_{Sv_3}} q_w. \end{array} \tag{90}$$

Clearly, from this form we can obtain a general formula of w_{s_k} *associated with cycle* k*, namely*

$$w_{s_k} = \frac{\rho_k}{\rho_k + \mu_{Su_k}} \frac{b_w}{b_w + \mu_{Sw_k}} \frac{b_k(N_h)}{b_k(N_h) + \mu_{Sv_k}} q_w, \quad k = 1, 2, 3, \tag{91}$$

and its value is completely determined by the parameters $b_k(N_h) = a_k \frac{N_h}{N_h+\kappa}$ *– the rate of flow of breeding site vectors in the reproductive stage* k *to human environs for questing,* b_w *a human biting rate of the mosquito,* q_w *– the probability of successfully acquiring a blood meal from the human and* ρ_k *– the rate of successful return of reproducing vectors in the reproductive stage* k *to the breeding site to lay their* $(k+1)$*-st batch of eggs.*

2. *The above allows us to generalise in the case where we consider up to* n *gonotrophic cycles before lumping, we may define, see also [20], the basic offspring number* $\mathcal{N}_n$ *after* n *gonotrophic cycles as*

$$\mathcal{N}_n = L\xi_v \frac{\nu_A}{\nu_A + \mu_{A,1}} \sum_{k=1}^{n} \alpha_k \prod_{j=1}^{k} w_{s_j}, \quad \alpha_1 = \alpha_2 = \cdots = \alpha_{n-1} = 1, \ \alpha_n = \frac{1}{1-\theta_{s_n} w_{s_n}}. \tag{92}$$

Since each $w_{s_i} < 1$*, our modelling results say that the dominant contribution to the basic offspring number* $\mathcal{N}_n$ *is from the first gonotrophic cycle, and this seems to agree with the general trend whereby the quality of the brood of eggs for Anopheles sp mosquitoes tend to decrease with increasing number of gonotrophic cycles*[4]*. This provides a justification for lumping higher gonotrophic cycles as explained in the introduction.*

To study the long term dynamics, we begin with the observation that system (80) is cooperative. We briefly recall the definition of a cooperative system, [24], and other definitions that may be useful for the understanding of some of the proofs and notation used below, in Appendix A. We note simply that for cooperative systems of autonomous ordinary differential equations, the global asymptotic stability of an equilibrium can be studied using the result of Theorem 7 stated in Appendix A. Thus, the dynamics of the unscaled version of system (80) can be summarized in the following theorem:

Theorem 2 *For any initial condition in* $\mathbb{R}^{10}_+$*, we have the following results:*

(i) When $\mathcal{N} \leq 1$*, the trivial equilibrium* $\mathbf{0}$ *is globally asymptotically stable in the closed subspace* $\mathbb{R}^{10}_+$*.*

(ii) When $\mathcal{N} > 1$*, the trivial equilibrium* $\mathbf{0}$ *is unstable, and the positive equilibrium* $\boldsymbol{x}^*$ *is asymptotically stable and* $\mathbb{R}^{10}_+ \setminus \{\mathbf{0}\}$ *is its basin of attraction.*

Proof: It suffices to verify the assumptions of Theorem 7 in Appendix A.

- Assume $\mathcal{N} \leq 1$. Then, there is only one equilibrium, $\mathbf{0}$. For sufficiently large $A > 0$, the following inequality holds:

$$\frac{(\nu_A + \mu_{A,1} + \mu_{A,2}A)}{\nu_A + \mu_{A,1}} \geq \frac{1}{\mathcal{N}^8}. \tag{93}$$

Thus, let $m > 0$ and A_m be sufficiently large so that (93) is verified. With the following variables

$$\begin{aligned} A_m &\geq m, \quad S_{v_1,m} = \frac{1}{\mathcal{N}} \frac{\xi_v \nu_A}{(\mu_{v_1} + b_1(H))} A_m \geq m, \\ S_{w_1,m} &= \frac{1}{\mathcal{N}^2} \frac{b_1(H)\xi_v \nu_A}{(b_{w,1} + \mu_{Sw_1})(\mu_{v_1} + b_1(H))} A_m \geq m, \quad S_{u_1,m} = \frac{w_1}{\mathcal{N}^3} A_m \geq m, \end{aligned}$$

and

$$\begin{aligned} S_{v_2,m} &= \frac{\rho_1}{(b_2(H) + \mu_{Sv_2})} \frac{w_1}{\mathcal{N}^4} A_m \geq m, \\ S_{w_2,m} &= \frac{2b_2(H)}{(b_{w,2} + \mu_{Su_2})} \frac{\rho_1}{(b_2(H) + \mu_{Sv_2})} \frac{w_1}{\mathcal{N}^5} A_m \geq m, \quad S_{u_2,m} = \frac{w_2 w_1}{\mathcal{N}^6} A_m \geq m, \end{aligned}$$

[4]Depending on the *Anopheles* mosquito species, and on the quality and size of the blood meal drawn, a female mosquito lays a batch of $50 - 200$ eggs during a single oviposition. Successive batches of eggs tend to decrease in size and the number of eggs laid may vary depending on the season [22], page 68. We have not considered issues of seasonal variations in this paper.

and

$$\begin{aligned} S_{v_3,m} &= \frac{\rho_2}{(b_3(H)+\mu_{Sv_3})}\frac{w_2w_1}{\mathcal{N}^7}A_m \geq m, \\ S_{w_3,m} &= \frac{2b_3(H)}{(b_{w,3}+\mu_{Su_3})}\frac{\rho_2}{(b_3(H)+\mu_{Sv_3})}\frac{w_3w_1}{\mathcal{N}^8}A_m \geq m, \quad S_{u_3,m} = \frac{w_3w_2w_1}{\mathcal{N}^9}A_m \geq m, \end{aligned}$$

chosen, such that $f_i < 0,\ i = 2, ..., 10$, where f_i is the right hand side of the i-th equation in (80). Finally, thanks to (93), and using the fact that $\mathcal{N} < 1$, we have

$$\begin{aligned} f_1 &= \left(b\left(\frac{w_3w_2w_1}{\mathcal{N}^9}+\frac{w_2w_1}{\mathcal{N}^6}+\frac{w_1}{\mathcal{N}^3}\right)-(\nu_A+\mu_{A,1}+\mu_{A,2}A_m)\right)A_m \\ &< \left(\frac{bw_1}{\mathcal{N}^9}(w_3w_2+w_2+1)-(\nu_A+\mu_{A,1}+\mu_{A,2}A_m)\right)A_m \\ &< (\nu_A+\mu_{A,1})\left(\frac{1}{\mathcal{N}^8}-\left(\frac{\nu_A+\mu_{A,1}+\mu_{A,2}A_m}{\nu_A+\mu_{A,1}}\right)\right)A_m < 0. \end{aligned}$$

Thus, choosing $\boldsymbol{b}_m = (A_m, S_{v1,m}, ..., S_{u_3,m})$ leads to $\boldsymbol{f}(\boldsymbol{b}_m) < 0$. Hence, with $\boldsymbol{a} = \boldsymbol{0}$, we can apply Theorem 7 in Appendix A, and deduce that $\boldsymbol{0}$ is GAS on $[\boldsymbol{0}, \boldsymbol{b}_m]$. However, since m can be chosen arbitrarily large, we deduce that $\boldsymbol{0}$ is GAS on $\mathbb{R}^{10}_+$.

- Assume $\mathcal{N} > 1$. Then the inequality

$$\frac{\nu_A+\mu_{A,1}+\mu_{A,2}A}{\nu_A+\mu_{A,1}} < \mathcal{N}, \tag{94}$$

holds for A sufficiently small. Let $\varepsilon > 0$, and let A_ε be sufficiently small for (94) to hold and

$$\begin{aligned} A_\varepsilon &\leq \varepsilon, \quad S_{v_1,\varepsilon} = \frac{\xi_v\nu_A\mathcal{N}}{(\mu_{v_1}+b_1(H))}A_\varepsilon \leq \varepsilon, \\ S_{w_1,\varepsilon} &= \frac{b_1(H)\xi_v\nu_A\mathcal{N}^2}{(b_{w,1}+\mu_{Sw_1})(\mu_{v_1}+b_1(H))}A_\varepsilon \leq \varepsilon, \quad S_{u_1,\varepsilon} = w_1\mathcal{N}^3A_\varepsilon \leq \varepsilon. \end{aligned}$$

Thus

$$\begin{aligned} S_{v_2,\varepsilon} &= \frac{\rho_1}{(b_2(H)+\mu_{Sv_2})}w_1\mathcal{N}^4A_\varepsilon \leq \varepsilon, \\ S_{w_2,\varepsilon} &= \frac{2b_2(H)}{(b_{w,2}+\mu_{Su_2})}\frac{\rho_1}{(b_2(H)+\mu_{Sv_2})}w_1\mathcal{N}^5A_\varepsilon \leq \varepsilon, \\ S_{u_2,\varepsilon} &= S_{w_2,\varepsilon} = w_2w_1\mathcal{N}^6A_\varepsilon \leq \varepsilon, \end{aligned}$$

and

$$\begin{aligned} S_{v_3,\varepsilon} &= \frac{\rho_2}{(b_3(H)+\mu_{Sv_3})}w_2w_1\mathcal{N}^7A_\varepsilon \leq \varepsilon, \\ S_{w_3,\varepsilon} &= \frac{2b_3(H)}{(b_{w,3}+\mu_{Su_3})}\frac{\rho_2}{(b_3(H)+\mu_{Sv_3})}w_3w_1\mathcal{N}^8A_\varepsilon \leq \varepsilon, \\ S_{u_3,\varepsilon} &= w_3w_2w_1\mathcal{N}^9A_\varepsilon \leq \varepsilon, \end{aligned}$$

so that

$$f_i > 0, \quad i = 2, ..., 10.$$

Finally, thanks to (94), and using the fact that $\mathcal{N} > 1$, we deduce

$$\begin{aligned} f_1 &= \left(b\left(w_3w_2w_1\mathcal{N}^9+w_2w_1\mathcal{N}^6+w_1\mathcal{N}^3\right)-(\nu_A+\mu_{A,1}+\mu_{A,2}A_\varepsilon)\right)A_\varepsilon \\ &> (\nu_A+\mu_{A,1})\left(\mathcal{N}-\left(\frac{\nu_A+\mu_{A,1}+\mu_{A,2}\varepsilon}{\nu_A+\mu_{A,1}}\right)\right)A_\varepsilon > 0. \end{aligned}$$

Hence, we deduce $\boldsymbol{f}(\boldsymbol{a}_\varepsilon) > 0$, with $\boldsymbol{a}_\varepsilon = (A_\varepsilon, ..., S_{u_3,\varepsilon})$.Thus, according to Theorem 7 in Appendix A, X^* is GAS in $[\boldsymbol{a}_\varepsilon, \boldsymbol{b}_m]$. Since $\boldsymbol{a}_\varepsilon$ can be chosen smaller than any $\boldsymbol{x} > 0$, and $\boldsymbol{b}_m$ can be chosen larger than any $\boldsymbol{x}$, we deduce that X^* is asymptotically stable on $\mathbb{R}^{10}_+$, with a basin of attraction being $\mathbb{R}^{10}_+ \setminus \{\mathbf{0}\}$ (because system (80) is cooperative; see Theorem 4 in [1]). This also implies that $\mathbf{0}$ is unstable.

However, we can go further. Define the following compact set

$$\Omega = \left\{\boldsymbol{x} \in \mathbb{R}^{10}_+ : \mathbf{0} \leq \boldsymbol{x} \leq \boldsymbol{x}^*\right\}.$$

Then using the fact that the disease free system is monotone, Ω is positively invariant with respect to the disease free system, meaning that if $X(0) \in \Omega$, then $X(t) \in \Omega$. Thus, Theorem 2 can be reformulated as

Theorem 3 *For any initial conditions in Ω, we have the following results:*

(i) When $\mathcal{N} \leq 1$, the trivial equilibrium $\mathbf{0}$ is globally asymptotically stable in Ω.

(ii) When $\mathcal{N} > 1$, $\boldsymbol{x}^* \neq \mathbf{0}$ exists. The trivial equilibrium $\mathbf{0}$ is unstable, and the positive equilibrium $\boldsymbol{x}^*$ is globally asymptotically stable in $\Omega \setminus \{\mathbf{0}\}$.

That is why for the rest of the paper we assume that the mosquito population belongs to Ω.

4 Analyzing the model's equations: The epidemiological model

In the last section we have examined the disease free model which, in the present framework, captured the mosquito only dynamics as a four stage system of equations, where the first stage, consisting of the aquatic stages of the mosquito population, is modelled by the state variable A, and the remaining three stages are used to model the gonotrophic cycles which the mosquito must complete for reproduction through laying viable eggs into the aquatic stage. We saw that the disease free model exhibited richer dynamics than is normally the case with most standard epidemiological models for insect borne diseases. Theorem 3 showed that when the basic offspring number $\mathcal{N} > 1$, the non trivial equilibrium solution for the disease free model is globally and asymptotically stable. This result points to the fact that under certain desirable conditions, the mosquito population will establish itself in a given locality. Are there other steady states for the full system?

4.1 Existence of steady states for the epidemiological model

The global stability of the non-trivial equilibrium vector population solution in the absence of disease, drawn from the fact the system is monotone cooperative, ensures establishment of a non-zero stable mosquito population in the system. This stability result is demographic in nature and is not related to the epidemiological model's consideration of a disease free state. The result however, provides a basis for the existence of the disease related solutions for the full epidemiological model since any other solutions for the full epidemiological model can only be constructed on the stable mosquito population as a base. What we would like to find in the present section is whether in the presence of the disease in the system, there exist other steady states in addition to the disease free equilibrium state (DFE). To answer this question we proceed by setting to zero the right hand side of the equations for the scaled epidemiological system, given by equations (51)-(75). We recall that, based on the scaling used, $s_h + i_h + t_h = 1 \Rightarrow s_h = 1 - i_h - t_h$ for all time $\tau \geq 0$ and that from equation (75), if t_h^* is a steady state solution, then we have $t_h^* = \frac{\delta}{\gamma} i_h^*$. So define $f, g : [0,1] \to \mathbb{R}$ by

$$f(i_h) = s_h + (1 - p_{hw})i_h + \alpha t_h,\ g(i_h) = s_h + i_h + \alpha t_h;\ s_h = 1 - i_h - t_h, t_h = \frac{\delta}{\gamma} i_h. \tag{95}$$

Then, if $\boldsymbol{x}^* \in \mathbb{R}^{24}_+$ is an equilibrium solution for system (51)-(75) written in the form (115), we have

$$s^*_{v_1} = s^*_{w_1} = a^*, \quad s^*_{u_1} = f(i^*_h)a^*, \quad i^*_{u_{1,1}} = a^* i^*_h, \tag{96}$$

$$\left.\begin{array}{rcl} s^*_{v_2} & = & s^*_{w_2} = f(i^*_h)a^*, \quad s^*_{u_2} = (f(i^*_h))^2 a^*, \quad i^*_{v_{2,1}} = a^* i^*_h, \\ i^*_{w_{2,1}} & = & i^*_{v_{2,1}}, \quad i^*_{u_{2,1}} = i^*_{w_{2,1}} g(i^*_h), \quad i^*_{u_{2,2}} = f(i^*_h)a^* i^*_h, \end{array}\right\} \tag{97}$$

$$\left.\begin{array}{rcl} s^*_{w_3} & = & s^*_{v_3} = \frac{(f(i^*_h))^2 a^*}{1-\gamma_{s_3} f(i^*_h)}, \quad s^*_{u_3} = \frac{(f(i^*_h))^3 a^*}{1-\gamma_{s_3} f(i^*_h)}, \quad i^*_{u_{3,3}} = \frac{(f(i^*_h))^2 a^*}{1-\gamma_{s_3} f(i^*_h)} i^*_h, \\ i^*_{v_{3,2}} & = & i^*_{u_{2,2}} + \gamma_{i_{3,3}} i^*_{u_{3,3}}, \quad i^*_{w_{3,2}} = i^*_{v_{3,2}}, \quad i^*_{u_{3,2}} = g(i^*_h) i^*_{w_{3,2}}, \\ i^*_{w_{3,1}} & = & \frac{i^*_{u_{2,1}} + \gamma_{i_{3,2}} i^*_{u_{3,2}}}{1-\gamma_{i_{3,1}} g(i^*_h)}, \quad i^*_{v_{3,1}} = i^*_{w_{3,1}}, \quad i^*_{u_{3,1}} = g(i^*_h) i^*_{w_{3,1}}, \end{array}\right\} \tag{98}$$

where a^* is a parameter still to be determined. The steady states in equations (96) are those for the mosquitoes at the first gonotrophic cycle, while those in equations (97) are for the second gonotrophic cycle and those in equations (98) for the third one. Since both $f(i_h)$ and $g(i_h)$, as defined in equation (95) are less than 1, the sizes of the steady states decrease with increasing gonotrophic cycles.

Now, if we substitute equations (96)-(98) into the equation for the aquatic stage, we get

$$a^* F(i^*_h) = \sum_{k=1}^{3} c_k s^*_{u_k} + \sum_{j=1}^{3} \sum_{k=j}^{3} c_{k,j} i^*_{u_{k,j}} = a^*(1 + a^*), \tag{99}$$

that leads to the solution $a^* = 0$, corresponding to the trivial equilibrium solution, where all variables are zero, and a non trivial solution $a^* \neq 0$, given by $a^*(i^*_h) = F(i^*_h) - 1$. The formula for $F(i^*_h)$ is directly read from the expression in the middle of (99), arising from that fact that a^* appears only linearly in all middle summand terms of that equation. We conjecture that F so identified will be linked to the epidemiological model's basic reproduction number which we shall compute below. We then note that a non-negative equilibrium solution for a^* will exists only when $F \geq 1$. The quantity F so constructed is a function of $i^*_h \in [0, 1]$, indicating the existence of an endemic human equilibrium state configuration, when $i^*_h \in (0, 1)$. When a non-zero equilibrium solution, $i^*_h \neq 0$, exists, it must satisfy the equation

$$\beta_i(1 - (1 + \frac{\delta}{\gamma})i^*_h) i^*_{w_{3,1}} - i^*_h = 0 \Rightarrow i^*_{w_{3,1}} = \frac{i^*_h}{\beta_i(1 - (1 + \frac{\delta}{\gamma})i^*_h)}, \tag{100}$$

so that a non-negative equilibrium solution, when it exists, must satisfy the equation

$$\frac{i^*_h}{\beta_i(1 - (1 + \frac{\delta}{\gamma})i^*_h)} = \frac{i^*_{u_{2,1}}(i^*_h) + \gamma_{i_{3,2}} i^*_{u_{3,2}}(i^*_h)}{1 - \gamma_{i_{3,1}} g(i^*_h)} \tag{101}$$

obtained by equating the two values of $i^*_{w_{3,1}}$ from (98) and (100). Note that $i^*_h = 0$ is always a solution and that, in this instance, $f(0) = g(0) = 1$ and the equilibrium computed above reduces to the disease free equilibrium computed earlier and shown in (87). It is easily established that (100) has at least one positive solution for $i^*_h \in (0, 1) \subset (0, (1 + \frac{\delta}{\gamma}))$.We have proved the following result.

Theorem 4 *The epidemiological model has at least one endemic equilibrium solution whenever the threshold condition $F > 1$ is satisfied.*

4.2 The epidemiological model's basic reproduction number

We consider now the full epidemiological model, given by either system of equations (16)-(40) or, equivalently, by the scaled system (51)-(75). System (16)-(40) is not monotone. It, however, admits the trivial equilibrium $\mathbf{0}$, which corresponds to the system with a full susceptible human population, without mosquitoes. It admits also a $X^{DFE} = \left(A^{DFE}, S^{DFE}_{v_1}, S^{DFE}_{w_1}, S^{DFE}_{u_1}, 0, \cdots, S^{DFE}_{u_3}, 0, 0, 0, 0\right)^T$,

which corresponds to a susceptible human population, $S_h = N_h$, and a susceptible mosquito population.

Let us compute the Basic Reproduction Number related to system. To do that, we follow the standard procedure, [28], and consider only the equations where the disease is in progression. Considering the scaled version of the model, we consider only the equations

$$\begin{aligned}
\frac{di_{u_{1,1}}}{d\tau} &= \rho_{i_{1,1}}(s_{w_1} i_h - i_{u_{1,1}}), \quad \frac{di_{v_{2,1}}}{d\tau} = b_{i_{2,1}}(i_{u_{1,1}} - i_{v_{2,1}}),\\
\frac{di_{w_{2,1}}}{d\tau} &= \tau_{i_{2,1}}(i_{v_{2,1}} - i_{w_{2,1}}), \quad \frac{di_{u_{2,2}}}{d\tau} = \rho_{i_{2,2}}(s_{w_2} i_h - i_{u_{2,2}}),\\
\frac{di_{u_{2,1}}}{d\tau} &= \rho_{i_{2,1}}((s_h + i_h + \alpha t_h) i_{w_{2,1}} - i_{u_{2,1}}),\\
\frac{di_{v_{3,2}}}{d\tau} &= b_{i_{3,2}}(i_{u_{2,2}} + \gamma_{i_{3,3}} i_{u_{3,3}} - i_{v_{3,2}}),\\
\frac{di_{v_{3,1}}}{d\tau} &= b_{i_{3,1}}(i_{u_{2,1}} + \gamma_{i_{3,2}} i_{u_{3,2}} + \gamma_{i_{3,1}} i_{u_{3,1}} - i_{v_{3,1}}),\\
\frac{di_{w_{3,2}}}{d\tau} &= \tau_{i_{3,2}}(i_{v_{3,2}} - i_{w_{3,2}}), \quad \frac{di_{w_{3,1}}}{d\tau} = \tau_{i_{3,1}}(i_{v_{3,1}} - i_{w_{3,1}}),\\
\frac{di_{u_{3,3}}}{d\tau} &= \rho_{i_{3,3}}(s_{w_3} i_h - i_{u_{3,3}}),\\
\frac{di_{u_{3,2}}}{d\tau} &= \rho_{i_{3,2}}((s_h + i_h + \alpha t_h) i_{w_{3,2}} - i_{u_{3,2}}),\\
\frac{di_{u_{3,1}}}{d\tau} &= \rho_{i_{3,1}}((s_h + i_h + \alpha t_h) i_{w_{3,1}} - i_{u_{3,1}}),\\
\frac{di_h}{d\tau} &= a_i(\beta_i s_h i_{w_{3,1}} - i_h).
\end{aligned} \tag{102}$$

Then, we rewrite the system as follows

$$\frac{d\boldsymbol{x}}{dt} = \mathcal{F}(\boldsymbol{x}) - \mathcal{V}(\boldsymbol{x}),$$

where $\boldsymbol{x} = (i_{u_{1,1}}, i_{v_{2,1}}, i_{w_{2,1}}, i_{u_{2,2}}, i_{u_{2,1}}, i_{v_{3,2}}, i_{v_{3,1}}, i_{w_{3,2}}, i_{w_{3,1}}, i_{u_{3,3}}, i_{u_{3,2}}, i_{u_{3,1}}, i_h)$,

$$\mathcal{F}(\boldsymbol{x}) = \begin{pmatrix}
\rho_{i_{1,1}} s_{w_1} i_h \\ 0 \\ 0 \\ \rho_{i_{2,2}} s_{w_2} i_h \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ \rho_{i_{3,3}} s_{w_3} i_h \\ 0 \\ 0 \\ a_i \beta_i s_h i_{w_{3,1}}
\end{pmatrix}, \qquad \mathcal{V}(\boldsymbol{x}) = \begin{pmatrix}
\rho_{i_{1,1}} i_{u_{1,1}} \\
-b_{i_{2,1}}(i_{u_{1,1}} - i_{v_{2,1}}) \\
-\tau_{i_{2,1}}(i_{v_{2,1}} - i_{w_{2,1}}) \rho_{i_{2,2}} i_{u_{2,2}} \\
-\rho_{i_{2,1}}((s_h + i_h + \alpha t_h) i_{w_{2,1}} - i_{u_{2,1}}) \\
-b_{i_{3,2}}(i_{u_{2,2}} + \gamma_{i_{3,3}} i_{u_{3,3}} - i_{v_{3,2}}) \\
-b_{i_{3,1}}(i_{u_{2,1}} + \gamma_{i_{3,2}} i_{u_{3,2}} + \gamma_{i_{3,1}} i_{u_{3,1}} - i_{v_{3,1}}) \\
-\tau_{i_{3,2}}(i_{v_{3,2}} - i_{w_{3,2}}) \\
-\tau_{i_{3,1}}(i_{v_{3,1}} - i_{w_{3,1}}) \\
\rho_{i_{3,3}} i_{u_{3,3}} \\
-\rho_{i_{3,2}}((s_h + i_h + \alpha t_h) i_{w_{3,2}} - i_{u_{3,2}}) \\
-\rho_{i_{3,1}}((s_h + i_h + \alpha t_h) i_{w_{3,1}} - i_{u_{3,1}}) \\
a_i i_h
\end{pmatrix}.$$

Then, we evaluate the Jacobians F^{DFE} and V^{DFE} of $\mathcal{F}$ and $\mathcal{V}$ at the X^{DFE}. Obviously, V^{DFE} is an M-Matrix such that $V^{DFE^{-1}}$ exists and is positive. After some computations, we can derive a formula for $F^{DFE} V^{DFE^{-1}}$. Then, we find the spectral radius $\varrho(F^{DFE} V^{DFE^{-1}}) = \max_\lambda\{|\lambda| : \lambda \text{ is an eigenvalue of } F^{DFE} V^{DFE^{-1}}\}$ that, as it is known, basic reproduction number. Since the matrix $F^{DFE} V^{DFE^{-1}}$ is sparse, we quickly obtain the spectral radius that we need. We note first

that at X^{DFE}, $s_h = 1$, $t_h = 0$, $s_{w_1}^{DFE}$, $s_{w_2}^{DFE}$, and $s_{w_3}^{DFE}$, are given by

$$s_{w_1}^{DFE} = s_{w_2}^{DFE} = a^*, \quad s_{w_3}^{DFE} = \frac{1}{1-\gamma_{s_3}} a^*, \tag{103}$$

where a^* is given by the last equation in (86). Direct computations yield

$$\varrho(FV^{-1}) = \frac{\sqrt{\beta_i}\sqrt{s_{w_1}^{DFE} + \gamma_{i_{3,2}}(s_{w_2}^{DFE} + \gamma_{i_{3,3}}.s_{w_3}^{DFE})}}{\sqrt{1-\gamma_{i_{3,1}}}} \tag{104}$$

Then, the basic reproduction number R_0 is such that $R_0^2 = \varrho(FV^{-1})^2$. We note that R_0^2 is split into the sum of three mutual parts where

$$R_0^2 = R_{0_1}^2 + R_{0_2}^2 + R_{0_3}^2, \tag{105}$$

where

$$R_{0_1}^2 = \frac{\beta_i s_{w_1}^{DFE}}{1-\gamma_{i_{3,1}}}, \quad R_{0_2}^2 = \frac{\beta_i \gamma_{i_{3,2}} s_{w_2}^{DFE}}{1-\gamma_{i_{3,1}}}, \quad R_{0_3}^2 = \frac{\beta_i \gamma_{i_{3,2}} \gamma_{i_{3,3}} s_{w_3}^{DFE}}{1-\gamma_{i_{3,1}}}. \tag{106}$$

We now examine the nature of the terms in the above expressions. To do this we return to the original variables of the model by using the relevant expressions from(43)-(50) and, by substitution, we easily see that the presence of the infection in the system also introduces contributions to the reproduction number in the form of terms such as in (90), but associated with the disease variables. Here these terms that represent contributions from the infected vectors at the reproductive stage k that were first infected at reproductive stage j are given as follows:

$$w_{i_{1,1}} = \frac{\rho_{1,1}}{\rho_{1,1}+\mu_{Iu_{1,1}}} \frac{b_w}{b_w+\mu_{Sw_1}} \frac{b_1(N_h)}{b_2(N_h)+\mu_{Iv_{2,1}}} q_w, \tag{107}$$

$$w_{i_{2,1}} = \frac{\rho_{2,1}}{\rho_{2,1}+\mu_{Iu_{2,1}}} \frac{b_w}{b_w+\mu_{Iw_{2,1}}} \frac{b_2(N_h)}{b_3(N_h)+\mu_{Iv_{3,1}}} q_w, \tag{108}$$

$$w_{i_{2,2}} = \frac{\rho_{2,2}}{\rho_{2,2}+\mu_{Iu_{2,2}}} \frac{b_w}{b_w+\mu_{Sw_2}} \frac{b_2(N_h)}{b_3(N_h)+\mu_{Iv_{3,2}}} q_w, \tag{109}$$

$$w_{i_{3,1}} = \frac{\rho_{3,1}}{\rho_{3,1}+\mu_{Iu_{3,1}}} \frac{b_w}{b_w+\mu_{Iw_{3,1}}} \frac{b_3(N_h)}{b_3(N_h)+\mu_{Iv_{3,1}}} q_w, \tag{110}$$

$$w_{i_{3,2}} = \frac{\rho_{3,2}}{\rho_{3,2}+\mu_{Iu_{3,2}}} \frac{b_w}{b_w+\mu_{Iw_{3,2}}} \frac{b_3(N_h)}{b_3(N_h)+\mu_{Iv_{3,1}}} q_w, \tag{111}$$

$$w_{i_{3,3}} = \frac{\rho_{3,3}}{\rho_{3,3}+\mu_{Iu_{3,3}}} \frac{b_w}{b_w+\mu_{Sw_3}} \frac{b_3(N_h)}{b_3(N_h)+\mu_{Iv_{3,2}}} q_w. \tag{112}$$

We also note that we require $\gamma_{i_{3,1}} < 1$ for the expressions for $R_{0_i}^2$, $i = 1, 2, 3$ to be positive. Using the definitions of this parameter grouping, we find that

$$\gamma_{i_{3,1}} = \theta_{i_{3,1}} w_{i_{3,1}} < 1, \quad \gamma_{i_{3,2}} = \theta_{i_{3,2}} \frac{w_{i_{3,2}} w_{i_{2,2}}}{w_{i_{2,1}} w_{i_{1,1}}} w_{s_1}, \quad \gamma_{i_{3,3}} = \theta_{i_{3,3}} p_{hw} w_{s_2} \frac{w_{i_{3,3}}}{w_{i_{2,2}}}, \tag{113}$$

$$\beta_i = w_{i_{1,1}} w_{i_{2,1}} \frac{\nu_A + \mu_{A,1}}{\mu_{A,2}} \frac{\xi_v \nu_A}{b_1(N_h)+\mu_{Sv_1}} \frac{b_3(N_h) b_w p_{hw} p_{wh} q_w}{N_h(\gamma_h+\delta_h+\mu_h)\left(\mu_{Iw_{3,1}}+b_w\right)}, \tag{114}$$

so that it is evident that $1-\gamma_{i_{3,1}} > 0$. It is clear from the above that the nonzero endemic equilibrium exists only when $\mathcal{N} > 1$, since the only way we can have a positive basic reproduction number is if $\mathcal{N} > 1$.

4.3 Global asymptotic stability of the DFE

First, according to [28], the following result holds:

Theorem 5 *When $\mathcal{R}_0^2 < 1$, the DFE is locally asymptotically stable. It is unstable, when $\mathcal{R}_0^2 > 1$.*

To show that the DFE is globally asymptotically stable, we will use [2]. Let us first rewrite the system in the following manner

$$\begin{cases} \dfrac{d\boldsymbol{x}}{dt} = \boldsymbol{f}(\boldsymbol{x}, \boldsymbol{i}), \\ \dfrac{d\boldsymbol{i}}{dt} = \boldsymbol{g}(\boldsymbol{x}, \boldsymbol{i}), \end{cases}$$

where $\boldsymbol{x}$ is the vector representing the state of different compartments of non-transmitting individuals (e.g. susceptible, immune) and the vector $\boldsymbol{i}$ represents the state of compartments of different transmitting individuals (e.g. infected, exposed). Here, for the purpose of this section,

$$\begin{aligned} \boldsymbol{x} &= (s_{v_1}, s_{w_1}, s_{u_1}, s_{v_2}, s_{w_2}, s_{u_2}, s_{v_3}, s_{w_3}, s_{u_3}, s_h, t_h)\,, \\ \boldsymbol{i} &= (i_{u_{1,1}}, i_{v_{2,1}}, i_{w_{2,1}}, i_{u_{2,2}}, i_{u_{2,1}}, i_{v_{3,2}}, i_{v_{3,1}}, i_{w_{3,2}}, i_{w_{3,1}}, i_{u_{3,3}}, i_{u_{3,2}}, i_{u_{3,1}}, i_h), \end{aligned}$$

so that $X^{DFE} = \big(s_{v_1}^{DFE}, s_{w_1}^{DFE}, s_{u_1}^{DFE}, s_{v_2}^{DFE}, s_{w_2}^{DFE}, s_{u_2}^{DFE}, s_{v_3}^{DFE}, s_{w_3}^{DFE}, s_{u_3}^{DFE}, 1, 0\big)$. From ((51)-(75)), we deduce, with $h(s_{u_k}, i_{u_{k,j}}) = \sum_{k=1}^{3} c_k s_{u_k} + \sum_{j=1}^{3}\sum_{k=j}^{3} c_{k,j} i_{u_{k,j}}$,

$$\boldsymbol{f}(\boldsymbol{x}, \boldsymbol{i}) = \begin{cases} c_0\left(h(s_{u_k}, i_{u_{k,j}}) - (1+a)a\right), \\ b_{s_1}(a - s_{v_1}), \\ \tau_{s_1}(s_{v_1} - s_{w_1}), \\ \rho_{s_1}((s_h + (1-p_{hw})i_h + \alpha t_h)s_{w_1} - s_{u_1}), \\ b_{s_2}(s_{u_1} - s_{v_2}), \\ \tau_{s_2}(s_{v_2} - s_{w_2}), \\ \rho_{s_2}((s_h + (1-p_{hw})i_h + \alpha t_h)s_{w_2} - s_{u_2}), \\ b_{s_3}(s_{u_2} + \gamma_{s_3} s_{u_3} - s_{v_3}), \\ \tau_{s_3}(s_{v_3} - s_{w_3}), \\ \rho_{s_3}((s_h + (1-p_{hw})i_h + \alpha t_h)s_{w_3} - s_{u_3}), \\ a_s(1 + r i_h + \gamma t_h - \beta_s i_{w_{3,1}} s_h - s_h), \\ a_t(\delta i_h - \gamma t_h). \end{cases} \quad \boldsymbol{g}(\boldsymbol{x}, \boldsymbol{i}) = \begin{cases} \rho_{i_{1,1}}(s_{w_1} i_h - i_{u_{1,1}}), \\ b_{i_{2,1}}(i_{u_{1,1}} - i_{v_{2,1}}), \\ \tau_{i_{2,1}}(i_{v_{2,1}} - i_{w_{2,1}}), \\ \rho_{i_{2,2}}(s_{w_2} i_h - i_{u_{2,2}}), \\ \rho_{i_{2,1}}((s_h + i_h + \alpha t_h)i_{w_{2,1}} - i_{u_{2,1}}), \\ b_{i_{3,2}}(i_{u_{2,2}} + \gamma_{i_{3,3}} i_{u_{3,3}} - i_{v_{3,2}}), \\ b_{i_{3,1}}(i_{u_{2,1}} + \gamma_{i_{3,2}} i_{u_{3,2}} + \gamma_{i_{3,1}} i_{u_{3,1}} - i_{v_{3,1}}), \\ \tau_{i_{3,2}}(i_{v_{3,2}} - i_{w_{3,2}}), \\ \tau_{i_{3,1}}(i_{v_{3,1}} - i_{w_{3,1}}), \\ \rho_{i_{3,3}}(s_{w_3} i_h - i_{u_{3,3}}), \\ \rho_{i_{3,2}}((s_h + i_h + \alpha t_h)i_{w_{3,2}} - i_{u_{3,2}}), \\ \rho_{i_{3,1}}((s_h + i_h + \alpha t_h)i_{w_{3,1}} - i_{u_{3,1}}), \\ a_i(\beta_i s_h i_{w_{3,1}} - i_h). \end{cases}$$

Clearly, according to the result of Theorem 3 on mosquito dynamics without diseases, X^{DFE} is GAS for the system $\dfrac{d\boldsymbol{x}}{dt} = \boldsymbol{f}(\boldsymbol{x}, \boldsymbol{0})$ (assumption 1 in [2]). Then, we can rewrite $\boldsymbol{g}$ as follows

$$g(\boldsymbol{x}, \boldsymbol{i}) = A\boldsymbol{i} - \hat{G}(\boldsymbol{x}, \boldsymbol{i}),$$

where $A = J_G(X^{DFE}, \boldsymbol{0})$. We need to show that A is an M-Matrix and $\hat{G}(\boldsymbol{x}, \boldsymbol{i}) \geq 0$ (assumption 2 in [2]). Since $J_G(X^{DFE}, \boldsymbol{0}) = V^{DFE}$, where V^{DFE} is an M-Matrix, it remains to show that $\hat{G}(\boldsymbol{x}, \boldsymbol{i}) \geq \boldsymbol{0}$.

In fact, we have

$$\hat{G}(\boldsymbol{x},\boldsymbol{i}) = \begin{pmatrix} \rho_{1,1} i_h \left(s_{w_1}^{DFE} - s_{w_1}\right) \\ 0 \\ 0 \\ \rho_{2,2} i_h \left(s_{w_2}^{DFE} - s_{w_2}\right) \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ \rho_{3,3} i_h \left(s_{w_3}^{DFE} - s_{w_3}\right) \\ 0 \\ 0 \\ 0 \end{pmatrix}.$$

The sign of $\hat{G}$ completely relies on the sign of $s_{w_i}^{DFE} - s_{w_1}$, for $i = 1, 2, 3$. However, the mosquito model being a monotone system, it means that if $\boldsymbol{x}(0) \leq X^{DFE}$ (see the Theorem 3 in the mosquito dynamic section) then $\boldsymbol{x}(t) \leq X^{DFE}$, for all $t \geq 0$, such that $s_{w_i}^{DFE} - s_{w_1} \geq 0$, and thus $\hat{G}(\boldsymbol{x},\boldsymbol{i}) \geq \mathbf{0}$, and this completes the proof. The conditions for the global stability of the disease free steady state as postulated by Castillo et al., [2], being verified, we can thus deduce

Theorem 6 *The DFE is globally asymptotically stable when* $\mathcal{R}_0^2 < 1$.

The result of Theorem 6 establishes the global stability of the disease free equilibrium, when $R_0^2 < 1$. This is a results which we earlier established when examining the disease free model and this outcome was expected. We also have seen that when $R_0^2 > 1$, an endemic equilibrium solution is possible and we believe that such an endemic solution will be stable for $R_0^2 > 1$. Since our main focus in this paper was to derive an improved formula for the basic reproduction number for a mosquito centered model that captures the mosquito's gonotrophic cycles, and identify vulnerable points in the evolutionary path of the spread of malaria disease within human and mosquito populations, we do not pursue the issue of stability of the endemic equilibrium state any further. Additionally, another main focus was to analyse relevant components of the reproduction number, in order to exploit it for control purposes, which can be done and explained without numerical simulations by studying the basic reproduction number, we do not deem it necessary, here, to carry out numerical simulations. We leave it for a future study, which also helps keep the length of this manuscript within reasonable limits. We indicate that from the form of the basic reproduction number, it is clear that if we apply control measures that can lead to the reduction of the basic offspring number, then we would find a way to control malaria transmission since we need a certain minimum threshold in the mosquito population size to sustain the mosquito population at a stable non-zero state. The formula for R_0^2, written in three parts (see equations (105) and (106)) shows clear dependence on the stable questing mosquito population densities (those categories of mosquitoes that interact with humans), which is a prerequisite to the existence of a viable mosquito population. We discuss this further in the next section, where we summarize the results of the current paper, discussing possible vulnerable spots in the malaria transmission chain and hence some possible control measures. We also indicate prospects for future work.

5 Discussion and Conclusion

The mosquito's gonotrophic cycle is an important and integral component of its demography. It is also central to the human malaria disease transmission and plays an important role in malaria dynamics because some aspects of the cycle ensure mosquito-human interactions presenting opportunities for

mosquitoes to acquire and transmit the malaria parasite. A successful interaction between humans and mosquitoes potentially also guarantees a successful mosquito reproduction, continuing the malaria cycle. Thus understanding the mosquito's gonotrophic cycle and examining it for areas that could be exploited for control is essential for the fight towards malaria eradication. Unfortunately, very little has been done to analyse the gonotrophic cycle from a mathematical perspective. This manuscript is one of the first steps towards understanding the gonotrophic cycle of the malaria transmitting mosquito from the mathematical perspective and looking at ways to exploit and influence it for a positive malaria control.

To this end, we developed a mathematical model of the mosquito life cycle, from the aquatic stages to the adult stages, incorporating the gonotrophic and feeding cycles of mosquitoes with focus on possible control mechanisms. The model provides a way to understand the dynamics of the malaria transmitting mosquitoes, in particular, their feeding and reproductive cycles and their interaction with the human population, revealing the key control points in the malaria disease chain. It extends the idea originally introduced in [20] in that we have incorporated the disease dynamics and introduced the aquatic stages of the mosquitoes, assuming a linear recruitment rate from the aquatic stages into the adult mosquito population. An advantage of this model over other malaria models is in the model formulation, that clearly demarcates the stages of the adult mosquito gonotrophic cycle involved in the disease transmission, and the contributions of the feeding stages towards the growth of the mosquito population. However, we had to decide how many stages, and hence how many gonotrophic cycle loops we can conveniently include in the model. This question, pertaining to the trade-off between mathematical tractability of the model and having a realistic model, is addressed below. Additionally, we incorporated a class of treated humans, treated with a high but safe dose of a mosquitocidal drug, in this case Ivermectin, based on a recent 2018 study [23], that can lead to the demise of the mosquito when the mosquito feeds on these class of humans.

Analysis of the model in the absence of malaria reveals the existence of the basic offspring number $\mathcal{N}$ defined in equation (89), whose size determines whether there is a thriving mosquito population or if the mosquito population goes extinct. Specifically, when $\mathcal{N} < 1$, the mosquito extinction equilibrium (a trivial mosquito equilibrium state with a positive susceptible human state) is globally and asymptotically stable, while when $\mathcal{N} > 1$ there exists a persistent positive vector population state that is globally asymptotically stable. A study of this basic offspring number reveals that its size is affected by the rate of oviposition per reproducing mosquito (denoted in this manuscript by L) and the bio-transition factor that measures the successful transition from aquatic to adult stage mosquitoes (denoted by ξ_v). The relationship is assumed to be linear for both cases. From the expression for $\mathcal{N}$ and the aforementioned linear relationship, it is easy to see that a 10% reduction of L, respectively ξ_v, will produce a corresponding 10% reduction of $\mathcal{N}$, regardless of the sizes of other parameters. Thus, these are desirable targets for control. In addition, an increase in the death rates of the aquatic stages of the mosquito, the resting/breeding site mosquitoes, the questing mosquitoes and the fed and reproducing mosquitoes, holding all other parameters fixed, would also lead to a decrease of $\mathcal{N}$. From the control perspective, the death rates of the aquatic stage mosquitoes and that of the breeding site mosquitoes can be increased by using human and environmentally friendly larvicides and pesticides at the breeding sites, while controlling the questing mosquito population would require a continuous use of, safe insecticide treated bed nets. Control of the fed and reproducing mosquito death rates would require, when possible, eliminating the breeding sites near human habitats, thus making it difficult for the mosquitoes to visit them and/or increasing the possibility of their deaths when they visit, because they may be too fatigued to fly back.

Other desirable targets for control that can directly affect the size of the basic offspring number are: the flow rate of vectors to human habitats in search of a blood meal, at each reproductive stage k, the human biting rate of mosquitoes, which is the probability of a mosquito successfully acquiring a blood meal from a human (denoted here by q_w), and the rate of successfully returning to the breeding site after a blood meal. Reducing the flow rates to and from human habitats requires removal of the breeding sites near human habitats, when possible, while reducing contacts between humans and

the questing mosquitoes would reduce the mosquito biting rates and the probability of a questing mosquito successfully acquiring a blood meal.

A question of importance in our work was how to explicitly incorporate the gonotrophic cycles in the modelling formulation without loosing mathematical tractability but at the same time preserve their effects on the basic offspring offspring number? From equation (89), it is evident that: (i) the magnitude of the basic offspring number increases with increasing number of gonotrophic cycles accounted for, (ii) the dominant contribution to the magnitude of the basic offspring number is from the first gonotrophic cycle and (iii) the largest size of the basic offspring number will not exceed $L\xi_v q_w \left(k - 1 + \frac{1}{1-\theta_{s_k}}\right) > 0$, for the case $k > 1$. Here, $\theta_{s_k} \in [0, 1]$ is the proportion of susceptible reproducing vectors at gonotrophic or reproductive stage k, that eventually survive to re-enter the chain, contributing to the the human-mosquito interaction. In Figure 1 (with all disease classes removed, i.e. just considering the first column terms), we chose $k = 3$, that is, we decided to use the three staged model, and we highlighted the results for this case.

Two further questions of interest in the model formulation were: how large should k be and how should we incorporate the mosquitoes that were in their final gonotrophic cycle in the model? Obviously, k is determined by both the lifespan of the mosquito as well as the length of the gonotrophic cycle - how often during its lifetime a mosquito feeds and returns to lay eggs. In fact, in [11], it was noted that the length of the mosquito's gonotrophic cycle is one of the most important bionomic parameters as, among others, it estimates the frequency of contacts between mosquitoes and humans and hence the opportunities available for the mosquito to acquire and transmit the malaria parasite. Thus, the way we incorporate this aspect in our model is of great importance and warrants further discussion. In [20], where the idea of explicitly modelling the mosquito's gonotrophic cycles in a model with no disease was first introduced, it was assumed that the mosquitoes in the final stage laid their eggs at the breeding site and died with no further interaction with the human population. This assumption makes sense if we consider a 2-3 day gonotrophic cycle counting them during the entire average lifespan of a mosquito. If such an assumption was made, then in the expression for the basic offspring number, which we can call $\mathcal{N}_{non-truncated}$, we would set θ_{s_k} to zero. For this case, the magnitude of $\mathcal{N}_{non-truncated}$ does not exceed $L\xi_v q_w k$, where k, as discussed, is the number of gonotrophic cycles. However, if we truncate the number of stages at k and account for the effects of the fed mosquitoes not only in increasing the aquatic stage population but also in increasing the size of the breeding site mosquitoes, as well as the effect of questing mosquitoes at this stage in the human-mosquito interaction, then we easily see that $\mathcal{N}_{non-truncated} < \mathcal{N}$, since $\frac{1}{1-\theta_{s_k}} \geq 1$. That is, the non-truncated model estimates the basic offspring number to be smaller as compared to a truncated model. Nonetheless, as the proportion of susceptible reproducing vectors at gonotrophic stage k that eventually survive to re-enter the chain (contributing to the human-mosquito interaction) approaches zero (i.e. as $\theta_{s_k} \to 0$) (which is the case when we account for more gonotrophic cycles), then $\mathcal{N} \to \mathcal{N}_{non-truncated}$. Furthermore, a model truncated and looped at the second gonotrophic cycle will give a smaller estimate for the basic offspring number compared to the one truncated and looped at the third, and thus higher, gonotrophic cycles.

In the presence of parasitemia in the human and mosquito populations, we obtained the model's epidemiological basic reproduction number R_0, which only exists when $\mathcal{N} > 1$. We showed that when $R_0^2 < 1$, and thus $R_0 < 1$, there exist a globally and asymptotically stable positive disease-free equilibrium (DFE) which becomes unstable as R_0 grows large passing through the value $R_0 = 1$. Thus, the model's dynamic predicts that reducing R_0 to a value less than 1 would lead to disease control and possibly disease eradication. The effects of truncating and looping versus not truncating on the size of the basic reproduction number is easily seen in the expression for R_0^2. Based on the analysis that led to the value of R_0^2, as shown in (105), it can be seen that for a k staged model, we will have $R_0^2 = \sum_{j=1}^{k} R_{0_j}^2$, where $R_{0_j}^2$ represents the contribution to disease dynamics from questing mosquitoes at

the gonotrophic stage j. Each term $R^2_{0_j}$, for the k staged model, has the form $R^2_{0_j} = \beta_i \frac{1}{1-\gamma_{i_{k,1}}} C_j s^{DFE}_{w_j}$, where $\gamma_{i_{k,1}} = \varkappa \theta_{i_{k,1}} q_w < \begin{cases} q_w \\ \theta_{i_{k,1}} \end{cases} < 1$, where $\varkappa < 1$ is a constant that depends on the model parameters. Here, $\theta_{i_{k,1}}$ is the proportion of the infected fed and reproducing mosquitoes at gonotrophic or reproductive stage k that were first infected with malaria at the first gonotrophic stage and survived to re-enter the chain of feeding, egg laying and human-mosquito interaction; q_w is, as earlier defined, the probability of successfully acquiring a blood meal from humans; and C_j, for $1 < j \leq k$, is a function of the parameters, that represent the fraction of the infected vectors at the reproductive stage k, that were first infected with the malaria parasite at the reproductive stage j, and that survived to re-enter the chain, contributing to the human-mosquito interaction effects as well as to the disease transmission. In fact, $C_1 = 1$, that is, all mosquitoes infected at the first gonotrophic cycle that survive to the k^{th} gonotrophic cycle play a central role in the propagation of the disease. Furthermore, $s^{DFE}_{w_j} = \mathcal{N} - 1$ for $1 \leq j < k$ and at the k^{th} gonotrophic cycle, $s^{DFE}_{w_k}$ is bounded above by $\dfrac{1}{1-\theta_{s_k}} (\mathcal{N} - 1)$. From the aforementioned discussion, it is clear that truncating the number of gonotrophic stages at k has an impact on the estimated size of the basic reproduction number. The easiest way to see this is by setting $\theta_{i_{k,1}} = 0$ and allowing $\theta_{s_k} \to 0$, then $\beta_i \frac{1}{1-\gamma_{i_{k,1}}} C_j s^{DFE}_{w_j} \to \beta_i C_j (\mathcal{N} - 1) < R^2_{0_j}$. Note that the expression $\beta_i C_j (\mathcal{N} - 1)$ gives the contribution from each gonotrophic stage to the basic reproduction number for the k-stages non-truncated model. It makes sense that the basic reproduction number for a truncated model is larger than that for the non-truncated model, because, in truncating and accounting for the effects of the mosquitoes at the k^{th} stage on the mosquito-human interaction and the disease dynamics, we introduce mosquitoes, a small proportion though, that can potentially live forever.

From the preceding discussions, and also as highlighted by the expressions $R^2_{0_j}$ and hence R^2_0 (see equations (105)-(114)), as well as the steady states defined in equations (96)-(98), it is evident that the greatest contribution to the magnitude of the basic reproduction number is from the mosquitoes infected at the first gonotrophic cycle that survive later gonotrophic cycles, exhausting the length of their life cycle. In fact, it highlights the fact that newly emerged mosquitoes that are infected with the malaria parasite during their first blood meal play an important and strong role in the size of the mosquito population as well as the malaria disease dynamics and burden. Thus targeting these mosquitoes will play a great role in reducing R_0 and hence the disease burden and transmission. Additionally, mosquitoes at later stages also impact the size of the basic reproduction number and hence the disease burden, but their contributions decreases with increasing gonotrophic cycle at which they were infected. In particular, if we inspect steady states defined in equations (96)-(98), we see that the steady state populations for the breeding site, reproducing and questing mosquitoes at later gonotrophic cycles are decreasing with increasing gonotrophic cycles.

From the expression for R^2_0, it is also evident that the aquatic mosquito stages have an impact on the disease burden and dynamics. Inhibiting the successful transition from the aquatic to the adult staged mosquitoes will lower ξ_v, and hence R_0, and this will reduce the disease burden. This can be achieved by reducing the density of mosquito eggs, larvae and pupa at breeding sites. Reducing the number of bites that a mosquito places on a human, as well as the probability of a successful meal, are all desirable targets, that can be achieved with the use of insecticide treated bednets, reducing contacts between humans and mosquitoes. Obstructing the flow between human habitats and the breeding sites by removing the breeding sites from human habitats will also lead to a lower R_0 value and hence towards a disease control.

One of the control methods we were interested in was the use of mosquitocidal drugs administered to infected individuals, that have a potential to kill mosquitoes that feed on these humans. The idea is based on a 2018 trial study that showed that *Anopheles sp* mosquitoes can be targeted and killed when they feed on humans treated with a high dose of a safe mosquitocidal drug such as ivermectin. From our mathematical model, and the conceptual model presented in Figure 2, the rate at which humans were recruited into the treated class is given by δ_h. From the expression for R^2_0, an increase in

δ_h would lead to a reduction in the size of R_0^2 and hence R_0. This means that if this drug combination is eventually approved for mass human use, it will play an important role in reducing the disease burden, especially if it is the first line drug used to treat malaria. Additionally, if the proportion of mosquitoes that survived, which we denoted here by α, was smaller then the size of the infected mosquitoes will reduce, hence also positively impacting the malaria control. This can easily be seen since the function g defined in (95) is 1 when $\alpha = 0$ and less than 1 for $\alpha \in [0, 1)$. Thus a smaller α means a smaller steady state mosquito population, as evident in equations (96)-(98). Thus, if this medication combination is found safe and approved for use by infected malaria patients, it will provide an additional way for better malaria control.

To conclude, we have presented a model that explicitly describes the roles of the mosquitoes at various gonotrophic cycles in the mosquito dynamics, and how they contribute to the basic offspring number in the absence of the malaria disease, as well as the basic reproduction number, in the presence of disease. The model clearly shows the complexity of the malaria problem and the fact that control must be applied at various fronts: eliminating breeding sites and breeding site mosquitoes, inhibiting contacts between humans and mosquitoes, inhibiting the successful transition from aquatic to adult stage mosquitoes and also reducing mosquito size. The presented model is a first step towards understanding the entire complex malaria problem. Further work will include analyzing the full malaria problem, studying the impact of the treatment class on the disease burden, amongst others.

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Appendix A: Some technical definitions (cooperative systems, partial order relation and order interval)

Definition 2 (Cooperative systems.) *Let $\boldsymbol{x} \in \Omega$ be a vector of state variables and consider an n-dimensional autonomous system of ordinary differential equations*

$$\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x}), \qquad \boldsymbol{x}(0) = \boldsymbol{x}_0, \tag{115}$$

where $\Omega \subseteq \mathbb{R}^n$ is an open subset, and $\boldsymbol{f} : \Omega \longrightarrow \mathbb{R}^n$ is a continuous function. System (115) is called cooperative if for every $i, j \in \{1, 2, ..., n\}$ such that $i \neq j$, the function $f_i(x_1, ..., x_n)$ is monotone increasing with respect to x_j.

Thus, if $\boldsymbol{f}$ is differentiable, it suffices to verify that $\dfrac{\partial f_i}{\partial x_j} \geq 0$ for every $i, j \in \{1, 2, ..., n\}, i \neq j$. It is easy to verify that the requirements of Definition 2 are verified for system (80), since $A(\boldsymbol{x})$ is an almost constant Metlzer matrix.

Definition 3 (Partial order relation.) *Let there be given an arbitrary set X. A partial order relation on X is a relation $\leq$ that is reflexive, transitive and antisymmetric in the sense that*

(i) $\forall x \in X, x \leq x$, *(reflexive);*

(ii) $\forall x, y, z \in X, x \leq y, y \leq z \Rightarrow x \leq z$, *(transitive);*

(iii) $\forall x, y \in X, x \leq y, y \leq x \Rightarrow x = y$ *(antisymmetric).*

In the context of Definition 3, we write $x < y$ if $x \leq y$ and $x \neq y$. We will use a partial order on $X = \mathbb{R}^n$ by defining for any $\boldsymbol{x}$, $\boldsymbol{y}$ in $\mathbb{R}^n$, $\boldsymbol{x} \leq \boldsymbol{y}$ if $x_i \leq y_i$ for all $i = 1, 2, 3 \cdots, n$.

Definition 4 (Order interval.) *If* $\boldsymbol{u}, \boldsymbol{v} \in \mathbb{R}^n$, *with* $\boldsymbol{u} \leq \boldsymbol{v}$, *then we write* $[\boldsymbol{u}, \boldsymbol{v}] \equiv \{\boldsymbol{y} \in X : \boldsymbol{u} \leq \boldsymbol{y} \leq \boldsymbol{v}\}$ *and call it the order interval generated by* $\boldsymbol{u}$ *and* $\boldsymbol{v}$.

The following is an important result in the theory of monotone systems that was used in establishing some results:

Theorem 7 (see Theorem 6 [1]) *Let* $\boldsymbol{a}$, $\boldsymbol{b} \in \Omega$ *such that* $\boldsymbol{a} \leq \boldsymbol{b}$, $[\boldsymbol{a}, \boldsymbol{b}] \subset \Omega$ *and* $\boldsymbol{f}(\boldsymbol{b}) \leq 0 \leq \boldsymbol{f}(\boldsymbol{a})$. *Then, (115) defines a (positive) dynamical system on* $[\boldsymbol{a}, \boldsymbol{b}]$. *Moreover, if* $[\boldsymbol{a}, \boldsymbol{b}]$ *contains a unique equilibrium* $\boldsymbol{p}$, *then* $\boldsymbol{p}$ *is globally asymptotically stable on* $[\boldsymbol{a}, \boldsymbol{b}]$.

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