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BSc Biology with a Modern Language
Robert Tucker Gilman

Modelling Malaria Transmission with Seasonal and Year-round Agriculture

Abstract

It has long been known that irrigation of rice paddies in Sub-Saharan Africa produces ideal aquatic conditions for the larvae of some *Anopheles* mosquito species, but empirical evidence has only recently suggested that this is translating into increased malaria transmission. In natural settings, malaria vector abundance is limited by rainfall, which in tropical regions only consistently occurs during the rainy season. However, since irrigation is usually conducted even through the dry season, providing a temporally stable supply of larval sites, rice paddies may alter typical phenological patterns of malaria transmission. We formulated a compartmental model to investigate how the relative addition to the system of mosquitos from seasonal and rice field larval sites affects malaria transmission at a range of mosquito abundances and biting rates. There were several scenarios where mean transmission was highest at intermediate relative contributions of rice and seasonal mosquitos, suggesting that the two habitats may sometimes interact to drive infection beyond levels that one alone would reach. We found that infection increased significantly with the introduction of rice fields at low baseline prevalence, but where baseline prevalence was high, the presence of rice fields reduced infection. We also found that at low mosquito biting rates, infection generally decreased with the introduction of rice fields, but at high mosquito biting rates, increasing presence of rice fields intensified infection. Since the direction and magnitude of the impact of rice fields on mean prevalence varied depending on interactions with other factors, more research is needed to examine if and when expansion of rice cultivation can be justified from a public health perspective. Our work represents the first attempt to mathematically model how irrigation influences malaria at a broad scale, and identifies several trends which merit further, more detailed investigation.

Lay Abstract

It is increasingly recognised that the irrigation of rice paddies may contribute to higher malaria transmission rates in surrounding human settlements. This is because some species of malaria-transmitting mosquito lay their eggs in the standing water provided by irrigated fields. Irrigation may also be disrupting seasonal patterns of malaria by supplying standing water all year round whereas in nature it would only be available during the rainy season of the Sub-Saharan African regions where malaria is most prevalent. We developed a theoretical model to assess how the presence of rice paddies could alter malaria transmission in systems containing two species of mosquito for which we varied abundances and biting rates. In some cases we found that the greatest number of humans became infected in settings with roughly equal amounts of irrigated and non-irrigated landscape features, suggesting that the two habitats may sometimes interact to drive infection beyond levels that one alone would reach. We also found that where malaria transmission was otherwise low, introducing rice fields substantially increased it. However, where transmission was already high, introducing rice fields reduced malaria. Overall, the effects of rice paddies on malaria transmission appear to be variable, and further research is needed to determine if and how expansion of rice cultivation can be reconciled with the potential risks to public health.

1. Introduction

Malaria is a vector-borne disease spread by mosquitos of the *Anopheles* genus and caused by *Plasmodium* parasites, particularly *Plasmodium falciparum* in the majority of serious cases. Malaria is a leading cause of illness and mortality, with the WHO reporting an estimated 247 million cases with 619,000 consequent deaths worldwide in 2021, most severely affecting young children and pregnant women (WHO, 2022). Challenges to malaria reduction efforts include increasing resistance of vectors to insecticides (Toé *et al*, 2014), emerging parasite resistance to artemisinins, the principal treatment for the disease (Xie *et al*, 2020), as well as the possibility that climate change could expand the ranges of vectors (Ryan *et al*, 2020). However, some research breakthroughs have presented cause for optimism, particularly the proposed rollout of the recently WHO-approved R21/Matrix-M™ *P. falciparum* vaccine (WHO, 2023), and the potential for vector control with CRISPR-Cas9-based gene drives (Hammond and Galizi, 2017).

Concerted campaigns to increase surveillance of malaria and develop and implement interventions to reduce its spread resulted in steady yearly declines in global case rates beginning in 2000 (Bhatt *et al*, 2016), but this stalled from 2015 onwards. Moreover, disruptions stemming from the Covid-19 pandemic coincided with elevated rates in 2020 and 2021 (Liu *et al*, 2021; WHO, 2022). The disease is most prevalent in tropical regions and its distribution is strongly correlated with poverty. Its continuing toll - despite the array of treatments and preventative measures available - is attributed in large part to the economic burden of the medical costs, loss of working hours and premature deaths which its endemicity entails (Sachs and Malaney, 2002).

One measure which the region worst afflicted by malaria, Sub-Saharan Africa (Oladipo *et al*, 2022), has taken to improve its economic situation is expansion of rice cultivation (Seck *et al*, 2010). Rice paddies are generally irrigated all year round, generating a constant supply of shallow puddles which provide ideal oviposition sites for some malaria vector species, whereas other stagnant water sources which *Anopheles* species rely on only appear ephemerally during the rainy season (Sinka *et al*, 2010). Notwithstanding, increasing rice farming has been justified by the so-called ‘paddies paradox’, a term coined in a seminal paper by Ijumba and Lindsay (2001) to describe a surprising lack of correlation between malaria incidence and the presence of irrigated rice fields. The explanation given for this was that the economic prosperity associated with growing this cash crop meant that inhabitants of the surrounding settlements were better able to access preventions and treatments against malaria.

However, Chan *et al* (2021) have since conducted a systematic review and meta-analysis which found that after concerted efforts were made around the turn of the millennium to make the distribution of these resources in Sub-Saharan Africa more equitable, prevalence of malaria has on average become significantly higher in rice-growing regions than other areas. This is not a universal phenomenon though, with several studies cited within the paper reporting the opposite or no effect of irrigation. Consequently, research is needed to investigate the precise mechanism by which rice fields modulate malaria prevalence and incidence, and if and how expansion of rice cultivation can be reconciled with malaria elimination efforts.

Of the four main malaria vector species present in Sub-Saharan Africa, the larvae of two - *Anopheles. funestus s.s.* and *Anopheles. coluzzii* - preferentially occupy large, permanent water sources such as rice paddies, although they are temporally separated from one another, favouring microhabitats fostered by different successional stages of crop growth (Sinka *et al*, 2010). *Anopheles. gambiae s.s.,* is more reliant on rain-dependent temporary larval sites such as puddles, with this preference thought to be a driving factor behind its ongoing speciation from *An. coluzzii* (Niang *et al*, 2020). *Anopheles arabiensis* is more opportunistic in its oviposition behaviour, equally content to use permanent and temporary larval sites (Chirebvu and Chimbari, 2015). *An. gambiae s.s.* has historically been considered as making the largest contribution to malaria transmission in Sub-Saharan Africa, but growing evidence suggests that *An. funestus s.s.* has overtaken it in much of the area where both are present (Msugupakulya *et al*, 2023). However, other species are more dominant at the regional level (Wiebe *et al*, 2017), and some studies have reported large contributions by less-studied ‘secondary’ vector species (Msugupakulya *et al*, 2023). Heterogeneities in the abundance and distribution of rice paddies in Sub-Saharan Africa are likely to influence species composition at the local and regional levels, and the different species’ relative effectiveness as vectors will determine malaria incidence.

Malaria is an extremely complex system, its spread underpinned by the convoluted life cycles of its vector and disease agent, an array of environmental and spatial factors, various human demographic and socio-economic variables, and the effects of any interventions implemented. As a consequence, malaria is an archetypal example of where mathematical modelling can provide key insights into patterns and mechanisms of response variables which cannot easily be observed or predicted from raw data alone (Smith *et al*, 2017). Ronald Ross (1915) was among the first to recognise this, and his compartmental model of malaria was able to demonstrate that female mosquitos were a fragile part of the system and interventions targeted at them could eliminate the disease if their population went below a specific threshold. This work proved foundational in the field of epidemiology as a whole and most subsequent malaria models have built on the framework he developed, incrementally introducing new complexity to more accurately represent reality (Brauer *et al*, 2017). The most significant development to the model has been credited to Macdonald (1956), who realised the importance of incorporating the latent period of infection in mosquitos due to its nonlinear interaction with vector control efforts. This is considered such a key contribution that modern compartmental malaria models are often referred to as ‘Ross-Macdonald models’ (Smith *et al*, 2012).

High-impact modelling frameworks which have assessed the association between availability of stagnant water larval sites and malaria transmission have generally - explicitly or implicitly - considered vector abundance as dependent on rainfall and other climatic factors (Hoshen and Morse, 2004; Tompkins and Ermert, 2013; Parham and Michael, 2010; Bomblies *et al*, 2009). This approach omits the potential contribution of irrigated crop fields to the preservation of important malaria vector species throughout the year, irrespective of rainfall levels. Updated modelling methods are needed to unravel how anthropogenic and natural water sources interact to mould population densities of different mosquito species. Jiang *et al* (2023) formulated an agent-based model which used climatic data, details of irrigation regimes, and hydrology to model the formation of larval habitats at high resolution in a specific region of Kenya. While undoubtedly useful, such highly specific strategies should be complemented by broad theoretical approaches which generate universal insights that provide context for more focused studies.

In this study we present a compartmental model of malaria which includes two vector classes: one which persists throughout the year thanks to its preference for larval sites provided by irrigated rice paddies, and one whose abundance spikes during the rainy season before dropping off sharply in the dry season. We vary biting rates and baseline malaria prevalence to show that introducing temporally stable mosquitos which use rice field larval sites to different biotic settings results in differing impacts on transmission. Although the model is relatively simple, it represents a useful initial foray into malaria modelling in the context of irrigation, demonstrating that transmission in this context is influenced by non-linear interactions which are not taken into account in other models.

2. Methods

2.1. Model Structure

We developed a deterministic compartmental model of malaria to examine how the presence of permanent larval habitats provided by irrigated rice paddies impacts transmission of *Plasmodium falciparum* (Figure 1). The model is a system of delay differential equations which incorporates classes, tracked in absolute numbers, for two vector species. One of these has a constant population size, representing mosquitos which oviposit in rice fields which are irrigated year-round. The population size of the other fluctuates seasonally, representing species which oviposit in ephemeral water sources that only appear during the rainy season. The system also includes a latency period before mosquitos become infectious after biting an infected human. In brief, humans can move from susceptible to the infected compartment, I_h, and back, while mosquitos may move between susceptible, exposed or infected compartments: either S_{m1}, E_{m1} and I_{m1} for the species which uses rice larval sites, or S_{m2}, E_{m2} and I_{m2} for the species which uses temporary larval sites. The model is explained in full below.

The system constitutes the following series of delay differential equations:

$$\frac{dS_{m1}}{dt} = (p \cdot M_r(t)) - (a_1 \cdot c \cdot I_h \cdot S_{m1}) - (\mu_2 \cdot S_{m1})$$

$$\frac{dE_{m1}}{dt} = (a_1 \cdot c \cdot I_h \cdot S_{m1}) - (\mu_2 \cdot E_{m1}) - (a_1 \cdot c \cdot I_h \cdot S_{m1}[t - \tau_m] \cdot e^{-\tau_m \cdot \mu_2})$$

$$\frac{dI_{m1}}{dt} = (a_1 \cdot c \cdot I_h \cdot S_{m1}[t - \tau_m] \cdot e^{-\tau_m \cdot \mu_2}) - (\mu_2 \cdot I_{m1})$$

$$\frac{dS_{m2}}{dt} = (p \cdot M_f(t)) - (a_2 \cdot c \cdot I_h \cdot S_{m2}) - (\mu_2 \cdot S_{m2})$$

$$\frac{dE_{m2}}{dt} = (a_2 \cdot c \cdot I_h \cdot S_{m2}) - (\mu_2 \cdot E_{m2}) - (a_2 \cdot c \cdot I_h \cdot S_{m2}[t - \tau_m] \cdot e^{-\tau_m \cdot \mu_2})$$

$$\frac{dI_{m2}}{dt} = (a_2 \cdot c \cdot I_h \cdot S_{m2}[t - \tau_m] \cdot e^{-\tau_m \cdot \mu_2}) - (\mu_2 \cdot I_{m2})$$

$$\frac{dI_h}{dt} = (H - I_h) \cdot b(a_1 \cdot I_{m1} + a_2 \cdot I_{m2}) - (r \cdot I_h)$$

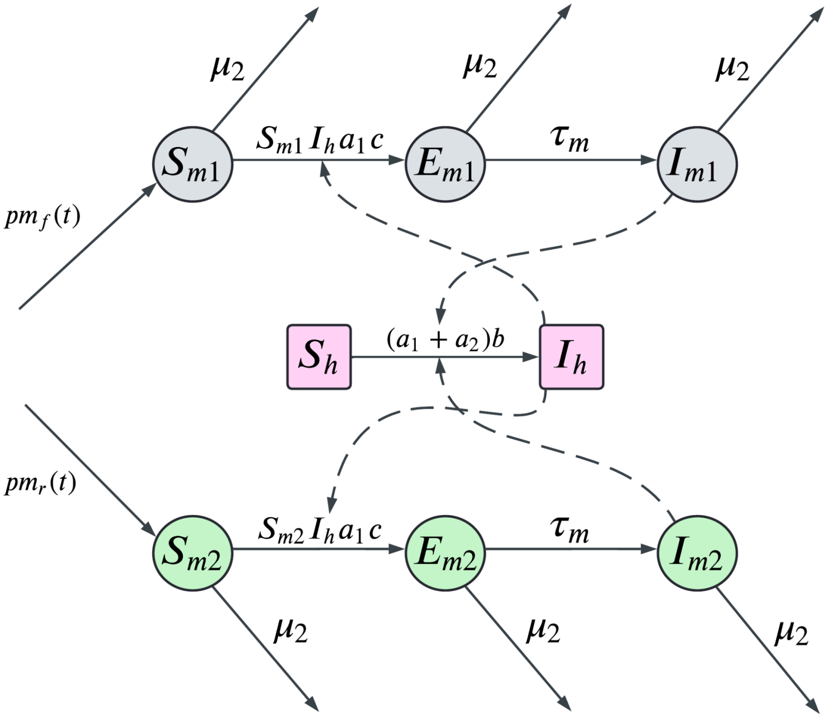

Figure 1 Flow diagram summarising the structure of the model and movement between compartments. Direct additions to compartments are shown by solid arrows. Indirect contributions by compartments to movements between compartments of another class are shown by dashed arrows.

Only female mosquitos are modelled, since males do not take blood meals and hence do not contribute to infection (Chavasse, 2002). The function $m_r(t)$ represents the temporally constant daily number of mosquitos of one species, hereafter referred to as 'rice mosquitos' which would emerge from a homogeneous landscape of permanent larval sites. $m_f(t)$ describes the fluctuating daily number of mosquitos of the second species, hereafter referred to as 'seasonal mosquitos', which would emerge from temporary larval sites, spiking in abundance during the rainy season. Mosquitos can move between the following compartments: susceptible, denoted by S_{m1} for rice mosquitos and S_{m2} for seasonal mosquitos; exposed, denoted by E_{m1} for rice mosquitos and E_{m2} for seasonal mosquitos, and infected, denoted by I_{m1} for rice mosquitos and I_{m2} for seasonal mosquitos.

To model heterogeneous landscapes, we introduce the parameter p which governs the relative land coverage of permanent and temporary larval sites. Overall, at each time step, rice mosquitos enter the system in the susceptible state at a rate defined by $M_r(t) \cdot p$, and susceptible seasonal mosquitos enter the system at a different rate defined by $M_f(t) \cdot (1 - p)$. *Anopheles* mosquitos may die at any point during their adult lives due to natural causes such as predation (Collins *et al*, 2019). This is represented in the model by removal from the system of a constant proportion of all mosquito compartments, defined by the parameter μ_2, the mosquito mortality rate.

After a mosquito takes a blood meal from an infected human, *Plasmodium* parasites may enter its gut in the form of gametocytes which have invaded human red blood cells. The probability that the mosquito contracts the infection is mediated by gametocyte concentration in the human bloodstream (Churcher *et al*, 2015). After gametocytes are taken up by a mosquito, they undergo a complex series of developmental and reproductive changes known collectively as sporogony. Until the parasites reach the final stage of this process, the release of infectious sporozoites into the salivary glands of the mosquito, their mosquito host will be unable to transmit malaria to humans even if they bite a susceptible individual (Ouologuem *et al*, 2023). The duration of time between when a mosquito contracts *Plasmodium* parasites and when it eventually becomes infectious is called the latent period, and it varies significantly depending on species and environmental factors (Stopard *et al*, 2021). In our model, those mosquitos that are in the latent period of infection are classed as exposed, represented by the E_{m1} and E_{m2} compartments, and only move into the infected class once a number of time steps equal to the value of the mosquito latent period (τ_m) has passed.

Mosquitos thus move from the susceptible to the exposed class at rates determined by the product of their species' biting rate, the proportion of bites by susceptible mosquitos on infectious humans which result in infection as determined by gametocyte density (c), and the abundance of infected humans, I_h. In our model, the biting rates (a_1 for rice mosquitos and a_2 for seasonal mosquitos) are spatial search rates which represent the fraction of the area, within which humans can be thought of as homogeneously distributed, that each mosquito of the corresponding species searches through at each time step, biting any human it finds. After the duration of the latent period, the exposed mosquitos that have survived will become infectious. As a result, the rate of transfer from the exposed to the infected compartments uses the same equation as defines movement from susceptible to exposed classes, but uses S_h abundance τ_m (mosquito latent period) days ago, and the product is also multiplied by a proportion equal to $e^{-\tau_m \cdot \mu_2}$ which corresponds to the survivorship given the cumulative mortality rate during the time steps in the latent period.

Humans move between susceptible and infected classes, although only the infected compartment, I_h, is explicitly modelled since the number of susceptible humans is just the abundance of infected humans subtracted from the total human population size, H. Humans are represented in absolute numbers, and their total population size remains constant. The human population is not structured spatially or by factors such as age or immunity, so every individual is considered equally at risk of infection. Susceptible humans may become infected and move into the I_h compartment at a rate dependent on how many infectious vectors are in the system, how likely these vectors are to encounter them, and the probability that they pass on their infection, which is related to the density of parasites in mosquitos' salivary glands (Churcher *et al*, 2017). Therefore, mathematically, the rate at which humans become infected by each species is defined by the product of that mosquito species' abundance (the value in the I_{m1} or I_{m2} compartment), its respective biting rate ($a_1$or a_2) and the proportion of infectious bites which result in infection (b). After a certain period of time, infected humans are able to remove *Plasmodium* gametocytes from their blood and thus are no longer infectious to mosquitos. This is represented in the model as a constant proportion of infected humans (r) continuously returning from the infected to the susceptible class.

The system was developed and run in R version 4.4.0 (R Core Team, 2023) using the *deSolve* package (Soetaert *et al*, 2010) for solving differential equations.

2.2. Data Collection

M_f is intended to represent the emergence of mosquitos which only use seasonal larval sites, so we used mosquito catch data collected in a rural Ethiopian village where irrigated agriculture is not practised, extracted from the literature, namely Jaleta *et al* (2013). The samples we used were taken using artificial pit shelters between February 2010 and January 2011, and we accessed them via the *MapVEu* tool

Table 1 Description of parameters. Values for b, c, r, τ_m and μ_2 were taken from literature ranges given in Mandal *et al* (2011). Vector abundance used for M_f was taken from Jaleta *et al* (2013), accessed via *VectorBase* (Alvarez-Jarreta *et al*, 2024).

Parameter	Description	Value/Value Range
a_1	Rice mosquito biting rate per human	0.00015 - 0.0005
a_2	Seasonal mosquito biting rate per human	0.00025 - 0.0005
b	Proportion of bites by an infectious mosquito which result in human infection	0.35
c	Proportion of bites by a susceptible mosquito on an infectious human which result in mosquito infection	0.5
H	Total human population size	1000
r	Human recovery rate	0.01
$M_r(t)$	Daily abundance of rice mosquitos	43.53
$M_f(t)$	Daily abundance of seasonal mosquitos	0 - 288
τ_m	Latent period of mosquitos	10
μ_2	Per capita mosquito mortality rate	0.1
p	Proportion of M_r which actually enters the system; $1 - p$ is the proportion of M_f which actually enters the system	0.1 - 0.9

hosted by *VectorBase* (Alvarez-Jarreta *et al*, 2024). M_r represents emergence of mosquitos whose larval habitats are permanent, so the daily abundance was kept constant throughout the year. We set this constant value at 43.53, which is the average value for M_f, in order to control for the effect of relative total vector species abundance.

Descriptions, and values, for all parameters used are listed in Table 1. Values for b, c, r, τ_m and μ_2 were selected from around the middle of the literature ranges given in Mandal *et al* (2011).

2.3 Parameter Manipulation and Output Measurement

An. gambiae, which uses temporary larval sites, is generally considered to have the strongest affinity for human hosts - a tendency known as anthropophily - of the malaria vectors present in Sub-Saharan Africa (Fahmy *et al*, 2015). Among the other most important vector species, all of which oviposit in permanent larval sites, *An. funestus* and *An. coluzzii* are also both regarded as anthropophilic, but slightly less so than *An. gambiae* (Akogbéto *et al*, 2018; Akoton *et al*, 2023). With this in mind, the biting rate a_2 for seasonal mosquitos was kept constant for each set of runs, whereas we varied a_1 from 60% to 100% of a_2 at increments of 10%. This was intended to reflect the range of possible relative biting rates of rice mosquitos compared to seasonal mosquitos in the absence of relevant empirical evidence on a per-individual-mosquito basis. We did not model a species based on *An. arabiensis*, which is considered zoophilic and equally uses temporary and permanent larval sites (Chirebvu and Chimbari, 2015).

Across all combinations of biting rates, the model was run 9 times varying p from 0.1 to 0.9 at increments of 0.1. This altered the proportions of mosquitos arriving from each source in the model, thus implicitly simulating landscapes with different relative proportions of irrigated rice fields versus seasonal larval habitats.

Anopheles biting rates are difficult to measure empirically, and may be altered by interventions such as bed nets (Mandal *et al*, 2011). To assess scenarios with low, medium and high biting rates, we conducted three sets of runs adjusting the values of a_2 to 0.00025, 0.000375 or 0.0005 respectively, while not altering M_f and still varying p from 0.1 to 0.9 and a_1 from 60 to 100% of a_2.

In their literature review, Chan *et al* (2021) assessed studies that compared malaria transmission in villages which practised rice cultivation with control villages 5 - 20 km away. In general, they found that where human malaria prevalence in control villages was low (≤25%), greater prevalence was seen in rice-growing villages; where control prevalence was intermediate (6 - 75%), prevalence was lower in rice-growing villages, and where control prevalence was high (>75%), there was no significant difference in comparison to rice-growing villages. We simulated each of these three control scenarios - at each configuration of p and relative biting rates - by manipulating the daily seasonal mosquito abundances given by $M_f(t)$, either halving them, keeping them the same as taken from the literature, or doubling them. These specific transformations were chosen because they resulted in annual maximum human malaria prevalences within the ranges mentioned above. For these runs, a_2 was set to 0.0003.

3. Results

3.1 Transmission Dynamics

Regardless of parameter configurations, the model outputs reached stable cycles for the frequencies of all compartments, with repeated phenological fluctuations (a representative example is shown in Figure 2). Seasonal spikes in input of susceptible seasonal mosquitos into the system prompted a cascade of corresponding peaks in abundance of exposed seasonal mosquitos, then infected seasonal mosquitos, then humans. Shortly after these peaks, abundance of susceptible, exposed and infected seasonal mosquitos fell off dramatically to near 0, and the frequency of infected humans also troughed to its lowest point. Levels of rice mosquitos changed much less through the year, with only small increases in the exposed and infected compartments and decreases in the susceptible compartment coinciding with rising human infections, and then subsequent changes in the opposite direction when infected human prevalence drops. The magnitude of all seasonal fluctuations increased as the relative proportion of rice compared to seasonal mosquitos (p) decreased.

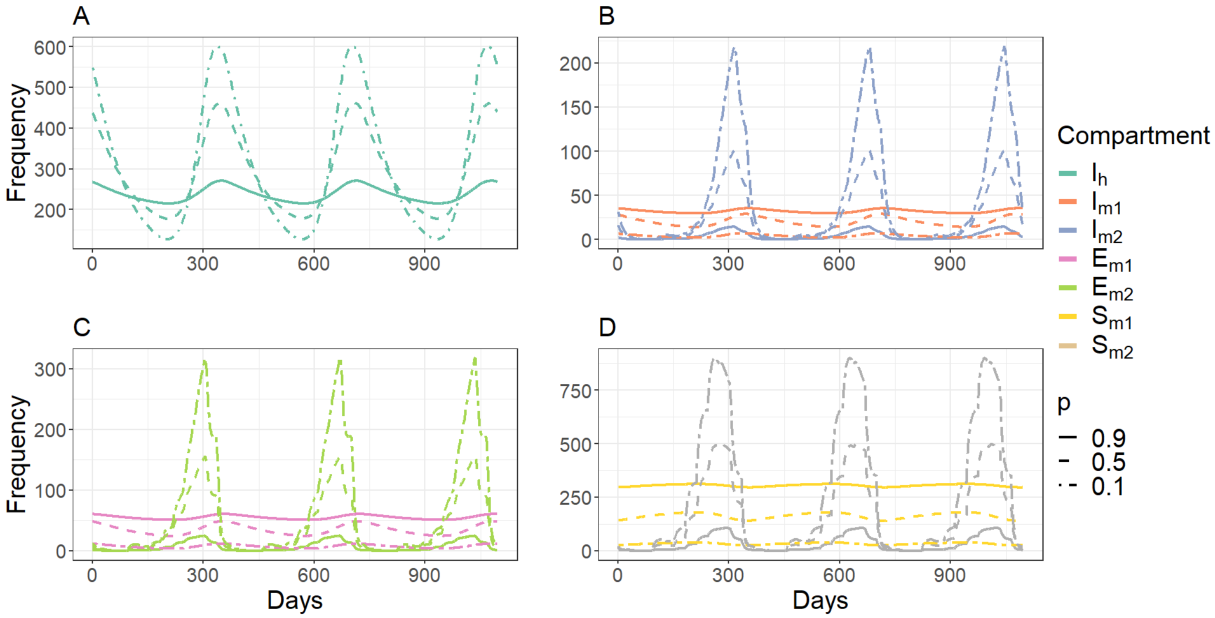

Figure 2 A representative example set of time series plots tracking the abundances in the compartments of our model, with intermediate values for $M_f(t)$, a_2 at 0.0003, a_1 at 0.00024 (80% of a_2), and p at 0.9 (solid line), 0.5 (dashed line) or 0.1 (dash dotted line). (A) Infected humans, I_h. (B) Infected rice and seasonal mosquitos, I_{m1} and I_{m2} respectively. (C) Exposed rice and seasonal mosquitos, E_{m1} and E_{m2} respectively. (D) Susceptible rice and seasonal mosquitos, S_{m1} and S_{m2} respectively.

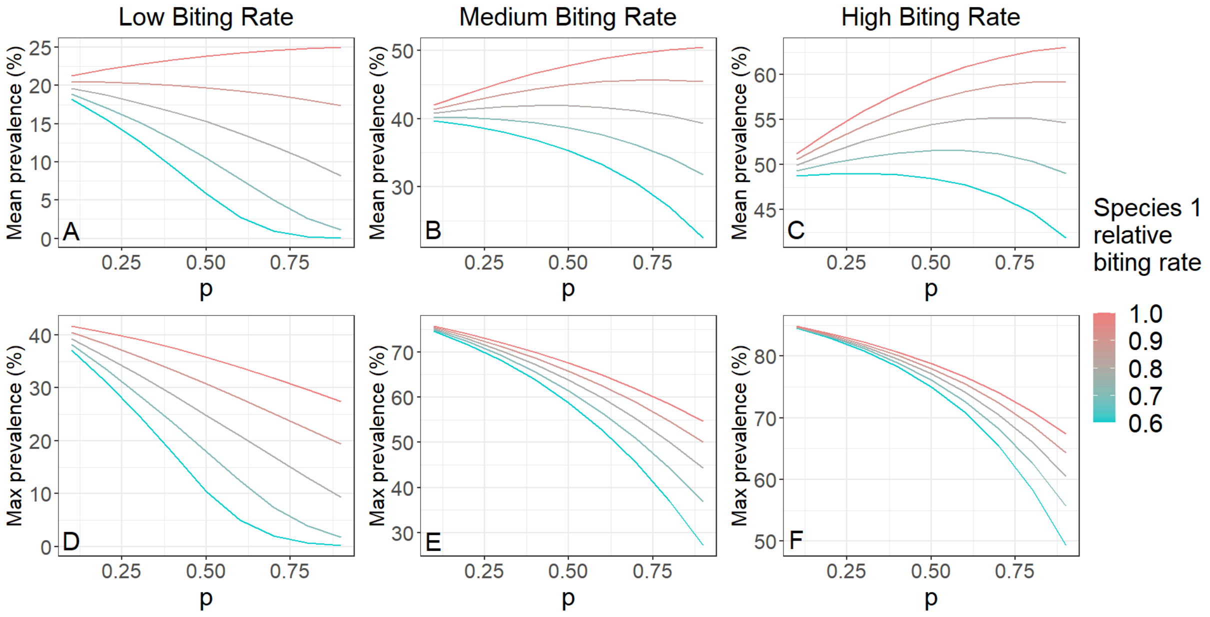

Figure 3 Plots of the mean (A-C) and maximum (D-F) human malaria prevalences as p varies from 0.1 to 0.9 at increments of 0.1. p is the proportion of rice mosquitos counted in M_r which enter the system, while $1 - p$ is the proportion of seasonal mosquitos from M_f which enter the system. Consequently, as p increases the relative contribution of rice mosquitos increases and the relative contribution of seasonal mosquitos decreases. The colour of the lines represent the relative biting rate of rice (a_1) versus seasonal (a_2) mosquitos for that run, from red (a_1 and a_2 are the same) to cyan (a_1 is 60% of a_2). (A,D) are for a value for a_2 of 0.00025. (B,E) are for a value for a_2 of 0.000375. (C,F) are for a value of a_2 of 0.0005.

3.2 Varying Mosquito Biting Rates

We ran the model across low, medium and high values of seasonal mosquito biting rate (a_2). The values for a_2 that we used were 0.00025 (low), 0.000375 (medium) and 0.0005 (high). For each value of a_2 we also varied a_1, the rice mosquito biting rate, from 60-100% of the value of a_2. We assessed differential effects of these characteristics on malaria transmission in different landscapes by additionally varying p, the relative contribution to the system of rice paddy larval sites compared to temporary larval sites. The values of p we used ranged from 0.1 to 0.9 at increments of 0.1 for each configuration of a_1 and a_2. From the resulting time series data, we calculated the mean and maximum human malaria prevalences at the stable state for each parameter configuration, presented in Figure 3. Across all outputs, mean and maximum prevalence always rose with a_1, meaning that as biting rates increased, infection increased.

For all three values of seasonal mosquito biting rate, the yearly maximum prevalence consistently decreased with p (Figure 3D-F), meaning the seasonal peaks of infection were always highest where the contribution of rice fields was lowest. However, the effects on mean prevalence were more varied (Figure 3A-C). Where a_1 and a_2 were equal (the red lines on the plots), mean prevalence always rose with p, and where a_1 was 60% of a_2 (the cyan lines on the plots), it always fell as p increased - so where biting rates were equal, more rice fields resulted in more infection, whereas where the rice mosquito biting rate was much lower, infection was higher when there were more temporary larval sites. At intermediate relative values of a_1 and low a_2, mean prevalence always reduced as p rose. However, mean prevalence often peaked at intermediate values of p from 0.5 to 0.8 at intermediate a_1 and medium and high values of a_2, meaning that in these scenarios, transmission was greatest where both types of larval habitat had intermediate contributions to the system.

3.3 Varying Baseline Prevalence

We ran the model across low, medium and high baseline malaria prevalences. To represent these three scenarios, we set the daily values for $M_f(t)$, the daily seasonal mosquito abundance if the whole landscape consisted only of temporary larval sites, as either half, unadjusted or double those that we extracted from the literature. We also varied a_1, the rice mosquito biting rate, from 60% to 100% of the value of a_2, the seasonal mosquito biting rate, for each baseline prevalence. In order to assess differential effects of introducing rice fields to the different baseline prevalence settings, we additionally varied p, the proportional relative contribution to the system of rice paddy larval sites compared to temporary larval sites. The values we used for this ranged from 0.1 to 0.9 at increments of 0.1 for each configuration of a_1 and baseline prevalence. From the resulting time series data, we calculated the mean and maximum human malaria prevalences at the stable state for each parameter configuration, presented in Figure 4. Across the three sets of outputs, mean and maximum prevalence always rose with a_1, meaning that as biting rates increased, infection increased.

At low baseline prevalence, Chan *et al* (2021) found that transmission increases with the presence of rice paddies. We found a linear trend corroborating this prediction in terms of mean prevalence (Figure 4A) at all but the lowest value of a_1 (the green line). Yearly maximum prevalence (Figure 4D) also increased with p at the three highest values of a_1 but decreased where a_1 was the lowest. Furthermore, maximum prevalence peaked at an intermediate value for p of 0.4 where a_1 was 70% of a_2, meaning that at this relative rice mosquito biting rate, the highest yearly peak of prevalence occurred where there were intermediate contributions of each type of larval habitat.

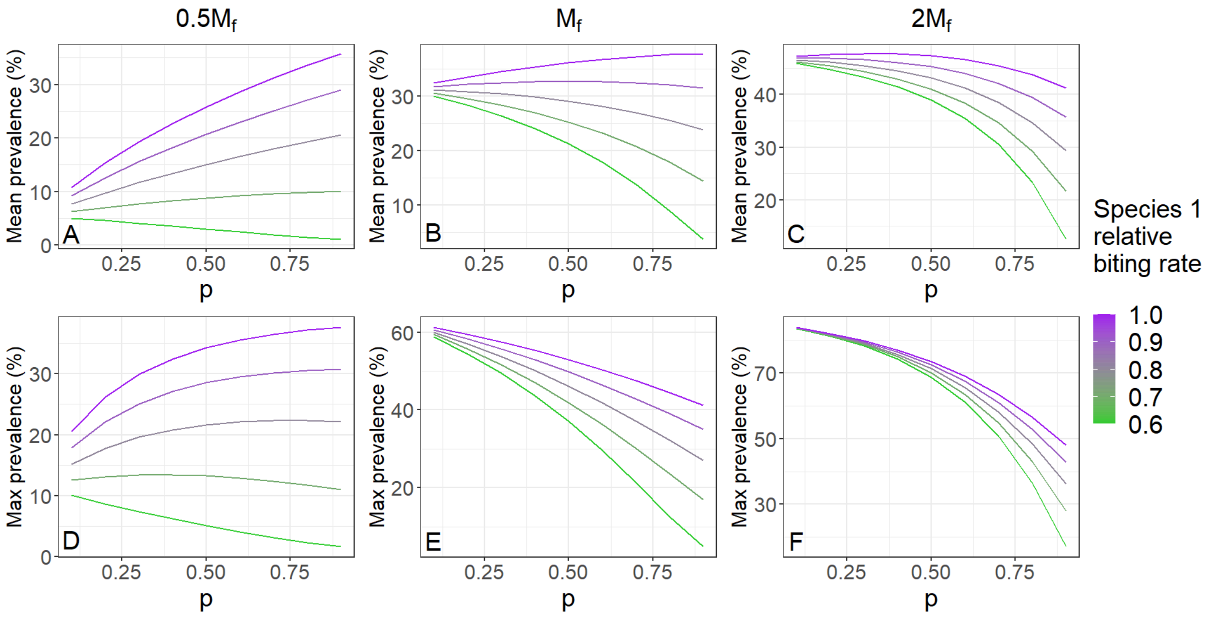

Figure 4 Plots of the mean (A-C) and maximum (D-F) human malaria prevalences as p varies from 0.1 to 0.9 at increments of 0.1. p is the proportion of rice mosquitos counted in M_r which enter the system, while $1 - p$ is the proportion of seasonal mosquitos from M_f which enter the system. Consequently, as p increases the relative contribution of rice mosquitos increases and the relative contribution of seasonal mosquitos decreases. The colour of the lines represent the relative biting rate of rice (a_1) versus seasonal (a_2) mosquitos for that run, from purple (a_1 and a_2 are the same) to green (a_1 is 60% of a_2). (A,D) are at low prevalence baseline prevalence i.e. values for $M_f(t)$ are halved. (B,E) are at intermediate baseline prevalence i.e. values for $M_f(t)$ are unaltered. (C,F) are at high baseline prevalence i.e. values for $M_f(t)$ are doubled.

Where baseline prevalence was intermediate, Chan *et al* (2021) found that transmission usually increases with the presence of rice paddies. Our model was in concordance with this in terms of yearly peak prevalence, which decreased as p rose at all values of a_1 (Figure 4E). However, trends in mean prevalence were more diverse (Figure 3B), with the direction of the effect of rice fields being mediated by the relative biting rate of rice mosquitos. Mean prevalence increased with p where the species' biting rates were the same, decreased with p where a_1 was 80% or less of a_2, and peaked at an intermediate value for p of 0.5 when a_1 was 90% of a_2.

Chan *et al* (2021) found that the presence of rice fields had no significant effect on malaria transmission in high baseline prevalence settings. Our model conflicted with this, instead suggesting that as the relative contribution of rice paddy mosquito species increased, both mean and maximum prevalences decreased (Figure 4C,F).

4. Discussion

The simple compartmental model we developed suggests that the presence of irrigated rice paddies, which provide a permanent habitat for some malaria vector species, modulates qualitative trends in malaria transmission in differing ways as other epidemiologically relevant biotic factors in the system vary.

One particularly noteworthy result was that mean malaria prevalence was frequently highest at intermediate values of p where neither type of larval site is dominant over the other in its contribution of mosquitos to the system. This somewhat calls into question the approach of empirical studies such as those assessed in Chan *et al* (2021) which treat the presence of a rice field as a binary factor, because in reality permanent and temporary larval sites may interact to drive malaria transmission to levels beyond what would be reached by one type alone. It may be worthwhile for future work which investigates the link between rice cultivation and malaria to take into account more detailed nuances with regard to the exact spatial setting of human settlements surveyed, and what the likely relative contribution of mosquito species which use different types of larval habitats is likely to be.

We found that the introduction of irrigated rice paddies raised malaria prevalence at the greatest rate in systems where malaria prevalence was otherwise low. This concurs with the empirical findings of Chan *et al* (2021). Given that the contribution to malaria transmission of the most important species which uses only seasonal larval sites, *An. gambiae s.s.*, appears to be diminishing (Msugupakulya *et al*, 2023), such low baseline transmission areas are likely to become increasingly common. As a result, rice paddies could sustain malaria prevalence when it would otherwise be decreasing, by supporting populations of species which are able to make use of rice field larval sites. The repercussions of this could be particularly harmful given that these species often bite diurnally and outdoors: this behaviour is well established in *An. funestus s.s.* (Sougoufara *et al*, 2014) and has recently been established in *An. arabiensis* and *An. coluzzii* (Doucoure *et al*, 2020). By not biting indoors and at night, these species are able to circumvent the long-lasting insecticide nets and indoor residual spraying strategies which are the main defences used against malaria vectors (Russell *et al*, 2011), thus making control operations challenging. While beyond the scope of this project, it may be worthwhile for future work which models malaria with irrigation to include the consequences of these behaviours on biting rate in contexts which include vector control interventions.

At high baseline prevalence, we found that increasing the relative contribution of mosquitos which use rice field larval sites generally reduced mean prevalence. This is intuitive from our model given that in this scenario more rice fields resulted in lesser overall mosquito abundance and a greater proportion of mosquitos with (in four out of five runs) lower biting rates. However, while we arbitrarily assigned the yearly abundance of rice mosquitos to equal the intermediate abundance of seasonal mosquitos, in reality mosquito abundance may be much higher in rice fields (Chan, 2021). This may explain why, in their review, Chan *et al* (2021) found that rice fields did not affect transmission in high prevalence settings, although the evidence for this was weak since the sample size of studies which met their criteria for inclusion in this category was only two. Moreover, it is possible that density-dependent effects may reduce the vectorial capacity of very large *Anopheles* populations (Diuk-Wasser *et al*, 2005). Overall, detailed models including a range of population sizes for mosquitos which use rice field larval sites, and density-dependent transmission, are likely needed to assess how rice fields impact malaria transmission in high baseline prevalence settings.

At intermediate baseline prevalence, Chan *et al* (2021) found that prevalence usually decreased with increasing relative contribution of mosquitos which use rice larval sites. Our results mostly concurred with this, but there was some variability in the directionality of the trends we saw depending on the relative biting rate of rice compared to seasonal mosquitos. The true biting rate of mosquitos which use rice larval sites is likely to depend on species composition and also may vary geographically (Akogbéto *et al*, 2018; Akoton *et al*, 2023; Sinka *et al*, 2010). Also, since mosquito behaviour is extremely challenging to track (Spitzen and Takken, 2018), and biting rate is generally reported per human rather than per mosquito in the form of the entomological inoculation rate (Tusting *et al*, 2014), it was difficult to extract biting rates with any true biological basis from the literature. For these reasons, we simulated a_1 over a range of values. The variability in our results in this scenario indicates that it may be difficult to predict the impact of rice fields on intermediate transmission areas in the absence of detailed entomological data which is not generally available.

Further evaluating the range of plausible values for biting rates, we also ran the model at low, medium, and high values for a_2, seasonal mosquito biting rate, while still varying a_1 from 60 to 100% of a_2. While the medium a_2 outputs were similar to the medium $M_f(t)$ result discussed previously, interestingly, the trends seen in the low and high transmission settings discussed previously are swapped: rice fields decrease mean prevalence at low a_2, and increase mean prevalence at high a_2. A potential explanation for the result at low a_2 could be that increasingly temporally evenly-spread mosquito abundance prevents infections from ever accumulating enough to be amplified rapidly in the population. At high a_2, the cause of the phenomenon seen could be that the maximum prevalences reached at higher proportions of seasonally-spiking mosquitos are limited by the total human population size. These insights indicate that interventions which reduce biting rate, such as bed nets (Musiime *et al*, 2019) and zooprophylaxis (Donnelly *et al*, 2015) may be particularly important in controlling malaria transmission in settings which contain rice paddies.

Across all configurations of M_f and a_2 other than the low M_f setting, we found that the maximum peaks of malaria prevalence reduced as the relative contribution of mosquito species which use rice field larval sites reduced, although this often did not correspond with decreasing mean prevalence. More homogenous malaria transmission throughout the year brought about by mosquitos which use rice field larval sites reduces the utility of interventions which have proved effective when timed around predicted yearly spikes of transmission, such as seasonal malaria chemoprevention (Cairns *et al*, 2012), seasonal vaccination campaigns (Greenwood *et al*, 2017), and indoor residual spraying campaigns (Selvaraj *et al*, 2018). Declining seasonality of malaria transmission could have complex and variable consequences on control efforts which merit further investigation.

In striving for generality for our model, we sacrificed some details which could have made it a more accurate reflection of reality. Most compartmental models include human populations which are structured by age and immunity, in which individuals may also die and be removed from the system (Mandal *et al*, 2011). Our model also inherits the most inaccurate assumption of the original Ross-Macdonald formulation, i.e. homogeneous mixing where mosquitos choose hosts at random (Simoy and Aparicio, 2020). Additionally, we treat irrigation as producing an entirely unchanging supply of larval habitats where in reality the physical landscape will change throughout the year depending on the specifics of the irrigation regime used (Jiang *et al*, 2023). Nevertheless, by maintaining simplicity we avoid overfitting our model and lay a foundation for future work examining specific regional scenarios in more detail.

5. Conclusions

Our model predicts that the presence of rice fields exerts effects of different direction and magnitude on malaria prevalence depending on other biotic factors. Our findings encompass some cases where the greatest prevalence came about from an interacting combination of rice paddy and seasonal larval sites, and large increases in prevalence due to introduction of rice fields in settings where otherwise there would be relatively little transmission. More nuanced investigation is thus needed regarding if and when expansion of rice cultivation can be justified in Sub-Saharan Africa.

Reflection

One personal attribute I cultivated during this process was resilience. At the beginning of the project, I embarked on an ambitious attempt to develop the system independently with only an outline of the project aims from my supervisor. However, when I presented my initial model to the lab group, it became evident that my approach had significant shortcomings, and I would need to start again, virtually from scratch. Initially, this setback left me feeling disheartened, but after processing the initial disappointment, my perspective began to shift as I realised there was still ample time to recover. It also soon occurred to me that I was likely to produce something much better if I learnt to balance independence with more input from my supervisor, who is an expert in the field and was happy to help me. Overall, the experience underscored the importance of leveraging available resources and expertise, particularly in complex endeavours like scientific research: from that point onward, I made a conscious effort to regularly consult with my supervisor. These frequent check-ins ensured that any errors in my work were identified early, preventing me from veering off course again.

I also developed my maths skills during this project. Although I selected this field of research because I was interested in theoretical modelling of biological processes, I did not even study maths at A-level and so I knew I would have some catching up to do. While the systems of differential equations I worked with initially seemed intimidating, I was eventually able to get to grips with them and now feel quite comfortable explaining how they work, as I feel I have done well in my methods section. Quantitative skills are widely applicable and highly desirable in both jobs and postgraduate research, so I believe that this process has made me a stronger applicant to future positions.

One area which I had identified as a personal weakness before the onset of the project was public speaking. As a consequence, I resolved to make a concerted effort to practise whenever I was offered the opportunity: as well as the mandatory FSB presentation, I also volunteered to give talks on my project in a research group lab meeting and a tutorial. Feedback I had received in previous years had complained that my presentation style was too deadpan and seemed unenthusiastic. My strategy to combat this was to avoid over-preparing in a way which meant that it seemed like I was just reading from a script, instead simply including prompts which encouraged me to speak more freely and naturally. While the lab meeting presentation could hardly be considered a success given that my model turned out to be wrong, I received a good mark for my FSB and I believe that my tutorial talk went down well, with my classmates reassuring me that they were able to understand the topic despite its complexity. Virtually every job involves some form of public speaking, so I am happy to have made progress refining this skill this year.

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Generative AI Statement

I sporadically used ChatGPT version 3.5 to debug the code I wrote.