Utilization of environmental and epidemiological indicators in the study of malaria dynamics

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ABSTRACT

This paper aims to analyze the behavior of malaria transmission in the Amazon region based on climatic and environmental changes, such as temperature, precipitation and deforestation, through proposed modifications to the SIR and SEI models, in order to contribute to the study of applications of external effects on the evolution of the disease. The Trajetórias Project, developed by the Synthesis Center on Biodiversity and Ecosystem Services (SinBiose/CNPq) was used as an initial reference for the study. This work employs a modified SIR/SEI methodology, based on work from Parham and Michael (2010) which takes into account rainfall and temperature, with further modifications to avoid delay equations. Primary results show that the model is too sensible on some parameters, and using values indicated by other papers did not give the same results, opening up future work to compare the modified model equations with the originals. With the obtained results, it was possible to verify a strong effect caused by increased contact of host and vectors on the transmission of the disease.

1. Introduction

The Amazon is one of the largest and most biodiverse tropical forests in the world, harboring numerous species of plants, animals, and microorganisms, including vectors and pathogens responsible for the transmission of various diseases. Among them, one of the most common is malaria, caused by protozoa of the genus *Plasmodium*, transmitted by the bite of the infected female mosquito of the genus *Anopheles*. It is present in 22 American countries, but the areas with the highest risk of infection are located in the Amazon region, encompassing nine countries, which accounted for 68% of infection cases in 2011 [1]. Although malaria is prevalent in the Americas, it is not limited to this continent and is found in countries in Africa and Asia, resulting in more than two million cases of infection and 445,000 deaths worldwide in 2016 [2], being endemic in a total of 84 countries in 2021 [3].

Notably, vector-borne disease transmission is closely related to environmental changes that interfere with the ecosystem of both transmitting organisms and affected organisms. In the case of the Amazon, agricultural and livestock settlements are among the factors that most favor disease transmission, both due to the deforestation they cause for establishment and the clustering of people in environments close to the vector's habitat [4], especially by clustering non-immune migrants near these natural and artificial breeding sites [5].

Additionally, other factors such as rainfall, wildfires, and mining also significantly influence disease transmission in the region. These events result in habitat loss, ecosystem fragmentation, and climate changes, affecting the distribution and abundance of vectors and hosts, as well as their interaction with pathogens. Furthermore, population growth and urbanization also play a crucial role in disease spread, increasing human exposure to vectors and infection risks.

In this context, this work aims to investigate vector-borne disease transmission in the Amazon and analyze how environmental impacts influence the dynamics of malaria transmission, the ecological and socioeconomic factors affecting this spread, and possible prevention and control strategies. The main reference for this research is the Trajetórias Project, developed by the Center for Biodiversity and Ecosystem Services (SinBiose/CNPq), which is a dataset including environmental, epidemiological, economic, and socioeconomic indicators for all municipalities in the Legal Amazon, analyzing the spatial and temporal relationship between economic trajectories linked to the dynamics of agrarian systems, whether they are family-based rural or large-scale agricultural and livestock production, the availability of natural resources, and the risk of diseases [6].

2. Model formulation

Based on previous work developed to model the transmission of malaria based on precipitation and temperature dynamics [7], we focus on two different sets of compartments: susceptible hosts (S_H), infected hosts (I_H), recovered hosts (R_H), susceptible vectors (S_M), exposed vectors (E_M) and infected vectors (I_M). The equations that describe the transmission are initially given as:

$$\frac{dS_H}{dt} = -ab_2\left(\frac{I_M}{N}\right)S_H \tag{1}$$

$$\frac{dI_H}{dt} = ab_2\left(\frac{I_M}{N}\right)S_H - \gamma I_H \tag{2}$$

$$\frac{dR_H}{dt} = \gamma I_H \tag{3}$$

$$\frac{dS_M}{dt} = b - ab_1\left(\frac{I_H}{N}\right)S_M - \mu S_M \tag{4}$$

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$$\frac{dE_M}{dt} = ab_1\left(\frac{I_H}{N}\right)S_M - \mu E_M - ab_1\left(\frac{I_H}{N}\right)S_M l(\tau_M) \tag{5}$$

$$\frac{dI_M}{dt} = ab_1\left(\frac{I_H}{N}\right)S_M l(\tau_M) - \mu I_M \tag{6}$$

However, the use of these equations proved to be unsuccessful for the modelling of the mosquito populations through the SEI equations, causing (5) to be very close to 0, and therefore mirroring the oscillations of S and I, a behavior not seen in nature.

To overcome this effect, the SEI equations were modified in order for b_1 to only be used in the transference between compartments S and E, and a new parameter, b_3 to move mosquitos from E to I. Being inversely related to the incubation period, the definition of this rate can be found in **Table A.2**. In addition to that, the parameter $a(T)$ that was in use in the transition between exposed and infected also had to be removed, as no further bites occur at this point. The parameter l also had to be disassociated from the infection rate of exposed individual (b_3).

The SIR equations were also modified, to take into consideration population dynamics, including a μ_H parameter as both a birth and mortality rate.

The finalized equations used in the model are as following:

$$\frac{dS_H}{dt} = \mu_H N - ab_2\left(\frac{I_M}{N}\right)S_H - \mu_H S_H \tag{7}$$

$$\frac{dI_H}{dt} = ab_2\left(\frac{I_M}{N}\right)S_H - \gamma I_H - \mu_H I_H \tag{8}$$

$$\frac{dR_H}{dt} = \gamma I_H - \mu_H R_H \tag{9}$$

$$\frac{dS_M}{dt} = b - ab_1\left(\frac{I_H}{N}\right)S_M - \mu S_M \tag{10}$$

$$\frac{dE_M}{dt} = ab_1\left(\frac{I_H}{N}\right)S_M - \mu E_M - b_3 E_M - l E_M \tag{11}$$

$$\frac{dI_M}{dt} = b_3 E_M - \mu I_M \tag{12}$$

The parameters are given in Table A1, while the variables are given in Table A2, which can be found in the Appendix. The selected human population was from the the rural area of Manaus, between the years of 2004 to 2008, as this locality had the highest incidence of malaria caused by *P. vivax* in the Amazon region [6]. This species of Plasmodium was chosen as it is responsible for the highest number of malaria cases in Brazil [10, 11], being the most common human malaria parasite in the region [12]. With the incidence function [6] we have that

$$\text{Inc} = \frac{\text{Cases}(d, m, z, t_1, t_2)}{\text{Pop}(m, z, (t_1 + t_2)/2) \times 5 \text{ years}} \times 10^5, \tag{13}$$

where $\text{Cases}(d, m, z, t_1, t_2)$ is the number of cases of disease d in zone z of municipality m, and t_1 and t_2 are the initial and final years of the interval, while $\text{Pop}(m, z, (t_1 + t_2)/2) \times 5$ years is the population in zone z of municipality m in the middle of the period multiplied by the total number of observation years. In this case, we could indicate as:

$$\text{Inc}(\text{Vivax, Manaus, Rural, } 2004, 2008) = \tag{14}$$

$$= \frac{\text{Cases(Vivax, Manaus, Rural, } 2004, 2008)}{\text{Pop(Manaus, Rural, } 2006) \times 5 \text{ years}} \times 10^5 \Rightarrow \tag{15}$$

$$\Rightarrow 184030.8 = \frac{78745}{5\text{Pop}} \times 10^5 \Rightarrow Pop \approx 8558 \tag{16}$$

Using data on the total population of Manaus in this period, with an incidence of 3106.429047 and a number of cases of 262264, the total population of the municipality was estimated to be 1688524 inhabitants, which corresponds to the value found in the official census [13]. Thus, the rural population could be considered as approximately 0.5% of the municipality's population.

Having estimated the percentage size of the rural population in the city, it was possible to calculate this population for each of the years of the analysis through linear interpolation using historical series data from IBGE [14]:

Table 1
Manaus' rural population from 2004 to 2009.

Year	Estimated rural population
2004	7717
2005	7889
2006	8061
2007	8233
2008	8492
2009	8751

Given there was only population data for the years of 2000, 2007, and 2010, interpolations were performed with different initial and final points, using data from 2000 to 2007 for 2004-2007 and from 2007 to 2010 for 2008-2009, ensuring the correct use of the 2007 population. Given the population growth between 2004 and 2009, the annual birth rate was estimated to be 206.8 births per year. Therefore, this corresponds to approximately 0.56657 births per day and 0.00007 births per day per person, which would be our μ_H.

Temperature and precipitation data were taken from the Mosqlimate Data API datastore [15], from January 1st 2004 to December 31st 2008, with the geocode 1302603.

As for the theory behind environmental factors, it is known that the removal of tree canopies allowed the resurgence of malaria in South America [16]. In deforested areas, without tree canopies covering the ground, water puddles under sunlight attract mosquitoes of the species

Anopheles darlingi, the main vector related to human malaria in the Amazon [17]. They are usually less commonly found in still intact forests. This is because light and heat favor the development of larvae and pupae, in addition to a greater availability of algae for larval feeding [18]. The increase in ambient temperature also favors the vectorial capacity of mosquitoes.

Deforestation also attracts and brings humans closer to take part in logging, agriculture, and road construction activities, bringing individuals infected with *Plasmodium* to an area where both the vector and the environment have already been modified to favor transmission. Furthermore, agriculture also promotes river sedimentation, providing suitable environments for breeding sites. Therefore, it can be considered a relevant change for the model to take into account deforestation, the increase in survival probabilities of eggs, larvae, and pupae, as well as increasing the proportion of bites that lead to infection, due to the increased human population density in areas near mosquito breeding sites.

As it was outside the scope of this project to collect samples of *A. darlingi in loco*, it was instead used an estimate for the number of mosquitos based in the literature. As the study was made around the rural population of the municipality, this would favour the clustering of adult mosquitos, given the proximity to bodies of water and recently open up areas of rainforest [19]. In fact, the municipality of Manaus has a great number of breeding sites in its' periurban and rural areas, both natural and man-made. Many of the city's fish farming tanks have been noted as breeding sites for *A. darlingi* [20].

3. Mathematical analysis of the model

3.1. Basic Reproduction Number ($\mathcal{R}_0$)

To derive the $\mathcal{R}_0$ of the model, X_s is defined as the set of all disease-free states,

$$X_s = \{x \geq 0 | x_i = 0, i = 1, \dots, m\},$$

where $X = (x_1, \dots, x_n)^T$, such that $x_i \geq 0$ represents the number of individuals in each compartment, and each function is assumed to be continuously differentiable at least twice in each variable (C^2) [21].

Rearranging the equations so that the first m equations contain the infected individuals, let $\mathcal{F}_i(x)$ be the rate of appearance of new infections in compartment i, $\mathcal{V}_i^+(x)$ be the rate of individuals entering compartment i by other means, and $\mathcal{V}_i^-(x)$ be the rate of individuals leaving compartment i. The disease transmission model consists of non-negative initial conditions together with the following system of equations:

$$\dot{x} = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x), i = 1, \dots, n,$$

where $\mathcal{V}_i(x) = \mathcal{V}_i^-(x) - \mathcal{V}_i^+(x)$. Here, $F = \left[\frac{\partial \mathcal{F}_i(x_0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial \mathcal{V}_i(x_0)}{\partial x_j}\right]$, where x_0 is a Disease-Free Equilibrium (DFE), and $1 \leq i, j \leq m$, and $\mathcal{R}_0 = \rho(FV^{-1})$.

Calculating $\mathcal{R}_0$ for both models, as wel as the full system SIR/SEI:

- **SIR:** In this case, $m = 1$, and the compartments are arranged as $[I_H, S_H, R_H]$. Since $\mathcal{R}_0$ is calculated with normalized values, the necessary equations are mulyiplied by N to remove the denominator. Specifically, for the SIR case, as R_H is not used in any of the equations, it can be expressed solely in terms of S and I. Therefore:

  $\mathcal{F}_i(x)$: rate of entrance of infected individuals in compartment i

  $$\mathcal{F} = \begin{bmatrix} ab_2 I_M S_H \end{bmatrix}$$

  Additionally, we have

  $\mathcal{V}_i(x)^-$: rate of leaving compartment i

  $\mathcal{V}_i(x)^+$: rate of entering compartment i

  Thus:

  $$\mathcal{V}^- = \begin{bmatrix} \gamma I_H + \mu_H I_H \end{bmatrix}$$
  $$\mathcal{V}^+ = \begin{bmatrix} 0 \end{bmatrix}$$
  $$\mathcal{V}_i(x) = \mathcal{V}_i(x)^- - \mathcal{V}_i(x)^+$$

  Therefore,

  $$\mathcal{V} = \begin{bmatrix} I_H(\gamma + \mu_H) \end{bmatrix}$$

  Hence

  $$F = \frac{\partial \mathcal{F}}{\partial I_M} = \begin{bmatrix} ab_2 S_H \end{bmatrix}$$
  $$V = \frac{\partial \mathcal{V}}{\partial I_H} = \begin{bmatrix} \gamma + \mu_H \end{bmatrix}$$

  At the equilibrium, $[S_H^*, I_H^*] = [1, 0]$, so

  $F = [ab_2]$, $V = [\gamma + \mu_H]$ and $\mathcal{R}_0 = \left|\frac{ab_2}{\gamma + \mu_H}\right|$.

- **SEI:** In this case, $m = 2$, and the compartments are arranged as $[E_M, I_M, S_M]$. Again, the necessary equations are multiplied by N to remove the denominator. Therefore:

  $$\mathcal{F} = \begin{bmatrix} ab_1 I_H S_M \\ 0 \end{bmatrix}$$

  $$\mathcal{V}^- = \begin{bmatrix} E_M(\mu + b_3 + l) \\ \mu I_M \end{bmatrix}$$

  $$\mathcal{V}^+ = \begin{bmatrix} 0 \\ b_3 E_M \end{bmatrix}$$

  $$\mathcal{V}_i(x) = \mathcal{V}_i(x)^- - \mathcal{V}_i(x)^+$$

Thus,

$$\mathcal{V} = \begin{bmatrix} E_M(\mu + b_3 + l) \\ \mu I_M - b_3 E_M \end{bmatrix}$$

Hence

$$F = \frac{\partial \mathcal{F}}{\partial E_M, I_H} = \begin{bmatrix} \frac{\partial a b_1 I_H S_M}{\partial E_M} & \frac{\partial a b_1 I_H S_M}{\partial I_H} \\ \frac{\partial 0}{\partial E_M} & \frac{\partial 0}{\partial I_H} \end{bmatrix} =$$

$$= \begin{bmatrix} 0 & a b_1 S_M \\ 0 & 0 \end{bmatrix}$$

$$V = \frac{\partial \mathcal{V}}{\partial E_M, I_M} = \begin{bmatrix} \frac{\partial E_M(\mu + b_3 + l)}{\partial E_M} & \frac{\partial E_M(\mu + b_3 + l)}{\partial I_M} \\ \frac{\partial \mu I_M - b_3 E_M}{\partial E_M} & \frac{\partial \mu I_M - b_3 E_M}{\partial I_M} \end{bmatrix} =$$

$$= \begin{bmatrix} \mu + b_3 + l & 0 \\ -b_3 & \mu \end{bmatrix}$$

At the equilibrium, $[S_M^*, E_M^*, I_M^*] = [1, 0, 0]$, so

$$F = \begin{bmatrix} 0 & a b_1 \\ 0 & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} \mu + b_3 + l & 0 \\ -b_3 & \mu \end{bmatrix}$$

and

$$\mathcal{R}_0 = \left| \frac{a b_1 b_3}{(b_3 + l + \mu)\mu} \right|.$$

- **SIR/SEI:** In this case, $m = 3$, and the compartments are arranged as $[I_H, E_M, I_M, S_H, S_M]$. Once again, the necessary equations are multiplied by N to remove the denominator. Therefore:

$$\mathcal{F} = \begin{bmatrix} a b_2 I_M S_H \\ a b_1 I_H S_M \\ 0 \end{bmatrix}$$

$$\mathcal{V}^- = \begin{bmatrix} \gamma I_H + \mu_H I_H \\ E_M(\mu + b_3 + l) \\ \mu I_M \end{bmatrix}$$

$$\mathcal{V}^+ = \begin{bmatrix} 0 \\ 0 \\ b_3 E_M \end{bmatrix}$$

$$\mathcal{V}_i(x) = \mathcal{V}_i(x)^- - \mathcal{V}_i(x)^+$$

Thus,

$$\mathcal{V} = \begin{bmatrix} I_H(\gamma + \mu_H) \\ E_M(\mu + b_3 + l) \\ \mu I_M - b_3 E_M \end{bmatrix}$$

Hence

$$F = \frac{\partial \mathcal{F}}{\partial I_H, E_M, I_M} = \begin{bmatrix} 0 & 0 & a b_2 S_H \\ a b_1 S_M & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$V = \frac{\partial \mathcal{V}}{\partial I_H, E_M, I_M} = \begin{bmatrix} \gamma + \mu_H & 0 & 0 \\ 0 & b_3 + l + \mu & 0 \\ 0 & -b_3 & \mu \end{bmatrix}$$

At the equilibrium, $[S_H^*, S_M^*, I_H^*, E_M^*, I_M^*] = [1, 1, 0, 0, 0]$, so

$$F = \begin{bmatrix} 0 & 0 & a b_2 \\ a b_1 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} \gamma + \mu_H & 0 & 0 \\ 0 & b_3 + l + \mu & 0 \\ 0 & -b_3 & \mu \end{bmatrix}$$

and $\mathcal{R}_0 = \left| \sqrt{\frac{a^2 b_1 b_2 b_3}{(b_3 + l + \mu)(\gamma + \mu_H)\mu}} \right| = \sqrt{\mathcal{R}_{0SIR} \times \mathcal{R}_{0SEI}}$.

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A. Appendix

Table A.1
List of model parameters.

Parameter	Definition	Formulation
$b(R,T)$	Mosquito birth rate (days^{-1})	$B_E p_E(R) p_L(R,T) p_P(R)/(\tau_E + \tau_L(T) + \tau_P)$
$a(T)$	Biting rate (days^{-1})	$(T - T_1)/D_1$
$\mu(T)$	Mosquito mortality rate per capita (days^{-1})	$-\log(p(T))$
$\tau_M(T)$	Duration of sporozoite cycle (days)	$DD/(T - T_{min})$
$\tau_L(T)$	Duration of larval development phase (days)	$1/(c_1 T + c_2)$
$p(T)$	Daily mosquito survival rate	$e^{(-1/(AT^2+BT+C))}$
$p_L(R)$	Probability of larval survival dependent on rainfall	$(4p_{ML}/R_L^2)R(R_L - R)$
$p_L(T)$	Probability of larval survival dependent on temperature	$e^{-(c_1 T + c_2)}$
$p_L(R,T)$	Probability of larval survival	$p_L(R)p_L(T)$
$l(\tau_M)(T)$	Probability of mosquito survival during sporozoite cycle (days^{-1})	$p(T)^{\tau_M(T)}$
$M(t)$	Total population of mosquitos	$S_M(t) + E_M(t) + I_M(t)$
$N(t)$	Total population of humans	$S_H(t) + I_H(t) + R_H(t)$

Table A.2
List of model variables.

Symbol	Definition	Units
b_1	Proportion of bites from susceptible mosquitoes on infected humans that result in infection	Dimensionless
b_2	Proportion of bites from infected mosquitoes on susceptible humans that result in infection	Dimensionless
γ	1/Average duration of infectiousness in humans	days^{-1}
T_1	Mean temperature in the absence of seasonality	$°C$
T_2	Amplitude of seasonal variability in temperature	Dimensionless
R_1	Average monthly precipitation in the absence of seasonality	mm
R_2	Amplitude of seasonal variability in precipitation	Dimensionless
ω_1	Angular frequency of seasonal oscillations in temperature	months^{-1}
ω_2	Angular frequency of seasonal oscillations in precipitation	months^{-1}
ϕ_1	Phase lag of temperature variability (phase shift)	Dimensionless
ϕ_2	Phase lag of precipitation variability (phase shift)	Dimensionless
B_E	Number of eggs laid per adult per oviposition	Dimensionless
p_{ME}	Maximum probability of egg survival	Dimensionless
p_{ML}	Maximum probability of larval survival	Dimensionless
p_{MP}	Maximum probability of pupal survival	Dimensionless
τ_E	Duration of the egg development phase	days
b_3	Infection rate in exposed mosquitoes ($1/\tau_M(T)$)	days^{-1}
τ_P	Duration of the pupal development phase	days
R_L	Rainfall threshold until breeding sites are eliminated, removing immature individuals	mm
T_{min}	Minimum temperature, below which there is no development of the parasite: 14.5	$°C$
DD	Degree-days for parasite development. “Sum of heat" for maturation: 105 [8, 9]	$°C$ days
A	Empirical sensitivity parameter	($°C^2$ days)$^{-1}$
B	Empirical sensitivity parameter	($°C$ days)$^{-1}$
C	Empirical sensitivity parameter	days^{-1}
D_1	Empirical sensitivity parameter: 36.5	$°C$ days
c_1	Empirical sensitivity parameter	($°C$ days)$^{-1}$
c_2	Empirical sensitivity parameter	days^{-1}
T'	Empirical temperature parameter	$°C$