

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 [?]. 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 [?], being endemic in a total of 84 countries in 2021 [?].

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 [?], especially by clustering non-immune migrants near these natural and artificial breeding sites [?].

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 [?].

2. Model formulation

Based on previous work developed to model the transmission of malaria based on precipitation and temperature dynamics [?], 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:

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

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

$$\frac{dR_H}{dt} = \gamma I_H \quad (3)$$

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

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

ORCID(s):

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

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:

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

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

$$\frac{dR_H}{dt} = \gamma I_H - \mu_H R_H \quad (9)$$

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

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

$$\frac{dI_M}{dt} = b_3 E_M - \mu I_M \quad (12)$$

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 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 [?]. This species of *Plasmodium* was chosen as it is responsible for the highest number of malaria cases in Brazil [? ?], being the most common human malaria parasite in the region [?]. With the incidence function [?] we have that

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

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 $\text{Pop}(m, z, (t_1 + t_2)/2) \times 5 \text{ years}$ 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:

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

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

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

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 [?]. 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 [?]:

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 [?], 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 [?]. 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 [?]. 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 [?]. 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 [?]. 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* [?].

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) [?].

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 $\mathcal{R}_0 = \rho(FV^{-1})$.

References

- [1] P.F.P. Pimenta et al., An overview of malaria transmission from the perspective of Amazon *Anopheles* vectors, *Memórias do Instituto Oswaldo Cruz*, Vol. 110 (1) (2015), 23-47, <https://doi.org/10.1590/0074-02760140266>.
- [2] G.A. Josling, K.C Williamson, M. Llinás, Regulation of Sexual Commitment and Gametocytogenesis in Malaria Parasites, *Annual Review of Microbiology*, Vol. 72 (1) (2018), 501-519, <https://doi.org/10.1146/annurev-micro-090817-062712>.
- [3] World Health Organization / World Malaria Report 2022, Global Malaria Programme, accessed 29 August 2024, <https://www.who.int/publications/i/item/9789240064898>.
- [4] M. Silva-Nunes et al., Malaria on the Amazonian frontier: transmission dynamics, risk factors, spatial distribution, and prospects for control, *American Journal of Tropical Medicine and Hygiene*, Vol. 79 (4) (2008), 624-635, <https://doi.org/10.4269/ajtmh.2008.79.624>.
- [5] M. Silva-Nunes et al., Amazonian malaria: Asymptomatic human reservoirs, diagnostic challenges, environmentally driven changes in mosquito vector populations, and the mandate for sustainable control strategies, *Acta Tropica*, Vol. 121 (3) (2012), 281-291, <https://doi.org/10.1016/j.actatropica.2011.10.001>.
- [6] A.C. Rorato, A.P. Dal'Asta, R.M. Lana et al., Trajetórias: a dataset of environmental, epidemiological, and economic indicators for the Brazilian Amazon, *Scientific Data*, Vol. 10 (1) (2023), 65, <https://doi.org/10.1038/s41597-023-01962-1>.
- [7] P.E.Parham, E. Michael, Modelling Climate Change and Malaria Transmission, *Modelling Parasite Transmission and Control*, *Advances in Experimental Medicine and Biology*, Vol. 673 (2010), 184-199, https://doi.org/10.1007/978-1-4419-6064-1_13.
- [8] G.C. McCord, Malaria ecology and climate change, *The European Physical Journal Special Topics*, Vol. 225 (3) (2016), 459-470, <https://doi.org/10.1140/epjst/e2015-50097-1>.
- [9] S. W. Lindsay, M. H. Birley, Climate change and malaria transmission, *Annals of Tropical Medicine & Parasitology*, Vol. 90 (1996), 573-588, <https://doi.org/10.1080/00034983.1996.11813087>.
- [10] J. Oliveira-Ferreira, M. V. Lacerda, P. Brasil et al., Malaria in Brazil: an overview., *Malaria Journal*, Vol. 9 (1) (2010), <https://doi.org/10.1186/1475-2875-9-115>.
- [11] C.T. Codeço, A.P. Dal'Asta, A.C. Rorato, R.M. Lana, T.C. Neves, C.S. Andreazzi, M. Barbosa, M.I.S. Escada, D.A. Fernandes, D.L. Rodrigues, I.C. Reis, M. Silva-Nunes, A.B. Gontijo, F.C. Coelho, A.M.V. Monteiro, Epidemiology, Biodiversity, and Technological Trajectories in the Brazilian Amazon: From Malaria to COVID-19, *Frontiers in Public Health*, Vol. 9 (2021), <https://doi.org/10.3389/fpubh.2021.647754>.
- [12] A. K. R. Galardo, M. Arruda, et al., Malaria vector incrimination in three rural riverine villages in the Brazilian Amazon, *The American Journal of Tropical Medicine and Hygiene*, Vol. 76 (3) (2007), 461-469, <https://www.ajtmh.org/view/journals/tpmd/76/3/article-p461.xml>.
- [13] Tabnet, Ministério da Saúde, accessed 12 August 2024, <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?ibge/cnv/popam.def>.
- [14] Censo - Séries históricas. Brasil / Amazonas / Manaus, IBGE, accessed 15 August 2024, <https://cidades.ibge.gov.br/brasil/am/manaus/pesquisa/43/0?tipo=grafico>.
- [15] Mosqlimate Data API / Datastore / climate, accessed 12 August 2024, <https://api.mosqlimate.org/datastore/>.

- [16] D. E. Norris, Mosquito-borne Diseases as a Consequence of Land Use Change, *EcoHealth*, Vol. 1 (1) (2004), 19-24, <https://doi.org/10.1007/s10393-004-0008-7>.
- [17] Anopheles, Fiocruz Rondônia, accessed 15 August 2024, <https://www.rondonia.fiocruz.br/pivem/anopheline/>.
- [18] M. Silva-Nunes, Environmental changes impact in malaria transmission and prospects for the disease control in brazilian amazon rural settlements, *Oecologia Australis*, Vol. 14 (3) (2010), 603-622, <https://revistas.ufrj.br/index.php/oa/article/view/7101>.
- [19] J. D. Charlwood, Biological variation in *Anopheles darlingi* Root, *Memórias do Instituto Oswaldo Cruz*, Vol. 91 (4) (1996), 391-398, <https://doi.org/10.1590/S0074-02761996000400001>.
- [20] G. R. de Lima, A.N. Arcos, E.V. dos Santos, R. C. Simões, C.A.P. Lima, W.P. Tadei, *Anopheles* Larval Abundance in Artificial Breeding Sites in the East Zone of Manaus, Amazon, *South American Journal of Basic Education, Technical and Technological*, Vol. 8 (1) (2021), 35-47, <https://periodicos.ufac.br/index.php/SAJEBTT/article/view/3399>.
- [21] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Mathematical Biosciences*, Vol. 180 (2002), 29-48, [https://doi.org/10.1016/S0025-5564\(02\)00108-6](https://doi.org/10.1016/S0025-5564(02)00108-6).

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 [? ?] | °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 |