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MODELING BURULI ULCER TRANSMISSION: SEIR-SEI ANALYSIS WITH IMMUNITY LOSS AND ARSENIC CONTAMINATION

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Abstract: This article presents a novel mathematical model to explore the transmission dynamics of *Mycobacterium ulcerans (MU)* infection, focusing on the waterborne spread. Using SEIR and SEI models for human and water-bug populations, it considers factors such as disease-related deaths and arsenic-contaminated water. The analysis determines the basic reproduction number (R_0), which dictates the stability of disease-free and endemic equilibria. The study underscores the importance of controlling Buruli ulcer transmission, offering valuable insights for global health management.

Keywords and Phrases: Arsenic, *Mycobacterium ulcerens*, Waterbug, Basic reproduction number, Next generation matrix, Global stability analysis.

2020 Mathematics Subject Classification: 34A34.

1. Introduction

Buruli ulcer's story begins in 1897 at Mengo Hospital in Uganda, where surgeon Albert Ruskin Cook first observed its devastating effects. It wasn't until fifty years later that MacCallum and his team, based at Melbourne University, unveiled the culprit bacterium in patients from southeastern Australia. Despite decades of clinical insight, the disease's enigmatic nature persisted until 1948 [8, 21].

Buruli ulcer (BU), caused by *Mycobacterium ulcerans (MU)*, is a devastating disease that predominantly affects Africa, leading to severe tissue damage. Ranked by the WHO as the third most prevalent mycobacterial infection, BU poses a major health threat, especially to children aged 4 to 15. The disease flourishes in tropical and subtropical regions, with water bugs acting as carriers in aquatic environments. Environmental shifts, like flooding and land use changes, drive its spread. Despite advances in understanding, the exact environmental source of MU and the triggers for BU infection remain a mystery [2, 9, 22, 23, 28, 30, 33, 38, 39, 41].

Several mathematical models analyze Buruli Ulcer epidemiology, focusing on human-water bug interactions [1, 3, 4, 15, 25]. Despite the link between vectors, arsenic concentration, and BU spread, neither has been extensively investigated.

Many experts suggested two views on the transmission dynamics of *Mycobacterium ulcerens*. They said it may occur through contaminated water or bug bites [1, 32, 34, 37, 40]. Water bugs can transmit MU through bites and arsenic-contaminated water.

Duker et al. [12] suggest environmental arsenic influences Buruli ulcer (BU) distribution by promoting *Mycobacterium ulcerans* (MU) accumulation in human tissues. Aidoo et al. [1] found a positive link between arsenic and MU spread, using a SIR model to explore BU transmission dynamics. Duker et al. [12] and Aidoo et al. [1] demonstrated positive associations between arsenic concentrations and the proliferation of *Mycobacterium ulcerans*, providing the empirical basis for modeling arsenic's influence on environmental contamination. Roche et al. [31] emphasize water bug biting, mortality rates, and arsenic concentration on BU prevalence. Bonyah et al. [4] propose a model with two BU transmission modes and a treatment function. Kimaro et al. [19] highlight arsenic's impact on MU proliferation, using optimal control theory to manage MU transmission via water bugs.

In our current investigation, we extend the framework proposed by Kimaro et al. [19], enhancing it to include separate compartments for the exposed and recovered individuals within the human population, and exclusively the exposed compartment within the vector populations. This refinement is biologically motivated by the nature of *Mycobacterium ulcerens* transmission: following exposure, humans undergo an incubation period before becoming infectious, necessitating an explicit Exposed class; moreover, individuals who recover from Buruli ulcer may experience waning immunity, justifying the inclusion of a Recovered class with possible return to susceptibility. For the vector populations, a latent period is also observed after pathogen acquisition before vectors become infectious, prompting the introduction of an Exposed compartment for vectors. Additionally, we tackle

the challenges related to immunity loss and disease-induced mortality attributed to *Mycobacterium ulcerans* infection within this demographic, as severe cases can lead to death if untreated.

Our primary objective is twofold: first, to establish stability properties of equilibria; second, to evaluate the basic reproduction number R_0, which serves as a determinant of endemicity. Notably, we observe a forward transcritical bifurcation around $R_0 = 1$. By formulating an appropriate Lyapunov function, we establish the global asymptotic stability of disease-free and endemic steady states. Our analysis underscores that if $R_0 \leq 1$, the disease-free state is globally asymptotically stable, leading to disease eradication. Conversely, if R_0 exceeds 1, a singular endemic state emerges as globally asymptotically stable, indicating disease persistence. Subsequently, we conduct numerical simulations to explore the influence of key parameters on the dissemination of vector-borne Buruli ulcers, validating our analytical conclusions and depicting potential behavioral scenarios. Our refined model yields more biologically grounded conclusions by integrating factors such as the exposed and recovered human populations and accounting for immunity loss and exposure dynamics in vectors. By addressing disease-induced mortality, our findings are enriched with greater realism, enhancing the validity and applicability of our results.

The research article follows this structure: introductory remarks and historical context in *Section 1*; description of model formulation, based on basic assumptions and hypotheses, in *Section 2*; presentation of preliminary results on solution existence and boundedness in *Section 3*; including study of the basic reproduction number using the next-generation operator; identification of equilibrium points, feasibility conditions, and local stability analysis in *Section 4 and 5*; demonstration of global asymptotic stability of disease-free and endemic steady states through construction of suitable Lyapunov functions in *Section 6*; numerical simulations illustrating model behavior in *Section 7*; and conclusion summarizing key findings in *Section 8*.

2. Model formulation

Within this segment, we have crafted an Ordinary Differential Equation (ODE) representation of a model delineating the transmission dynamics of a vector-borne disease among a host population. Our approach entails the utilization of an SEIR model for human populations and an SEI model for vector populations.

Our inquiry delves into the intricate transmission dynamics of Buruli ulcer (BU), encompassing three pivotal components: human hosts, water bugs, and the contamination of water sources with both Arsenic and *Mycobacterium ulcerans*.

In formulating our present model, we operate under the following foundational

assumptions:
(A1) The disease's etiology posits that it does not propagate through human-to-human transmission.
(A2) Human populations, waterbug habitats, and contaminated zones demonstrate spatial homogeneity.
(A3) Human individuals encounter random bites from water bugs upon contact.
(A4) Our model accounts for the immunocompromised status of recovered patients.
(A5) We assume simplified vector dynamics (constant birth-death processes) for tractability, as detailed vector ecology data are scarce. More complex models can be used in future work.
(A6) Immunity development does not occur among the vector class; once infected, the bugs persistently harbor M. ulcerans until death without clearing the infection. This observation is supported by Roche et al. [16], who found that infected aquatic bugs maintain M. ulcerans throughout their lifespan, and by Demange et al. [10], who similarly reported long-term persistence of the pathogen in aquatic vectors.
(A7) Elevated arsenic levels in water have been linked to higher *Mycobacterium ulcerans* presence, suggesting arsenic may facilitate BU transmission, as supported by findings from Duker et al. [14] and Gyasi et al. [17].

$$\left.\begin{array}{l} \textit{For human population} \\ \frac{dS_H}{dt} = A - \beta_H S_H I_W + \theta_H R_H - \mu_H S_H. \\ \frac{dE_H}{dt} = \beta_H S_H I_W - (\alpha_H + \mu_H) E_H. \\ \frac{dI_H}{dt} = \alpha_H E_H - (\gamma_H + \sigma_H + \mu_H) I_H \\ \frac{dR_H}{dt} = \gamma_H I_H - (\theta_H + \mu_H) R_H \\ \textit{For vector population} \\ \frac{dS_W}{dt} = B - \beta_W S_W I_H - \beta_E S_W \eta_E - \mu_W S_W. \\ \frac{dE_W}{dt} = \beta_W S_W I_H - \alpha_W E_W + \beta_E S_W \eta_E - \mu_W E_W. \\ \frac{dI_W}{dt} = \alpha_W E_W - (\mu_W + \delta_W) I_W. \\ \textit{For contaminated water containing MU} \\ \frac{d\eta_E}{dt} = a - \eta_E \nu_E. \end{array}\right\} \tag{2.1}$$

The dynamics of the total human population in the model (2.1) is obtained by adding associated human sub-classes to get

$$\frac{dN_H}{dt} = A - \sigma_H I_H - N_H I_H \tag{2.2}$$

the total dynamics of water-bug population in model (2.1) is given by

$$\frac{dN_W}{dt} = B - \delta_W I_W - N_W I_W \tag{2.3}$$

and the total population of *Mycobacterium ulceran* is given by

$$\frac{dN_E}{dt} = a - \eta_E \nu_E \tag{2.4}$$

In this classical epidemic model, the overall host population at time t, represented are stratified into three distinct epidemiological subclasses: susceptible $S_H(t)$, exposed $E_H(t)$, infected $I_H(t)$, and individuals in the recovery phase from infection $R_H(t)$. Mathematically, this division is expressed as $N_H(t) = S_H(t) + E_H(t) + I_H(t) + R_H(t)$.

The comprehensive vector population at time t, denoted as $N_W(t)$ is categorized into two distinctive epidemiological subclasses: susceptible water bug $S_W(t)$ and infectious water-bug $I_W(t)$. This partition is succinctly expressed as $N_W(t) = S_W(t) + E_W(t) + I_W(t)$.

In our consideration of disease transmission, we incorporate the environmental factor and introduce a distinct epidemiological component termed water contamination $\rho_E(t)$, encompassing *Mycobacterium ulcerans* (MU) due to arsenic.

State variables	Description of variables
N_H	The overall population size of human hosts
S_H	The count of uninfected, susceptible individuals within the human population
E_H	The tally of individuals in the human population who have encountered the infection
I_H	The tally of presently contagious individuals within the human population
R_H	The rate at which humans with latent infections receive treatment
N_W	The complete count of water bug vectors in the population
S_W	The number of water bugs in the vector population that are susceptible
E_W	The count of water bugs within the vector population that are in the exposed state
I_W	The number of infectious water bugs in the vector population.
η_E	Depicts environmental contamination with *Mycobacterium ulcer* (MU) in the water

Table 1: **Equation (2.1) uses state variables to describe the system's behavior over time**

Parameters	Description of parameters	Unit
a	Arsenic concentration rate in surface water	$\mu gl^{-1}year^{-1}$
μ_H	The intrinsic birth and death rates within the human population	$year^{-1}$
μ_W	The inherent birth and death rates within the vector population	$year^{-1}$
β_H	The likelihood of transmission from water bugs (vectors) to humans	$unitless$
β_W	The probability of transmission from humans to water bugs (the vector species)	$unitless$
β_E	Infectious rate of vector which is contact with contamination water	$persion^{-1}year^{-1}$
γ_H	The recovery rate in the Human population	$year^{-1}$
θ_H	The loss of immunity of recovered Humans	$unitless$
ν_E	The rate at which decontamination takes place in the aquatic environment	$year^{-1}$

Table 2: **Explanation of the parameters employed in the model's equation (2.1)**

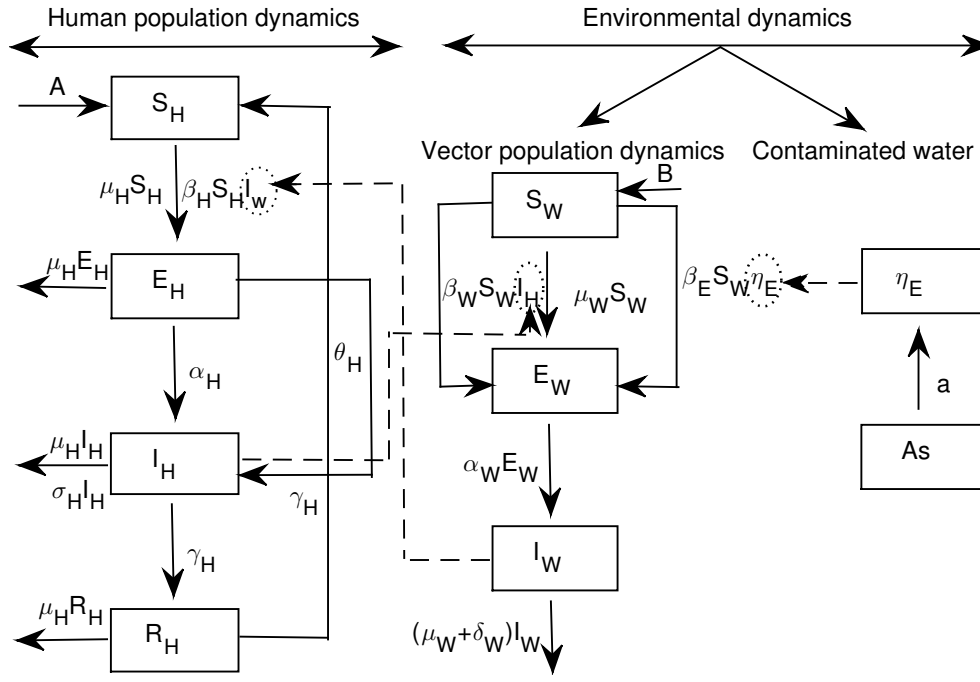

Figure 1: **The diagram shows the Buruli ulcer model**

3. Basic properties of the Buruli ulcer model

Theorem 3. *Let $S_H(0), E_H(0), I_H(0), R_H(0), S_W(0), E_W(0), I_W(0), \eta_E(0)$ be non-negative initial condition, then the system (2.1) has a non-negative solution for all instant $t > 0$. In addition, $limsup_{t\to\infty} N_H(t) \leq \frac{A}{\mu_H}$, $limsup_{t\to\infty} N_W(t) \leq \frac{B}{\mu_W}$ and $limsup_{t\to\infty} N_E(t) \leq \frac{a}{\eta_E}$. Furthermore if $N_H(0) \leq \frac{A}{\mu_H}$ then $N_H(t) \leq \frac{A}{\mu_H}$, if $N_W(0) \leq \frac{B}{\mu_W}$ then $N_W(t) \leq \frac{B}{\mu_W}$ and if $N_E(0) \leq \frac{a}{\eta_E}$ then $N_E(t) \leq \frac{a}{\eta_E}$. The feasible region in the model (2.1) is*

$$\Omega = \Omega_H \cup \Omega_W \cup \Omega_E \subset R_+^4 X R_+^3 X R_+^1 \tag{3.1}$$

where $\Omega_H = \{(S_H, E_H, I_H, R_H) \in R_+^4 : N_H(t) \leq \frac{A}{\mu_H}\}$, $\Omega_W = \{(S_W, E_W, I_W) \in R_+^3 : N_W(t) \leq \frac{B}{\mu_W}\}$ and $\Omega_E = \{\rho_E \in R_+^1 : N_E(t) \leq \frac{a}{\eta_E}\}$ is positively invariant and attracting with respect to model (2.1).

Proof. Using the first equation of model (2.1) gives rise to
$\frac{dS_H}{dt} + (\mu_H + \lambda)S_H \geq 0$, where $\lambda = \beta_H I_W$
This is a first-order linear differential equation. Here integrating factor is $\exp((\mu_H)t + \int_0^t \lambda(s)\mathrm{ds})$. Integrating (2.1) from time $t = 0$ to $t = t$ resulted into

$\frac{d}{dt}[S_H(t)\exp\{(\mu_H)t + \int_0^t \lambda(s)ds\}] \geq 0$
It means that $S_H(t) \geq S_H(0)\exp\{-(\mu_H t + \int_0^t \lambda(s)ds)\}$, for all $t \geq 0$
We have followed similar approach to establish that $E_H, I_H, R_H, S_W, I_W, \rho_E$ are non-negative for all instant $t > 0$.
We prove the other part of the theorem using Eqs. (2.2) - (4.2) to show that system (2.1) is positively invariant so that
$N_H(t) \leq N_H(0)e^{-\mu_H t} + \frac{A}{\mu_H}(1 - e^{-\mu_H t})$,
$N_W(t) \leq N_W(0)e^{-\mu_W t} + \frac{B}{\mu_W}(1 - e^{-\mu_W t})$,
$\eta_E(t)_E \leq \eta_E(0)e^{-\eta_E t} + \frac{a}{\eta_E}(1 - e^{-\eta t})$.
It follows that as $t \mapsto \infty$ $N_H(t) \leq \frac{A}{\mu_H}$, $N_W(t) \leq \frac{B}{\mu_W}$, and $\eta(t)_E \leq \frac{a}{\nu_E}$. Furthermore if $N_H(0) \leq \frac{A}{\mu_H}$ then $N_H(t) \leq \frac{A}{\mu_H}$, if $N_W(0) \leq \frac{B}{\mu_W}$ then $N_W(t) \leq \frac{B}{\mu_W}$ and if $\eta(0) \leq \frac{a}{\nu_E}$ then $\eta(t)_E \leq \frac{a}{\nu_E}$.
Thus it is clear that Ω is positively invariant. The boundedness of the solutions inside Ω is hereby proven. We conclude that the solutions to model (2.1) are positively invariant and attractive in a region Ω. According to the theorem, we deduced that system (2.1) is biologically feasible and well-posed mathematically in Ω.

4. Estimating the Basic Reproduction Number (R_0) with the Next-Generation matrix (NGM) method

The basic reproduction number, symbolized as R_0, is a fundamental pillar in epidemic theory. It provides insight into the expected number of secondary cases arising from a single infection within a completely susceptible population over the entire infectious period.

We employ the next-generation matrix approach to calculate the basic reproduction number, denoted as R_0, for the model (2.1). Within this framework, a disease-free equilibrium state is established at $E_0(S_H^0 = \frac{A}{\mu_H}, E_H^0 = 0, I_H^0 = 0, R_H^0 = 0, S_W^0 = \frac{B}{\mu_W}, I_W^0 = 0, \eta_E^0 = 0)$.
The infected compartments in the system (2.1) encompass various classes, including $E_H(t)$, $I_H(t)$, $E_W(t)$, $I_W(t)$, and $\eta_E(t)$. By the next-generation matrix approach, we determine both the non-negative infection matrix F and the non-singular transition matrix V at the disease-free equilibrium state E_0 as follows:

$$\therefore F(E_0) = \begin{pmatrix} 0 & 0 & 0 & \beta_H S_H^0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \beta_W S_W^0 & 0 & 0 & 0 & \beta_E S_W^0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{4.1}$$

$$V(E_0) = \begin{pmatrix} k_1 & 0 & 0 & 0 & 0 \\ 0 & k_2 & 0 & 0 & 0 \\ 0 & 0 & k_4 & 0 & 0 \\ 0 & 0 & 0 & k_5 & 0 \\ 0 & 0 & 0 & 0 & \nu_E \end{pmatrix} \tag{4.2}$$

Each term in the infection matrix F corresponds to the incidence rate of new infections per unit time, ensuring units of (1/time). Similarly, each term in the transition matrix V corresponds to rates of transfer between compartments (e.g., progression, recovery, or death), also measured in (1/time). Consequently, FV^{-1} becomes a dimensionless matrix, which complies with the requirement that the basic reproduction number R_0 must be dimensionless. The grouping of terms in V was logically structured based on biologically similar transition processes to ensure analytical tractability while maintaining dimensional consistency.
So, the next generation matrix FV^{-1} is

$$FV^{-1} = \begin{pmatrix} 0 & 0 & \frac{\beta_H S_H^0 \alpha_W}{K_4 k_5} & \frac{\beta_H S_H^0}{k_5} & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_W S_W^0 \alpha_H}{K_1 K_2} & \frac{\beta_W S_W^0}{K_2} & 0 & 0 & \frac{\beta_E S_W^0}{\nu_E} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{4.3}$$

The eigenvalues of FV^{-1} can be expressed as follows:
$\{0, 0, 0, -\sqrt{\frac{\beta_H \beta_W \alpha_H \alpha_W S_H^0 S_W^0}{k_1 k_2 K_4 K_5}}, \sqrt{\frac{\beta_H \beta_W \alpha_H \alpha_W S_H^0 S_W^0}{k_1 k_2 K_4 K_5}}\}$.
Among these eigenvalues, we focus on the largest dominant eigenvalue, which represents the basic reproduction number of the next-generation matrix, denoted as R_0^{ng}. It is defined as [11, 36] $\rho(FV^{-1})$ and can be expressed as: $R_0^{ng} \equiv \rho(FV^{-1}) = R_0 = \sqrt{\frac{\beta_H \beta_W \alpha_H \alpha_W S_H^0 S_W^0}{k_1 k_2 K_4 K_5}}$.
To further understand the influence of model parameters on R_0, a preliminary sensitivity analysis using Partial Rank Correlation Coefficients (PRCC) can be conducted. PRCC is a global sensitivity analysis method that quantifies the strength and direction of the relationship between input parameters and model outputs, accounting for the effects of other variables. This technique has been effectively utilized in infectious disease modeling to identify key parameters influencing R_0. Future work will explore this direction to refine parameter prioritization and enhance the model's predictive capabilities.

4.1. Steady state analysis

The model system (2.1) exhibits two distinct non-negative steady states:
(i) The Disease-free Axial Steady State (DFASS) denoted as $D_1(S_H^0, 0, 0, 0, S_W^0, 0, 0, 0)$.
(ii) The Endemic Steady State (ESS) represented as $D^*(S_H^*, E_H^*, I_H^*, R_H^*, S_W^*, E_W^*, I_W^*, \eta_E^*)$.

5. Stability analysis

This part of the paper focuses on analyzing the local stability of the system (2.1) around each of these steady states. The stability criteria of the system (2.1) around steady states D and D_* are stated in the following theorem.

Theorem 5.1. *(a) Within the realm of positive real space R_+^8, the elegance of the local asymptotic stability of the disease-free steady-state unfolds gracefully, elegantly asserted when $R_0 < 1$ and (b) The presence of an endemic steady-state, denoted as $D^*(S_H^*, E_H^*, I_H^*, R_H^*, S_W^*, E_W^*, I_W^*, \eta_E^*)$ in the system (2.1), indicates its local stability if $R_0 > 1$.*

Proof. When $R_0 < 1$, it signifies that either no infections are present in the water bug population, or they serve exclusively as carriers.
To perform a local stability analysis of the system (2.1) around the disease-free equilibrium (DFE), denoted as $E_0(S_H^0, E_H^0, I_H^0, R_H^0, S_W^0, E_W^0, I_W^0, \eta_E^0)$, we calculate the Jacobian matrix. The initial conditions are specified as follows: $S_H^0 = \frac{A}{\mu_W}$, $E_H^0 = 0$, $I_H^0 = 0$, $R_H^0 = 0$, $S_W^0 = \frac{B}{\mu_W}$, $E_W^0 = 0$, $I_W^0 = 0$, and $\eta_E^0 = 0$.

$$So, J_{E_0} = \begin{pmatrix} -\mu_H & 0 & 0 & \theta_H & 0 & 0 & \beta_H S_H^0 & 0 \\ 0 & -k_1 & 0 & 0 & 0 & 0 & \beta_H S_H^0 & 0 \\ 0 & \alpha_H & -k_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_H & -k_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_W S_W^0 & 0 & -\mu_W & 0 & 0 & -\beta_E S_W^0 \\ 0 & 0 & \beta_W S_W^0 & 0 & 0 & -k_4 & 0 & \beta_E S_W^0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_W & -k_5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\nu_E \end{pmatrix} \tag{5.1}$$

Hence $\det|E_0 - \lambda I_8|$.

$$\begin{pmatrix} -\mu_H-\lambda & 0 & 0 & \theta_H & 0 & 0 & \beta_H S_H^0 & 0 \\ 0 & -k_1-\lambda & 0 & 0 & 0 & 0 & \beta_H S_H^0 & 0 \\ 0 & \alpha_H & -k_2\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_H & -k_3-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_W S_W^0 & 0 & -\mu_W-\lambda & 0 & 0 & -\beta_E S_W^0 \\ 0 & 0 & \beta_W S_W^0 & 0 & 0 & -k_4-\lambda & 0 & \beta_E S_W^0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_W & -k_5-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\nu_E-\lambda \end{pmatrix}$$

The characteristic equation of $\det|E_0 - \lambda I_8|$ is in the form

$$P(\lambda) = (\mu_H + \lambda)(k_3 + \lambda)(\mu_W + \lambda)(\nu_E + \lambda)T(\lambda), \tag{5.2}$$

Now the eigen values of $P(\lambda) = 0$ are $\lambda_1 = -\mu_H, \lambda_2 = -\mu_W, \lambda_3 = -k_3, \lambda_4 = -\nu_E$ and $T(\lambda) = 0$ with $T(\lambda) = a_4\lambda^4 + a_3\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0$ where
$a_4 = 1$,
$a_3 = k_1 + k_2 + k_4 + k_5$,
$a_2 = k_1k_2 + k_4k_5 + (k_1 + k_2)(k_4 + k_5) + k_1k_2k_4k_5$,
$a_1 = k_1k_2(k_4 + k_5) + k_4k_5(k_1 + k_2)$,
$a_0 = k_1k_2k_4k_5(1 - R_0^2)$
To ascertain the system's stability, we meticulously analyze its eigenvalues, ensuring their compliance with the Routh-Hurwitz Criteria, as expounded by LaSalle in 1976 [20]. Specifically, we necessitate that $a_i > 0$ for $i = 0, 1, 2, 3$, and that $a_3a_2a_1 > a_1^2 + a_3^2a_0$.

Under the condition where $R_0 < 1$ this prerequisite is met, guaranteeing that $a_i > 0$ for $i = 0, 1, 2, 3$. As a result, every eigenvalue of the characteristic equation associated with (5.2) showcases a negative real component, thereby confirming the local asymptotic stability of the disease-free equilibrium denoted as E_1

The endemic steady state and its stability analysis

To identify the endemic equilibria of the system (2.1), where at least one of the infected components is non-zero, we follow these steps:

Let $E_2 = (S_H^*, E_H^*, I_H^*, R_H^*, S_W^*, E_W^*, I_W^*, \eta_E^*)$ represent an arbitrary endemic equilibrium of the model (2.1). To determine the values of these variables at steady state, we solve the equations of the system (2.1):

$$\eta_E^* = \frac{a}{\nu_E}, \tag{5.3}$$

$$E_H^* = (\frac{k_2}{\alpha_H})I_H^*, \tag{5.4}$$

$$R_H^* = (\frac{\gamma_H}{k_3})I_H^* \tag{5.5}$$

$$S_H^* = \frac{k_1}{\beta_H I_W^*}E_H^* \tag{5.6}$$

$$S_W^* = \frac{B}{(\beta_W I_H^* + \beta_E \frac{\alpha}{\nu_E} + \mu_W)}, \tag{5.7}$$

$$E_W^* = \frac{(\beta_W I_H^* + \beta_E \frac{\alpha}{\nu_E})B}{k_4(\beta_W I_H^* + \beta_E \frac{\alpha}{\nu_E} + \mu_W)} \tag{5.8}$$

$$I_W^* = \frac{\alpha_W}{k_4} E_W^* \tag{5.9}$$

I_H^* is the solution of the following cubic equation

$$f(I_H^*) = L_1(I_H^*)^2 + L_2(I_H^*) + L_3 = 0, \tag{5.10}$$

where

$$L_1 = B\beta_H\beta_W\alpha_W(\frac{\theta_H\gamma_H}{k_3} - \frac{k_1k_2}{\alpha_H}) - \frac{k_1k_2k_4\mu_H\beta_W}{\alpha_H} \tag{5.11}$$

$$L_2 = B\beta_H\alpha_W\beta_E\frac{a}{\nu_E}(\frac{\theta_H\gamma_H}{k_3} - \frac{k_1k_2}{\alpha_H}) - \frac{a\mu_H\beta_Ek_1k_2k_4k_5}{\nu_E\alpha_H} - \frac{\mu_H\mu_Wk_1k_2k_4k_5}{\alpha_H}(1 - R_0^2) \tag{5.12}$$

$$L_3 = AB\beta_H\alpha_W\beta_E\frac{a}{\nu_E} \tag{5.13}$$

Since all parameters in (2.1) are non-negative, it is easily numerically verified from (5.10) that $L_1 < 0$ and $L_3 > 0$. Furthermore, $L_2 > 0$ or $L_2 < 0$ when $R_0 > 1$ and $R_0 < 1$ respectively. Using the Descartes Rule of Signs, a positive solution of the equation $f(I_H^*) = 0$ exists, so there will always be a unique endemic equilibrium point.

Theorem 5.2. *The model has a unique endemic equilibrium point.*

5.0.1. Forward transcritical bifurcation

Our qualitative analysis of the model (2.1) reveals two distinct equilibrium points: one representing a disease-free state and the other characterizing an endemic state. The stability of the disease-free equilibrium is contingent upon the value of the basic reproduction number, R_0: it is stable when $R_0 < 1$ and unstable when $R_0 > 1$ Conversely, the stability of the endemic equilibrium depends on R_0: it is stable when $R_0 > 1$ and unstable when $R_0 < 1$, subject to certain conditions. This exchange of stability occurs precisely at the critical threshold $R_0 = 1$, a phenomenon known as a forward transcritical bifurcation. Notably, in this scenario, the equilibrium points undergo a stability switch as they cross the value of 1, with the endemic equilibrium exhibiting a forward transcritical bifurcation.

Biologically, the forward transcritical bifurcation at $R_0 = 1$ implies that if control measures reduce R_0 is below unity, the disease can be eradicated. In contrast, if R_0 exceeds unity, the Buruli ulcer persists in the population.

For a visual representation, refer to Figure 2, illustrating the bifurcation diagram of model (2.1).

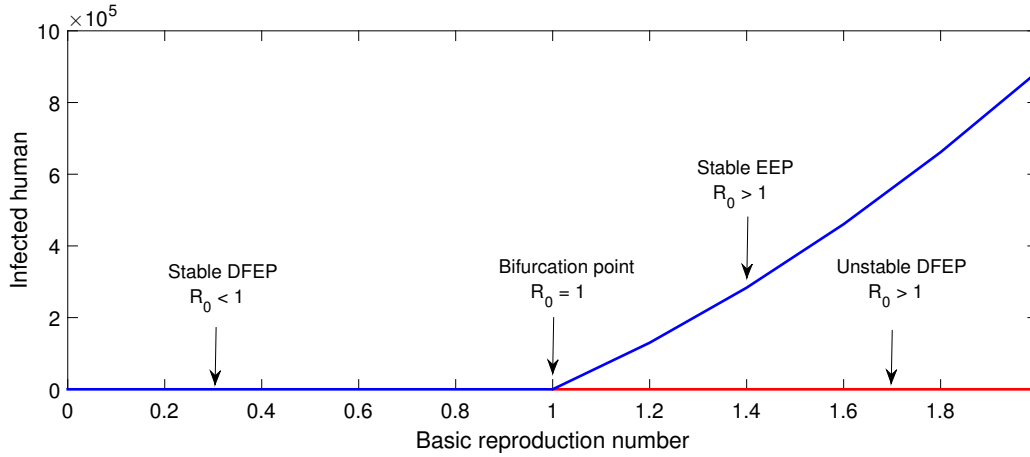

Figure 2: **The visualization portraying the relationship between infected human (I_H) and basic reproduction number (R_0) unveils a forward transcritical bifurcation centered around the critical value of $R_0 = 1$. In this specific context, the chosen parameter values are as follows:** $\mu_W = 0.3333333$, $\beta_W = 0.000015$, $\beta_E = 0.000001$, $\psi_{\beta_H} = 1.2$, $\alpha_H = 0.0018$, $\theta_H = 0.04$, $\gamma_H = 0.5$, $\nu_E = 0.9123$, **and** $\alpha_W = 1.5$.

6. Global Stability analysis

In this section, we embark on a meticulous global analysis, delving deep into the intricacies of the disease-free and endemic equilibria. Our chosen path employs the venerable direct Lyapunov method, a technique demanding the artful construction of a function endowed with particular properties. To facilitate this analytical voyage, we shall unveil the following pivotal findings.

Global stability of disease-free equilibrium with Lyapunov function
The following theorem elucidates a pivotal global characteristic of the disease-free equilibrium, denoted as E_1, in the framework of the system (2.1).

Theorem 6.1. *If α and θ_H both equal zero, then the disease-free equilibrium point E_0 of the system described by equations (2.1) exhibits global asymptotic stability within the region Γ_ε when $R_0 \leq 1$.*

Proof. To ascertain the global stability of the disease-free equilibrium, known as E_0, we will harness the versatility of a nonlinear Lyapunov function aptly named L. This function's realm of definition resides within the well-defined domain denoted as Γ_ϵ^+, and its role in our analysis is nothing short of pivotal. Before we dive into the intricacies, let's map out the flexible steps that will guide our journey:
Definition of the Lyapunov function L on the domain L_ϵ^+. Now, let's embark on the

journey of computing the time derivative of L as we traverse along the solutions of the system equation (2.1):
$\dot{L} = W_0\frac{(S_H-S_H^0)}{S_H}(A-\beta_H S_H I_W+\theta_H R_H-\mu_H S_H)+W_1(\beta_H S_H I_W-k_1 E_H)+W_2(\alpha_H E_H-k_2 I_H)+W_3(\gamma_H I_H-k_3 R_H)+W_4\frac{(S_W-S_W^0)}{S_W}(B-\beta_W S_W I_H-\beta_E S_W\eta_E-\mu_W S_W)+W_5(\beta_W S_W I_H+\beta_E S_W\eta_E-k_4 E_W)+W_6(\alpha_W E_W-k_5 I_W)+W_7(\alpha-\eta_E\nu_E)$
The '.' notation, perched atop, signals our intent to differentiate concerning the temporal variable 't'. When we infuse this notation with the initial conditions $S_H^0=\frac{A}{\mu_H}$ and $S_W^0=\frac{B}{\mu_W}$, the equation gracefully transforms into:
$\dot{L} = -W_0\mu_H\frac{(S_H-\frac{A}{\mu_H})^2}{S_H}-W_4\mu_W\frac{(S_W-\frac{B}{\mu_W})^2}{S_W}+(W_1-W_0)\beta_H S_H I_W+(W_5-W_4)\beta_W S_W I_H+(W_0\frac{(S_H-S_H^0)}{S_H}\theta_H-W_3k_3)R_H+(W_2\alpha_H-W_1k_1)E_H+(W_3\gamma_H+W_4\beta_W S_W^0-W_2k_2)I_H+(W_5-W_4)\beta_E S_W\eta_E+(W_4S_W^0\beta_E-W_7\nu_E)\eta_E+(W_6\alpha_W-W_5k_3)E_W+(W_0\beta_H S_H^0-W_6k_4)I_W+W_7\alpha$
Given the widespread awareness created through media channels in developed and developing countries, we can assume that the arsenic concentration rate tends towards zero, i.e., $\alpha=0$. Furthermore, if the disease provides permanent immunity against re-infection, the term θ_H becomes unnecessary, and we can set $\theta_H=0$. We can choose the following values for the parameters: $W_0=W_1=1, W_2=\frac{k_1}{\alpha_H}$, $W_3=\frac{\theta_H}{k_3}$, $W_4=W_5=\frac{\beta_H\alpha_W S_H^0}{k_4k_5}$, $W_6=\frac{\beta_H S_H^0}{k_5}$, $W_7=\frac{\beta_E S_W^0}{\nu_E}$.
Now, by substituting these values into the expression for L and performing some rearrangements, the expression simplifies to:

$$\dot{L} < -\mu_H\frac{(S_H-\frac{A}{\mu_H})^2}{S_H}-\mu_W\frac{(S_W-\frac{B}{\mu_W})^2}{S_W}-\frac{k_1k_2}{\alpha_H}(1-R_0^2) \tag{6.1}$$

By analyzing the time derivative $\dot{L}$, we have established that $\dot{L}$ is negative if $R_0\leq 1$. Furthermore, we observe that $\dot{L}=0$ if and only if the following conditions are met: $S_H^0=\frac{A}{\mu_H}, S_W^0=\frac{B}{\mu_W}$, $E_H^0=I_H^0=R_H^0=0$, $E_W^0=I_W^0=0$, and $\eta_E^0=0$. As a result, the largest compact invariant set in $(S_H,E_H,I_H,R_H,S_W,E_W,I_W,\eta_E)\in\Gamma_\varepsilon:\dot{L}=0$ consists of the singleton E_1, where E_1 represents the disease-free equilibrium point. By applying Lasalle's invariant principle [20], we conclude that E_1 is globally asymptotically stable within Γ_ε, thereby completing the proof.

Global Stability of endemic equilibrium with Lyapunov function
Our objective now is to demonstrate the global stability of the endemic equilibrium $E_1(S_H^*,E_H^*,I_H^*,R_H^*,S_W^*,E_W^*,I_W^*,\eta_E^*)$, where $S_H^*,E_H^*,I_H^*,R_H^*,S_W^*,E_W^*,I_W^*,\eta_E^*$ are the solutions to the following equations:

$$\left.\begin{array}{rcl} A-\beta_H S_H^* I_W^* + \theta_H R_H^* - \mu_H S_H^* &=& 0 \\ \beta_H S_H^* I_W^* - (\alpha_H + \mu_H) E_H^* &=& 0 \\ \alpha_H E_H^* - (\gamma_H + \sigma_H + \mu_H) I_H^* &=& 0 \\ \gamma_H I_H^* - (\theta_H + \mu_H) R_H^* &=& 0 \\ B - \beta_W S_W^* I_H^* - \beta_E S_W^* \eta_E^* - \mu_W S_W^* &=& 0 \\ \beta_W S_W^* I_H^* - \alpha_W E_W^* + \beta_E S_W^* \eta_E^* - \mu_W E_W^* &=& 0 \\ \alpha_W E_W^* - (\mu_W + \delta_W) I_W^* &=& 0 \\ a - \eta_E^* \nu_E &=& 0 \end{array}\right\} \tag{6.2}$$

We have the following theorem.

Theorem 6.2. *In the presence of $R_0 > 1$, the unique endemic equilibrium, denoted as E_2, in the Buruli ulcer model (2.2), exudes an aura of asymptotic stability. It gracefully resides within a discerning subset, Γ_0, nestled within the expansive expanse of Γ_ε. This subset is meticulously defined as follows:*
$\Gamma_0 = \{(S_H, E_H, I_H, R_H, S_W, E_W, I_W, \eta_E) \in \Gamma_\varepsilon : V_1 = 1 + \frac{R_H S_H^*}{R_H^* S_H} - \frac{R_H}{R_H^*} - \frac{S_H^*}{S_H} \geq 0.\}$
Proof. In our pursuit of establishing the global stability of the endemic equilibrium E_2, we shall introduce an ingenious nonlinear Lyapunov function, denoted as L, which maps from the positive region of Γ_ϵ to the real numbers. This function is characterized by the following: $\Gamma^+\epsilon = \{S_H, E_H, I_H, R_H, S_W, E_W, I_W, \eta_E \in \Gamma\varepsilon : S_H > 0, E_H > 0, I_H > 0, R_H > 0, S_W > 0, E_W > 0, I_W > 0, \eta_E > 0\}$ This function is defined as:

$$\begin{array}{rcl} L(t) &=& W_0(S_H - S_H^* - S_H^* \log \frac{S_H}{S_H^*}) + W_1(E_H - E_H^* - E_H^* \log \frac{E_H}{E_H^*}) \\ && + W_2(I_H - I_H^* - I_H^* \log \frac{I_H}{I_H^*}) + W_3(R_H - R_H^* - R_H^* \log \frac{R_H}{R_H^*}) \\ && + W_4(S_W - S_W^* - S_W^* \log \frac{S_W}{S_W^*}) + W_5(E_W - E_W^* - E_W^* \log \frac{E_W}{E_W^*}) \\ && + W_6(I_W - I_W^* - I_W^* \log \frac{I_W}{I_W^*}) + W_7(\eta_E - \eta_E^* - \eta_E^* \log \frac{\eta_E}{\eta_E^*})\dot{\eta_E} \end{array} \tag{6.3}$$

The Layapunov function L is continuous for all $S_H, E_H, I_H, R_H, S_W, E_W, I_W, \eta_E > 0$. In our pursuit of establishing the global stability of the endemic equilibrium E_2, we introduce an intricate nonlinear Lyapunov function denoted as L. This function elegantly maps the positive region of Γ_ϵ to the real numbers. Its time derivative along the trajectories of the system (2.1) is computed as follows:
$\dot{L}(t) = W_0(1 - \frac{S_H^*}{S_H})\dot{S}_H + W_1(1 - \frac{E_H^*}{E_H})\dot{E}_H + W_2(1 - \frac{I_H^*}{I_H})\dot{I}_H + W_3(1 - \frac{R_H^*}{R_H})\dot{R}_H$
$+ W_4(1 - \frac{S_W^*}{S_W})\dot{S}_W + W_5(1 - \frac{E_W^*}{E_W})\dot{E}_W + W_6(1 - \frac{I_W^*}{I_W})\dot{I}_W + W_7(1 - \frac{\eta_E^*}{\eta_E})\dot{\eta}_E.$
It follows that the first equation of (2.1)

$$\begin{aligned}(1-\tfrac{S_H^*}{S_H})\dot{S}_H &= (1-\tfrac{S_H^*}{S_H})(A-\beta_H S_H I_W+\theta_H R_H-\mu_H S_H)\\ &= \mu_H S_H^*(2-\tfrac{S_H^*}{S_H}-\tfrac{S_H}{S_H^*})+\beta_H S_H^* I_W^*(1-\tfrac{S_H^*}{S_H}-\tfrac{S_H I_W}{S_H^* I_W^*}+\tfrac{I_W}{I_W^*})\\ &-\theta_H R_H^*(1-\tfrac{S_H^*}{S_H}-\tfrac{R_H}{R_H^*}+\tfrac{R_H S_H^*}{R_H^* S_H}).\end{aligned} \tag{6.4}$$

Similarly, remaining eight equations in (2.1) we have

$$\begin{aligned}(1-\tfrac{E_H^*}{E_H})\dot{E}_H &= (1-\tfrac{E_H}{E_H^*})(\beta_H S_H I_W-k_1 E_H)\\ &= \beta_H S_H^* I_W^*(1+\tfrac{S_H I_W}{S_H^* I_W^*}-\tfrac{E_H}{E_H^*}-\tfrac{S_H I_W E_H^*}{S_H^* I_W^* E_H})\end{aligned} \tag{6.5}$$

$$\begin{aligned}(1-\tfrac{I_H^*}{I_H})\dot{I}_H &= (1-\tfrac{I_H^*}{I_H})(\alpha_H E_H-k_2 I_H)\\ &= \alpha_H E_H^*(1+\tfrac{E_H}{E_H^*}-\tfrac{I_H}{I_H^*}-\tfrac{E_H I_H^*}{E_H^* I_H}).\end{aligned} \tag{6.6}$$

$$\begin{aligned}(1-\tfrac{R_H^*}{R_H})\dot{R}_H &= (1-\tfrac{R_H}{R_H^*})(\gamma_H I_H-k_3 R_H)\\ &= \gamma_H I_H^*(1+\tfrac{I_H}{I_H^*}-\tfrac{R_H}{R_H^*}-\tfrac{I_H R_H^*}{I_H^* R_H}).\end{aligned} \tag{6.7}$$

$$\begin{aligned}(1-\tfrac{S_W^*}{S_W})\dot{S}_W &= (1-\tfrac{S_W^*}{S_W})(B-\beta_W S_W I_H-\beta_E S_W \eta_E-\mu_W S_W)\\ &= \beta_W S_W^* I_H^*(1-\tfrac{S_W^*}{S_W}-\tfrac{S_W I_H}{S_W^* I_H^*}+\tfrac{I_H}{I_H^*})+\beta_E S_W^* \eta_E^*(1-\tfrac{S_W^*}{S_W}-\tfrac{S_W \eta_E}{S_W^* \eta_E^*}+\tfrac{\eta_E}{\eta_E^*})\\ &+\mu_W S_W^*(2-\tfrac{S_W}{S_W^*}-\tfrac{S_W^*}{S_W}).\end{aligned} \tag{6.8}$$

$$\begin{aligned}(1-\tfrac{E_W^*}{E_W})\dot{E}_W &= (1-\tfrac{E_W^*}{E_W})(\tfrac{\beta_W S_W I_H}{N}+\beta_E S_W \eta_E-k_5 E_W)\\ &= \beta_W S_W^* I_H^*(1+\tfrac{S_W I_H}{S_W^* I_H^*}-\tfrac{E_W}{E_W^*}-\tfrac{S_W I_H E_W^*}{S_W^* I_H^* E_W})\\ &+\beta_E S_W^* \eta_E^*(1+\tfrac{S_W \eta_E}{S_W^* \eta_E^*}-\tfrac{E_W}{E_W^*}-\tfrac{S_W \eta_E E_W^*}{S_W^* \eta_E^* E_W}).\end{aligned} \tag{6.9}$$

$$\begin{aligned}(1-\tfrac{I_W^*}{I_W})\dot{I}_W &= (1-\tfrac{I_W^*}{I_W})(\alpha_W E_W-\mu_W I_W).\\ &= \alpha_W E_W^*(1+\tfrac{E_W}{E_W^*}-\tfrac{I_W}{I_W^*}-\tfrac{E_W I_W^*}{E_W^* I_W}).\end{aligned} \tag{6.10}$$

$$\begin{aligned}(1-\tfrac{\eta_E^*}{\eta_E})\dot{\eta}_E &= (1-\tfrac{\eta_E^*}{\eta_E})(\alpha-\eta_E \nu_E).\\ &= \alpha(2-\tfrac{\eta_E}{\eta_E^*}-\tfrac{\eta_E^*}{\eta_E}).\end{aligned} \tag{6.11}$$

Substituting the expression from system (2.1) at the endemic steady state, we have:

$$\left.\begin{aligned}&\dot{L}=W_0\{\mu_H S_H^*(2-\tfrac{S_H^*}{S_H}-\tfrac{S_H}{S_H^*})+\beta_H S_H^* I_W^*(1-\tfrac{S_H^*}{S_H}-\tfrac{S_H I_W}{S_H^* I_W^*}+\tfrac{I_W}{I_W^*})-\theta_H R_H^*(1-\tfrac{S_H^*}{S_H}-\tfrac{R_H}{R_H^*}+\tfrac{R_H S_H^*}{R_H^* S_H})\}\\ &+W_1\{\beta_H S_H^* I_W^*(1+\tfrac{S_H I_W}{S_H^* I_W^*}-\tfrac{E_H}{E_H^*}-\tfrac{S_H I_W E_H^*}{S_H^* I_W^* E_H})\}+W_2\{\alpha_H E_H^*(1+\tfrac{E_H}{E_H^*}-\tfrac{I_H}{I_H^*}-\tfrac{E_H I_H^*}{E_H^* I_H})\}\\ &+W_3\{\gamma_H I_H^*(1+\tfrac{I_H}{I_H^*}-\tfrac{R_H}{R_H^*}-\tfrac{I_H R_H^*}{I_H^* R_H})\}+W_4\{\beta_W S_W^* I_H^*(1-\tfrac{S_W^*}{S_W}-\tfrac{S_W I_H}{S_W^* I_H^*}+\tfrac{I_H}{I_H^*})+\beta_E S_W^* \eta_E^*(1-\tfrac{S_W^*}{S_W}-\\ &\tfrac{S_W \eta_E}{S_W^* \eta_E^*}+\tfrac{\eta_E}{\eta_E^*})+\mu_W S_W^*(2-\tfrac{S_W}{S_W^*}-\tfrac{S_W^*}{S_W})\}+W_5\{\beta_W S_W^* I_H^*(1+\tfrac{S_W I_H}{S_W^* I_H^*}-\tfrac{E_W}{E_W^*}-\tfrac{S_W I_H E_W^*}{S_W^* I_H^* E_W})\\ &+\beta_E S_W^* \eta_E^*(1+\tfrac{S_W \eta_E}{S_W^* \eta_E^*}-\tfrac{E_W}{E_W^*}-\tfrac{S_W \eta_E E_W^*}{S_W^* \eta_E^* E_W})\}+W_6\{\alpha_W E_W^*(1+\tfrac{E_W}{E_W^*}-\tfrac{I_W}{I_W^*}-\tfrac{E_W I_W^*}{E_W^* I_W})\}\\ &+W_7\{a(2-\tfrac{\eta_E}{\eta_E^*}-\tfrac{\eta_E^*}{\eta_E})\}.\end{aligned}\right\} \tag{6.12}$$

Here, the system of equations is given below

$$\left.\begin{array}{rcl} W_0\beta_H S_H^* I_W^* - W_6\alpha_W E_W^* &=& 0 \\ W_1\beta_H S_H^* I_W^* - W_0\beta_H S_H^* I_W^* &=& 0 \\ W_2\alpha_H E_H^* - W_1\beta_H S_H^* I_W^* &=& 0 \\ W_3\gamma_H I_H^* - W_2\alpha_H E_H^* + W_4\beta_W S_W^* I_H^* &=& 0 \\ W_4\beta_E S_W^* \eta_E^* - W_7 a &=& 0 \\ W_5\beta_W S_W^* I_H^* - W_4\beta_W S_W^* I_H^* &=& 0 \\ W_6\alpha_W E_W^* - W_5\beta_W S_W^* I_H^* - W_5\beta_E S_W^* \eta_E^* &=& 0 \end{array}\right\} \tag{6.13}$$

Next, setting the values of the coefficients

$$\left.\begin{array}{l} W_0 = W_1 = \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*} \\ W_2 = \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\alpha_H E_H^*} \\ W_3 = \frac{\beta_E S_W^* \eta_E^*}{\gamma_H I_H^*} \\ W_4 = W_5 = 1 \\ W_6 = \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\alpha_W E_W^*} \\ W_7 = \frac{\beta_E S_W^* \eta_E^*}{a} \end{array}\right\} \tag{6.14}$$

in equation (6.17). After some calculation, we have

$$\left.\begin{array}{l} \dot{L} = \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}\{\mu_H S_H^*(2 - \frac{S_H^*}{S_H} - \frac{S_H}{S_H^*}) + \beta_H S_H^* I_W^*(1 - \frac{S_H^*}{S_H} - \frac{S_H I_W}{S_H^* I_W^*} + \frac{I_W}{I_W^*}) - \theta_H R_H^*(1 - \frac{S_H^*}{S_H} - \\ \frac{R_H}{R_H^*} + \frac{R_H S_H^*}{R_H^* S_H})\} + \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}\{\beta_H S_H^* I_W^*(1 + \frac{S_H I_W}{S_H^* I_W^*} - \frac{E_H}{E_H^*} - \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H})\} + \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\alpha_H E_H^*} \\ \{\alpha_H E_H^*(1 + \frac{E_H}{E_H^*} - \frac{I_H}{I_H^*} - \frac{E_H I_H^*}{E_H^* I_H})\} + \frac{\beta_E S_W^* \eta_E^*}{\gamma_H I_H^*}\{\gamma_H I_H^*(1 + \frac{I_H}{I_H^*} - \frac{R_H}{R_H^*} - \frac{I_H R_H^*}{I_H^* R_H})\} + \{\beta_W S_W^* I_H^*(1 - \\ \frac{S_W^*}{S_W} - \frac{S_W I_H}{S_W^* I_H^*} + \frac{I_H}{I_H^*}) + \beta_E S_W^* \eta_E^*(1 - \frac{S_W^*}{S_W} - \frac{S_W \eta_E}{S_W^* \eta_E^*} + \frac{\eta_E}{\eta_E^*}) + \mu_W S_W^*(2 - \frac{S_W}{S_W^*} - \frac{S_W^*}{S_W})\} \\ + \{\beta_W S_W^* I_H^*(1 + \frac{S_W I_H}{S_W^* I_H^*} - \frac{E_W}{E_W^*} - \frac{S_W I_H E_W^*}{S_W^* I_H^* E_W}) + \beta_E S_W^* \eta_E^*(1 + \frac{S_W \eta_E}{S_W^* \eta_E^*} - \frac{E_W}{E_W^*} - \frac{S_W \eta_E E_W^*}{S_W^* \eta_E^* E_W})\} + \\ \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\alpha_W E_W^*}\{\alpha_W E_W^*(1 + \frac{E_W}{E_W^*} - \frac{I_W}{I_W^*} - \frac{E_W I_W^*}{E_W^* I_W})\} + \frac{\beta_E S_W^* \eta_E^*}{a}\{a(2 - \frac{\eta_E}{\eta_E^*} - \frac{\eta_E^*}{\eta_E})\}. \end{array}\right\} \tag{6.15}$$

After a little rearrangement, we obtain,

$$\left.\begin{array}{l} \dot{L} = -\theta_H R_H^* \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}(1 - \frac{S_H^*}{S_H} - \frac{R_H}{R_H^*} + \frac{R_H S_H^*}{R_H^* S_H}) - \mu_H S_H^* \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}(\frac{S_H^*}{S_H} + \frac{S_H}{S_H^*} - 2) \\ -\mu_W S_W^*(\frac{S_W}{S_W^*} + \frac{S_W^*}{S_W} - 2) + \beta_W S_W^* I_H^*(6 - \frac{S_H^*}{S_H} - \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} - \frac{E_H I_H^*}{E_H^* I_H} - \frac{S_W^*}{S_W} - \frac{S_W I_H E_W^*}{S_W^* I_H^* E_W} - \frac{E_H I_W^*}{E_W^* I_W}) \\ +\beta_E S_W^* \eta_E^*(9 - \frac{S_H^*}{S_H} - \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} - \frac{E_H I_H^*}{E_H^* I_H} - \frac{I_H R_H^*}{I_H^* R_H} - \frac{R_H}{R_H^*} - \frac{S_W^*}{S_W} - \frac{S_W \eta_E E_W^*}{S_W^* \eta_E^* E_W} - \frac{E_W I_W^*}{E_W^* I_W} - \frac{\eta_E^*}{\eta_E}). \end{array}\right\} \tag{6.16}$$

$$\text{Therefore,} \quad \dot{L} = U_i + V_j + W_k. \tag{6.17}$$

$$\text{Where } i = 1, 2; j = 1, 2, 3, 4; k = 1, 2, 3.$$

Now, by the inequality, we know that the arithmetic mean is greater than or equal

to the geometric mean:

$$\begin{aligned} U_1 = \frac{S_H}{S_H^*} + \frac{S_H^*}{S_H} &\geq 2. \\ U_2 = \frac{S_W}{S_W^*} + \frac{S_W^*}{S_W} &\geq 2. \end{aligned} \tag{6.18}$$

By the mean equality, we obtain,

$$\begin{aligned} W_1 = \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}(2 - \frac{I_H E_H^*}{I_H^* E_H} - \frac{E_H I_H^*}{E_H^* I_H}) \\ \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}\{2 - 2(\frac{I_H E_H^*}{I_H^* E_H} . \frac{E_H I_H^*}{E_H^* I_H})^{\frac{1}{2}}\}. \end{aligned} \tag{6.19}$$

$$= 0 \ \forall \ I_H > 0, E_H > 0.$$

The equality holds if and only if $\frac{I_H}{I_H^*} = \frac{E_H}{E_H^*}$

Proceeding in this similar way, we get

$$\begin{aligned} W_2 = \beta_W S_W^* I_H^* (6 - \frac{S_H^*}{S_H} - \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} - \frac{E_H I_H^*}{E_H^* I_H} - \frac{S_W^*}{S_W} - \frac{S_W I_H E_W^*}{S_W^* I_H^* E_W} - \frac{E_H I_W^*}{E_W^* I_W}) \\ \leq \beta_W S_W^* I_H^* \{6 - (\frac{S_H^*}{S_H} . \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} . \frac{E_H I_H^*}{E_H^* I_H} . \frac{S_W^*}{S_W} . \frac{S_W I_H E_W^*}{S_W^* I_H^* E_W} . \frac{E_H I_W^*}{E_W^* I_W})^{\frac{1}{6}}\}. \end{aligned} \tag{6.20}$$

$$= 0 \ \forall \ S_H > 0, E_H > 0, I_H > 0, S_W > 0, E_W > 0, I_W > 0.$$

The equality hold if and only if $S_H = S_H^*, S_W = S_W^*, \frac{E_H}{E_H^*} = \frac{I_H}{I_H^*} = \frac{I_W}{I_W^*}$.

$$\begin{aligned} W_3 = \beta_E S_W^* \eta_E^* (9 - \frac{S_H^*}{S_H} - \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} - \frac{E_H I_H^*}{E_H^* I_H} - \frac{I_H R_H^*}{I_H^* R_H} - \frac{R_H}{R_H^*} - \frac{S_W^*}{S_W} - \frac{S_W \eta_E E_W^*}{S_W^* \eta_E^* E_W} - \frac{E_W I_W^*}{E_W^* I_W} - \frac{\eta_E^*}{\eta_E}) \\ \leq \beta_E S_W^* \eta_E^* \{9 - (\frac{S_H^*}{S_H} . \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} . \frac{E_H I_H^*}{E_H^* I_H} . \frac{I_H R_H^*}{I_H^* R_H} . \frac{R_H}{R_H^*} . \frac{I_H R_H^*}{I_H^* R_H} . \frac{S_W^*}{S_W} . \frac{S_W \eta_E E_W^*}{S_W^* \eta_E^* E_W} . \frac{E_W I_W^*}{E_W^* I_W} . \frac{\eta_E^*}{\eta_E})^{\frac{1}{9}}\}. \end{aligned} \tag{6.21}$$

$$= 0 \ \forall \ S_H > 0, E_H > 0, I_H > 0, R_H > 0, S_W > 0, E_W > 0, I_W > 0, \eta_E > 0$$

The equality hold if and only if $S_H = S_H^*, R_H = R_H^*, \eta_E = \eta_E^*, \frac{E_H}{E_H^*} = \frac{I_H}{I_H^*} = \frac{I_W}{I_W^*} = \frac{E_W}{E_W^*}$.

By the mean inequality, we obtain

$$\left.\begin{aligned} W_1 = \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}(2 - \frac{I_H E_H^*}{I_H^* E_H} - \frac{E_H I_H^*}{E_H^* I_H}) \leq 0. \\ W_2 = \beta_W S_W^* I_H^* (6 - \frac{S_H^*}{S_H} - \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} - \frac{E_H I_H^*}{E_H^* I_H} - \frac{S_W^*}{S_W} - \frac{S_W I_H E_W^*}{S_W^* I_H^* E_W} - \frac{E_H I_W^*}{E_W^* I_W}) \leq 0. \\ W_3 = \beta_E S_W^* \eta_E^* (9 - \frac{S_H^*}{S_H} - \frac{S_H I_W E_H^*}{S_H^* I_W^* E_H} - \frac{E_H I_H^*}{E_H^* I_H} - \frac{I_H R_H^*}{I_H^* R_H} - \frac{R_H}{R_H^*} - \frac{S_W^*}{S_W} - \frac{S_W \eta_E E_W^*}{S_W^* \eta_E^* E_W} - \frac{E_W I_W^*}{E_W^* I_W} - \frac{\eta_E^*}{\eta_E}) \leq 0. \end{aligned}\right\} \tag{6.22}$$

Now, we assume the condition

$$V_1 = (1 + \frac{R_H S_H^*}{R_H^* S_H} - \frac{R_H}{R_H^*} - \frac{S_H^*}{S_H}) \ \geq \ 0 \tag{6.23}$$

Thus the conditions (6.22) and (6.23) ensures that $\dot{L} \leq 0$ for all $(S_H, E_H, I_H, R_H, S_W, E_W, I_W, \eta_E) \in \Gamma_0$, and the strict equality $\dot{L} = 0$ holds only for $S_H = S_H^*, E_H = E_H^*, I_H = I_H^*, R_H = R_H^*, S_W = S_W^*, E_W = E_W^*, I_W = I_W^*, \eta_E = \eta_E^*$. Then, the equilibrium state E_2 is the only positive invariant set of system (2.1) contained

entirely in $\Gamma_\epsilon^+ = \{(S_H, E_H, I_H, R_H, S_W, E_W, I_W, \eta_E), S_H = S_H^*, E_H = E_H^*, I_H = I_H^*, R_H = R_H^*, S_W = S_W^*, E_W = E_W^*, I_W = I_W^*, \eta_E = \eta_E^*.\}$ and hence by the asymptotic stability theorem [20], the positive endemic equilibrium state E_2 is globally asymptotically stable on Γ_ε. This completes the proof.

Note: It's important to emphasize that the additional condition involving $-\theta_H R_H^* \frac{(\beta_W S_W^* I_H^* + \beta_E S_W^* \eta_E^*)}{\beta_H S_H^* I_W^*}(1 - \frac{S_H^*}{S_H} - \frac{R_H}{R_H^*} + \frac{R_H S_H^*}{R_H^* S_H})$ is not required when the disease provides permanent immunity against re-infection. In such cases, θ_H equals zero, causing the first term of (6.16) to vanish.

7. Numerical analysis and simulation

Numerical experiments

Some parameter values were sourced from existing studies [1, 19, 24], while others (e.g., α_W, σ_H, δ_W, ν_E) were assumed due to the lack of empirical data. Future calibration with field data is needed. Finally, for the numerical experiments, we used the set of parameter values of the model (2.1) given in table 3.

Table 3: **Values of parameter used for simulations**

Parameters	Description of parameters	Reference
N_H	1000	[24]
N_W	7000	Hypothetical
μ_H	0.0004566	[1]
μ_W	0.15	[1]
β_H	0.0014	[19]
β_W	0.0015	[1]
β_E	0.002	[19]
γ_H	0.05	[1]
θ_H	0.4	[1]
α_H	0.7	[1]
α_W	0.5	Hypothetical
σ_H	0.0003	Hypothetical
δ_W	0.65	Hypothetical
a	100	[1, 19]
ν_E	0.05	Hypothetical

With a specific set of parameter values, including $N_H = 1000$, $N_W = 10,000$, $\mu_H = 0.004566$, $\mu_W = 0.3333333$, $\beta_H = 0.0000014$, $\beta_W = 0.00000015$, $\beta_E = 0.000000000001$, $\sigma_H = 0.05$, $\theta_H = 0.04$, $a = 100$, $\alpha_H = 0.0018$, $\alpha_W = 1.5$, $\gamma_H = 0.4$,

and $\eta_E = 0.9123$, we calculate the basic reproduction number as $R_0 = 0.0101$, which is less than 1, indicating that the disease is unlikely to result in an outbreak.

The equilibrium points for this system are as follows: E_0, representing the disease-free equilibrium, is $(10000, 0, 0, 0, 70,000, 0, 0, 0)$; and E^*, representing a non-trivial equilibrium where the disease is present, is $(9, 200, 95, 289, 38, 376, 51, 265, 10, 218, 8, 515, 250)$ The stability analysis reveals that the characteristic roots of the Jacobian matrix corresponding to the system (2.1) at the disease-free equilibrium point $E_0 = (219010, 0, 0, 30,000, 0, 0, 0, 0)$ are as follows: $\lambda_1 = -0.0046$, $\lambda_2 = -0.0446$, $\lambda_3 = -0.3333$, $\lambda_4 = -1.8333$, $\lambda_5 = -0.0063$, $\lambda_6 = -0.1147$, $\lambda_7 = -0.3333$, and $\lambda_8 = -0.9123$. Based on these eigenvalues, we can conclude that the disease-free equilibrium point is stable. The characteristic roots of the same Jacobian matrix corresponding to the system (2.1) at the endemic equilibrium point $E^* = (1793600941049739, 56382849, 885857, 1192645, 376, 21449, 1554, 6995, 10)$ are as follows: $\lambda_1 = 11.5663$, $\lambda_2 = -0.00456$, $\lambda_3 = -0.04456$, $\lambda_4 = -0.33333$, $\lambda_5 = -0.60671 - 12131i$, $\lambda_6 = -0.60671 + 1213i$, $\lambda_7 = -0.9123$, and $\lambda_8 = -12783$. Consequently, the endemic equilibrium point is determined to be unstable.

We explore an alternative parameter set for our model, featuring the following values: $N_H = 1,000$, $N_W = 10,000$, $\mu_H = 0.0004566$, $\mu_W = 0.006666$, $\beta_H = 0.000014$, $\beta_W = 0.000015$, $\beta_E = 0.004444$, $\sigma_H = 0.05$, $\theta_H = 0.004$, $a = 100$, $\alpha_H = 0.018$, $\alpha_W = 0.02$, $\delta_W = 0.04$, $\gamma_H = 0.02$, and $\eta_E = 0.0003123$. Given these specific parameter values, the computed basic reproduction number emerges as $R_0 = 3.9178\text{x}10^2$, comfortably surpassing the pivotal threshold 1.

The equilibrium points associated with this parameter set include $E_0 = (2.1901 X10^6, 0, 0, 0, 1.5002\text{X}10^6, 0, 0, 0)$ and $E^* = (30743974729, 145, 37, 166, 7, 375007, 160 719, 320204)$.

At the state of disease-free equilibrium, they denoted as $E_0 = (2.1901\text{X}10^6, 0, 0, 0, 1.5002\text{X}10^6, 0, 0, 0)$, the eigenvalues of the Jacobian matrix, governing the system (2.1), are elegantly characterized as $\lambda_1 = -0.0005$, $\lambda_2 = -0.6205$, $\lambda_3 = -0.4005$, $\lambda_4 = -0.0002$, $\lambda_5 = -0.8025$, $\lambda_6 = -0.5002$, $\lambda_7 = -0.0020$, $\lambda_8 = 0.0012$, $\lambda_9 = -0.9900$. Consequently, the disease-free equilibrium point is deemed unstable.

At the distinctive endemic equilibrium point $E^* = (22, 168, 605, 123, 79, 855, 27, 69, 116, 250)$, the eigenvalues of the Jacobian matrix exhibit the following pattern: $\lambda_1 = -0.00031$, $\lambda_2 = -0.00317$, $\lambda_3 = -0.02014$, $\lambda_4 = -0.02712$, $\lambda_5 = -0.45910$, $\lambda_6 = -0.07045$, $\lambda_7 = -2.2505$, $\lambda_8 = -14230$. Hence, the stability of the endemic equilibrium point has been verified.

Further insights on the transcritical bifurcation can be found in section 4.

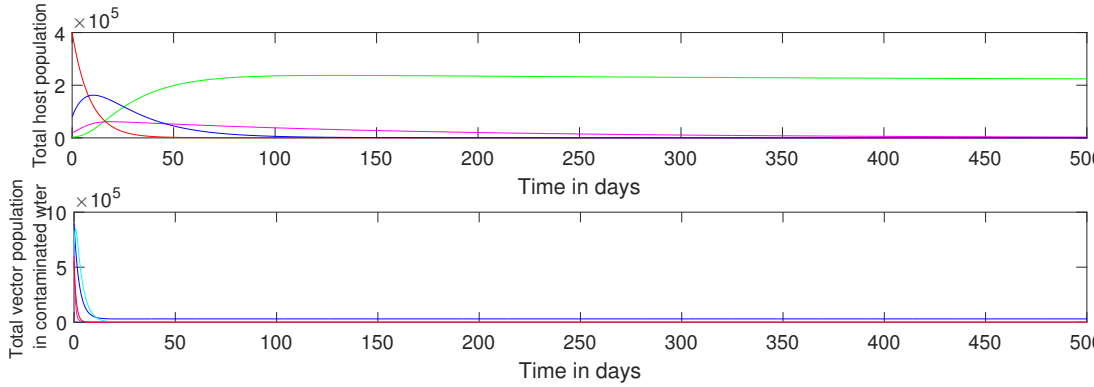

Figure 3: **The trajectories of state variables when** $R_0 = 0.0914 < 1$

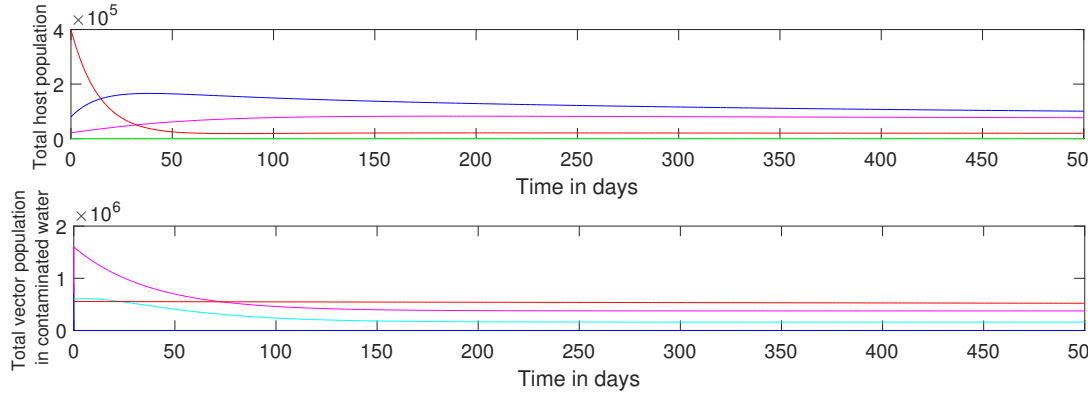

Figure 4: **The trajectories of state variables when** $R_0 = 3.9178 * 10^2 > 1$

8. Conclusion

In this study, we introduced and systematically analyzed an adapted SEIR-SEI model in an arsenic-contaminated environment. We specifically addressed individuals affected by the environmental pathogen *Mycobacterium ulcerans*. Our primary objective was to explore the transmission dynamics of Buruli ulcer disease.

To enhance the model's realism, we incorporated latent individuals, disease-induced mortality, and dynamic population changes in both host and vector populations. Within the epidemiological framework, we identified two key equilibrium states: a disease-free equilibrium representing the absence of infection and an en-

demic equilibrium signifying its sustained presence. Our analysis revealed the occurrence of forward bifurcation, where a locally asymptotically stable disease-free state can coexist with a stable endemic state when $R_0 < 1$. Using Lyapunov functions, we further established the global asymptotic stability of both equilibrium states, reinforcing the critical role of the basic reproduction number, R_0, in determining disease persistence. Specifically, when $R_0 < 1$, the disease-free equilibrium remains globally stable, whereas, for $R_0 > 1$, a unique endemic equilibrium prevails with global asymptotic stability.

This refined model, which integrates latent compartments and disease-induced mortality in human and vector populations, offers deeper biological insights into Buruli ulcer transmission. It is a valuable tool for understanding and mitigating the spread of this debilitating disease by capturing key epidemiological dynamics.

Future work will focus on validating the model using epidemiological datasets from Buruli ulcer endemic regions, enhancing predictive robustness.

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