

An Age- Structured Model for the spread of Buruli ulcer: Analysis and Simulation in Ghana

Abstract

Despite the advances in medical research on treatment and the intensive public education on prevention and control, Buruli ulcer (BU) continues to be a major public health problem that continues to overwhelm authorities in Ghana. Ghana is the second most endemic country after the Ivory Coast at the global level. Whereas it is common knowledge in literature that the disease can affect people of all ages, the mode of transmission is still evasive. The studied model is expressed as a system of hyperbolic (first order) partial differential equations in addition to an ordinary differential equation. We first, employ a representation from the method of characteristics and a fixed point argument and also prove the existence and uniqueness of a solution to our nonlinear system. Then we present a numerical scheme to model the dynamics of BU. The simulation results showed that Mycobacterium ulcer has peak period of spread and reduced subsequently.

Keywords: Buruli ulcer, SIR, Hyperbolic transport, Finite difference

Introduction

Buruli ulcer, also known as Bairnsdale ulcer is a chronic, indolent, and necrotizing disease of the skin tissue caused by Mycobacterium ulcerans [5]. The disease usually begins as a painless nodule or papule and may progress to massive skin ulceration [9]. It also appears that different mode of transmission occurs in different geographical and epidemiological setting [19]. Though the disease can affect people of all ages, children less the 15 years of age are particularly more vulnerable in many tropical and subtropical countries [12]. Buruli ulcer causes serious pain as well as permanent physical damage. The physical signs visually mark the individual and deprive them of societal standards of beauty. Additionally, physical deformities may prevent the individual from participating in any economic and social activities.

The study of Buruli ulcer continues to be an important problem in mathematical epidemiology as outbreaks of M. ulcerans continues to pose a public health challenge [1]. The mode of transmission the ulcer is not well explained, however residence near aquatic environment has been identified as a risk factor for the ulcer in Africa [12, 13]. It appears that different mode of transmission occurs in different geographical and epidemiological setting [19]. In Africa, it is estimated that almost 30, 000 cases have been reported between 2005 and 2010 [14]. Buruli ulcer is severe **disfiguring** disease which affect all age group but particularly children less the 15 years

of age in many tropical and subtropical countries [18] . The disease has emerged over the past two or more decades, especially in Central and West Africa and has been confirmed by laboratory test in 26 countries with reports in other countries around the world [19].

The known common of model for the spread of an infectious disease is the S, I, R model and which is .based on the categorization of individuals in the classes of susceptible, infected and removed populations. SIR models of Buruli ulcer developed at the moment are time dependent models which lead to system of ordinary differential equations (ODEs), see [2]. In order to model the pathway of infection clearly, we propose a model which considers the role of *M. ulcerans* introduced to the water reserves by disturbed environment.

Age is one of the vital characteristics in the modeling of populations and infectious disease. Different age groups of populations may have different reproduction and survival capacities. Disease may be in variation with respect to infection and mortality rate for different age groups [3]. In reality, individuals of varying age group may exhibit different behaviours. Behavioural changes are vital in control and prevention of many infectious diseases. Young individuals are known to be more active in interaction with or between population, and in disease transmissions. This paper therefore, in tends to use an age-structured model to study the spread of Buruli ulcer.

At the heart of an age-structured model, is a coupled system of hyperbolic partial differential equations (PDEs). The introduction of a system of PDEs instead of a system of ODEs gives rise to the interconnectivity of the problem greatly. Although using age-structured models to study the spread of diseases is not something new, however, to the best of our knowledge no such model has been proposed for the case of Buruli ulcer. The equation which accounts for the growth of the *M. ulcerans* will not have age structure and therefore, remain as ODE.

Further background of age-structured models, we entreat readers to see [20, 23]. The evolution of the equilibrium analysis of an age-structured composition model [21], was begun by the introduction of the existence results and formulation of age-structured models Gurtin and MacCamy [16] and Venturino [11]. Barbu [15] developed mathematical theory behind age-structured populations [3] and studied nonlinear age-dependent population and predator prey dynamics.

The dynamics of increasing mathematics complex issues and nonlinearities age structured models has brought about new dimension of analyzing them. One of these powerful tools is method semi-groups of linear and nonlinear operator in Banach space.

This paper sought to develop an age-structured BU model and provide a theoretical and numerical analysis of the model. The system differential equations along with initial and boundary conditions that form our disease model will be discussed. We will further prove the existence and uniqueness of solution in L^1 and L^∞ to our PDE system using a fixed point argument on a representation derived from the method of characteristics. Finally the numerical methods and its implementation will be discussed.

2 The model and its analysis

2.1 Model formulation

We consider a particular human population which we partition into three subgroups: the susceptible, infected and recovered. Within each category, the age density and population changes over time were taken into account. The number of people in each subsection was expressed as $S = S(a, t)$, $I = I(a, t)$ and $R = R(a, t)$ as a function of age a and time t . In order to use a dimensional approach in this model, we formally apply units of weeks for the age of humans a and days for the simulation time t . However, conventional units of years are also used in some instances to elucidate the age of human population. The number of susceptible

people between, say age a_1 , and a_2 at a time t is expressed as $\int_{a_1}^{a_2} S(a, t) da$ applying convectional

understanding that all humans from $a = a_0$ year to $a = a_0 + 1$ year taken a_0 year old. Similar methods are also used for infected and recovered humans $I(a, t)$ and $R(a, t)$ respectively. There is one water bug compartment of infective Buruli ulcer Mycobacterium denoted by $B_H = B_H(t)$.

The four quantities S, I, R, B_H are dependent variable of the model. Buruli ulcer is considered a water-borne disease and in most cases of transmission of the disease is through contact with contaminated water bodies [24, 25]. To put in various factors that influence the dynamics of a BU epidemic, we have initiated in the model an extra coefficient function which maybe constant or may vary with age or time (or both). A disturbed environment was taken into account such as

stagnant water in the model formulation. We include human demographics recruitment term $\Lambda(a, t)$ alongside natural death rate. $\mu_H(a)$

The possible interrelations between humans, the Mycobacterium ulcerans are represented by the schematic diagram below (fig 1).

Model formulation

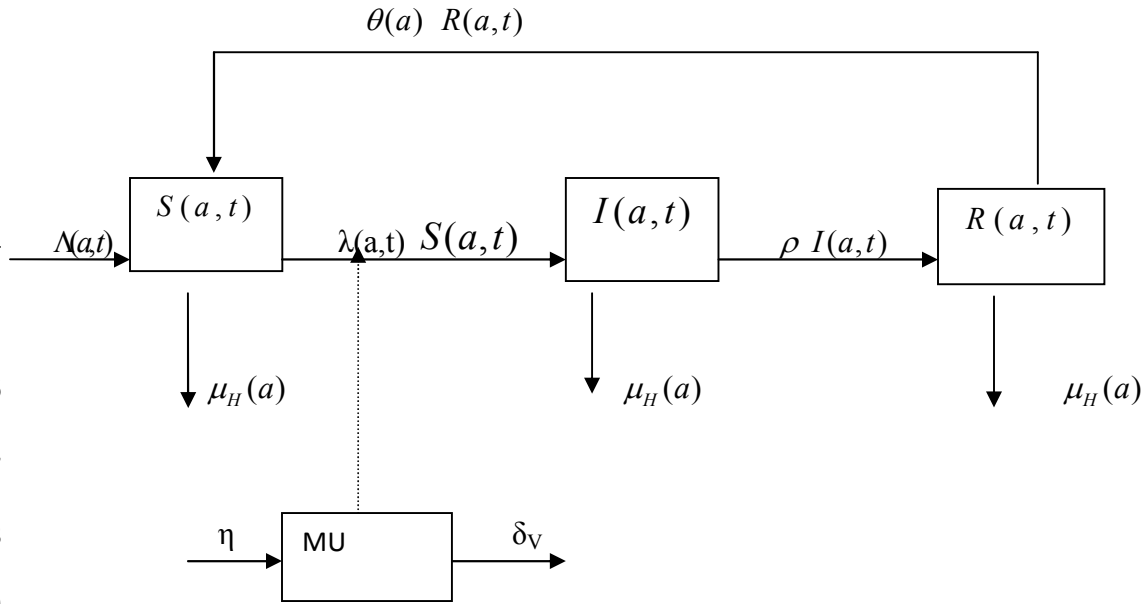


Figure 1: Proposed transmission dynamics of the Buruli ulcer between humans and MU in the environment.

The susceptible individuals become infected through ingesting of M. ulcerans at rate $B_H(a)$ with MU concentration measured with respect to infectious dose denoted by g_H . Individuals recover from BU at a rate $\theta(a)$ which depends on age. M. ulcerans bacteria experience a natural removal rate of δ_V owing to death or predation. A strategy $g(a, t)$ that can help reduce the spread of BU that represent antibiotic treatment was included in the model. This reduces the duration and quantity of infected humans concentration to the concentration of M.ulcerans bacteria in the environment.

We are interested in investigating the existence of a solution to this nonlinear system using numerical concept. We study the age-time domain $P = (0, A) \times (0, T)$ with intervention $g(a)$ in

$$\Omega = \left\{ (g) \in (L^\infty(Q))^2 \mid 0 \leq g(a, t) \leq Bi.eP \right\} \quad (1)$$

where $B_1 < 1$ represent maximum fractions of intervention. The variables, (S, I, R, B_H) , can be said to satisfy the system.

$$\frac{\partial S}{\partial t} + \alpha \frac{\partial S}{\partial a} = \Lambda(a, t) - \beta_H(a) \frac{B_H(t)}{k_H(a) + B_H(t)} S(a, t) - \mu_H(a) S(a, t) + \theta(a) R(a, t), \quad (2a)$$

$$\frac{\partial I}{\partial t} + \alpha \frac{\partial I}{\partial a} = \beta_H(a) \frac{B_H(t)}{k_H(a) + B_H(t)} S(a, t) - \mu_H(a) I(a, t) - \rho_1(1 - g(a, t)) I(a, t) - \rho_2 g(a, t) I(a, t) \quad (2b)$$

$$\frac{\partial R}{\partial t} + \alpha \frac{\partial R}{\partial a} = \rho_1(1 - g(a, t)) I(a, t) + \rho_2 g(a, t) I(a, t) - \mu_H(a) R(a, t) - \theta(a) R(a, t) \quad (2c)$$

$$\frac{dB_H}{dt} = \eta B_H(t) - \delta_V B_H(t) \quad (2d)$$

For the above equations $\alpha = \frac{1 \text{ week}}{7 \text{ days}}$ is the coefficient introduced to balance the units of age a in weeks and time t in days. With respect to infected class, the multiplicative factors $\rho_1(1 - g)$ and $\rho_2 g$ represent the rates of recovery for the individuals who have had no antibiotic treatment and those who have undergone such treatment respectively.

The Boundary and Initial Conditions

Buruli ulcer disease does not transmit vertically from parent to infants and therefore we can infer that children have some immunity. In this regard, newborns will appear in the R class in S, I, R model. This is significantly different from most S, I, R model. We translate this consideration to state the boundary conditions.

$$S(0, t) = 0, \quad (3a)$$

145 $I(0,t) = 0$, (3b)

146
$$R(0,t) = \int_0^A (S(a,t) + I(a,t) + R(a,t)) f(a) da,$$
 (3c)

147 where the fecundity function f is stated as

148
$$f(a) = \begin{cases} \frac{1}{5} \sin^2 \left(\pi \frac{(a-15)}{30} \right) & \text{if } 15 \leq a \leq 40; \\ 0 & \text{otherwise} \end{cases}$$

149 The fecundity function $f(\cdot)$ is stated here in units of per year for easier readability and assumes
 150 that from age 15 to 40 years a woman will give generally give birth to three children, since

151 $\int_0^{a^+} f(a) da = 3$, where $a^+ = 60$ is the largest age allowed for the simulation

152 The initial conditions are stated as

153 $S(a,0) = S_0(a)$, $I(a,0) = I_0(a)$, $R(a,0) = R_0(a)$ and $B_H(0) = B_H 0$. (4a)

Quantity	Descriptions
$S(a,t)$	susceptible humans of age a at t divided uniformly over all ages
$I(a,t)$	infected humans of age a at t
$R(a,t)$	removed and immune humans of age a at time t
$B_H(t)$	Mycobacterium ulcerans population
$\Lambda(a,t)$	recruitment rate of number of susceptible human entering population of age a at time t
$g(a,t)$	antibiotic treatment rate for humans of age a at time t
β_H	ingestion rate of MU at age a
$f(a)$	maternity rate
$\theta(a)$	rate of waning immunity of human at age a
k_H	saturation constant of MU at age a
$\theta(a)$	natural mortality rate of human at age a
k_H	
μ_H	recovery rate of untreated Buruli ulcer
ρ_1	
ρ_2	recovery rate of treated Buruli ulcer
ρ_1	
ρ_2	concentration rate of Mycobacterium ulcerans in the environment
η	
η	conc rate of MU in the environment
δ_L	deat

Table 1: Model parameters and their respective units

Existence of the solution to the state system

We determine solution of the system applying the method of characteristics [22]. By using Banach contraction mapping principle, we prove the existence and uniqueness of the solutions of the system. To compute the solution representation for the system (1a)-(1c), we add new notation to the right hand side of the partial differential equation (PDEs): a is age and t is time expressed in weeks and days respectively. $S(a, t)$ deals with susceptible humans of age a at time t divided uniformly over all ages with a unit of human per week. $I(a, t)$ has to do with infected humans of age a at time t of human per week. The $R(a, t)$ represents removed and immuned humans of age a at time t of human per week. The Mycobacterium ulcerans population is represented by $B_H(t)$ of cells per ml. α is the proportionality factor and $\Lambda(a, t)$ is the recruitment rate of susceptible humans population of age a at time t per week. $k_H(a)$ is the saturation constant of MU age a one per day. $\mu(a)$ is the natural mortality rate of humans at age t of one per day. $\theta(a)$ also deals with rate of waning of immunity from recovered humans at age a per day. ρ_1 and ρ_2 are rate of untreated and treated Buruli ulcer per day. δ_V also explains death rate of MU in the environment per day. The antibiotic rate of treatment is denoted by $g(a, t)$ for humans of age a at time t . η is the concentration rate of Mycobacterium ulcerans in the environment per day.

The method of characteristics to determine the existence of a solution of system state was applied. The Banach contraction mapping principle to prove the existence and uniqueness of solution was applied. In order to find solution representation for the system (2a-b-c-d)-(3a-b-c)-4a, the following notation for the right hand sides of the partial differential equation (PDEs) was created:

$$f_1(B_H(t), S(a, t), R(a, t)) = \Lambda(a, t) - \beta_H(a) \frac{B_H(t)}{k_H(a) + B_H(t)} S(a, t) + \theta(a) R(a, t)$$

(5a)

$$f_2(B_H(t), S(a, t), I(a, t), g(a, t)) = \beta_H(a) \frac{B_H(t)}{k_H(a) + B_H(t)} S(a, t) - \rho_1(1 - g(a, t)) I(a, t) - \rho_2 g(a, t) I(a, t) \quad (5b)$$

$$f_3(S(a, t), I(a, t), R(a, t), g(a, t)) = \rho_1(1 - g(a, t)) I(a, t) + \rho_2 g(a, t) I(a, t) - \theta(a) R(a, t) \quad (5c)$$

A notice was made that, $\mu_H(a)S(a, t)$, $\mu_H(a)I(a, t)$ and $\mu_H(a)R(a, t)$ were not part of the f_i for $i = 1, 2, 3$ terms. They were added in the left side of the three partial differential equations (4a)-(4c) to make use in the representation of the solution based on characteristics.

Let B be chosen such that

$$0 \leq S_0(a), I_0(a), R_0(a),$$

$$\int_0^A S_0(a) da \leq B, \int_0^A I_0(a) da \leq B, \int_0^A R_0(a) da \leq B,$$

$$\text{and } 0 \leq B_{H0} \leq B,$$

The state solution is defined as

$$Y = \{(S, I, R, B_H) \in (L^\infty(0, T; L^1(0, A)))^3 \times (L^\infty(0, T))\}$$

$$\sup_t \int_0^A |S(a, t)| da \leq 2B, \sup_t \int_0^A |I(a, t)| da \leq 2B,$$

$$\sup_t \int_0^A |R(a, t)| da \leq 2B, |B_H(t)| \leq 2B\}$$

By applying the method of characteristics, we can determine the representation of the solution and then use that **representation** to construct the map to be employed in the fixed point argument for existence and uniqueness. Now we define a map

$L : Y \rightarrow Y$ such that

$$L(S, I, R, B_H) = (L_1(S, I, R, B_H), L_2(S, I, R, B_H), L_3(S, I, R, B_H), L_4(S, I, R, B_H))$$

where L_1 is associated with equation (2a) and L_2 is associated with equation (1b) and where

$$\begin{aligned}
200 \quad L_1(S, I, R, B_H)(a, t) = & \left\{ \begin{aligned} & e^{-\int_0^t \mu_H(\alpha\tau - \alpha t + a) d\tau_{S_0(a-\alpha t)}} \\ & + \int_0^t e^{-\int_s^t \mu_H(\alpha\tau - \alpha t + a) d\tau} \times \\ & (f_1(B_H(s), S(\alpha s + a - \alpha t, s), \\ & R(\alpha s + a - \alpha t, s))) ds \\ & \text{if } a > \alpha t \\ & \left(\frac{1}{\alpha} \right) \int_0^a e^{-\int_s^a \frac{\mu_H(\tau)}{\alpha} d\tau} \times \\ & (f_1(B_H(\frac{s + \alpha t - a}{\alpha}), S(s, \frac{s + \alpha t - a}{\alpha}), R(s, \frac{s + \alpha t - a}{\alpha}))) ds \\ & \text{if } a < \alpha t, \end{aligned} \right. \\
201 \quad L_2(S, I, R, B_H)(a, t) = & \left\{ \begin{aligned} & e^{-\int_0^t \mu_H(\alpha\tau - \alpha t + a) d\tau_{I_0(a-\alpha t)}} \\ & + \int_0^t e^{-\int_s^t \mu_H(\alpha\tau - \alpha t + a) d\tau} \times \\ & (f_2(B_H(s), S(\alpha s + a - \alpha t, s), I(\alpha s + a - \alpha t, s) \\ & g(\alpha s + a - \alpha t, s)) ds \\ & \text{if } a > \alpha t \\ & \left(\frac{1}{\alpha} \right) \int_0^a e^{-\int_s^a \frac{\mu_H(\tau)}{\alpha} d\tau} \times \\ & (f_2(B_H(\frac{s + \alpha t - a}{\alpha}), S(s, \frac{s + \alpha t - a}{\alpha}), I(s, \frac{s + \alpha t - a}{\alpha}), \\ & g(s, \frac{s + \alpha t - a}{\alpha}))) ds \\ & \text{if } a < \alpha t, \end{aligned} \right.
\end{aligned}$$

$$L_3(S, I, R, B_H)(a, t) = \begin{cases} e^{-\int_0^t \mu_H(\alpha\tau - \alpha t + a) d\tau_{R_0(a-\alpha t)}} \\ + \int_0^t e^{-\int_s^t \mu_H(\alpha\tau - \alpha t + a) d\tau} \times \\ f_3(S(\alpha s + a - \alpha t, s), I(\alpha s + a - \alpha t, s), R(\alpha s + a - \alpha t, s)) \\ g(\alpha s + a - \alpha t, s)) ds \\ \text{if } a > \alpha t \\ \left(\frac{1}{\alpha} \right) \int_0^a e^{-\int_s^a \frac{\mu_H(\tau)}{\alpha} d\tau} \times \\ (f_3(S(s, \frac{s + \alpha t - a}{\alpha}), I(s, \frac{s + \alpha t - a}{\alpha}), R(s, \frac{s + \alpha t - a}{\alpha}))) ds \\ g(s, \frac{s + \alpha t - a}{\alpha}) ds \\ \text{if } a < \alpha t, \end{cases}$$

202

203 with

$$L_4(S, I, R, B_H)(t) = B_{H0} e^{-\delta_L t} + \int_0^t \eta e^{-\delta_L(t-s)} B_H(s) ds.$$

204 (6)

205 The fixed point of the map L was derived, meeting the conditions

206 A prove was made to show that the map $L_4(S, I, R, B_H) = (L_1, L_2, L_3, L_4)(S, I, R, B_H)$ with
 207 everyone of $S(a, t), I(a, t), R(a, t)$ and B_H being positive will be a solution
 208 $(S, I, R, B_H) = (S, I, R, B_H)(g)$ to the system of the model.

209

210 *Theorem (Existence and Uniqueness of solution). For $g \in \Omega$ as defined in (1) and Ω sufficiently*
 211 *small, there exists a unique solution (S, I, R, B_H) to the system 2a – 2d with boundary and initial*
 212 *conditions 3a – 3c and 4*

213

214 Proof : We prove that the map

215

$$L : Y \rightarrow Y$$

216 stated above is a strict contraction. Note that the function f_1, f_2 and f_3 used in the SIR
 217 equations are Lipschitz in their arguments with the Lipschitz constants base on coefficients and
 218 parameters from our model and also on B, an addition to the bounds on S, I, R from the set Y .

219 The definition of the map L, was given to show that L maps Y into Y and the definition of the Li
 220 functions for $i = 1, 2, 3$ was expressed as

$$221 \int_0^A |L_i(S, I, R, B_H)| (a, t) da \leq D_1 B \Omega + B \leq 2B$$

222 where the single B in the first inequality obtained from the bound of $\int_0^A S_0(a) da, \int_0^A I_0(a) da$, or

223 $\int_0^A R_0(a) da$, respectively for $i = 1, 2, 3$. By the fact Ω is sufficiently minimal, then the above

224 estimate is less than or equal to $2B$. In an addition for $j = 1, 2, 3$,
 225 $|L_j(S, I, R, B_H)| \leq \max\{B_{H0}\} + D_2 B \Omega \leq 2B$ was obtained. The constants D_1 and D_2 hinge upon
 226 the coefficients and the parameters in the model. Also for Ω to be sufficiently small, we get the
 227 estimates above and hence, the L maps Y into Y. Note that for the contraction property, for
 228 $i = 1, 2, 3$ this contraction property was taken into account

229 $\int_0^A |L_i(S_1, I_1, R_1, B_{H1}) - L_i(S_2, I_2, R_2, B_{H2})| (a, t) da$. There is a need to examine some of the terms on

230 the model such as $\beta_H(a) \frac{B_H(t)}{k_H(a) + B_H(t)} S(a, t)$ and in specific their differences. For instance, the
 231 expression (7) below was investigated

$$232 \frac{B_{H1}(t)}{k_H(a) + B_H(t)} |S_1 - S_2| (a, t) + \frac{S_2(a, t) k_H |B_{H1} - B_{H2}| (t)}{k_H + B_{H1}(t))(k_H + B_{H2}(t))} \quad (7)$$

233 and consider from equations (3.1) and (3.2). In order to make things simple, we show an estimate
 234 of such a term for $a > \alpha t$ in $L_1(S, I, R, B_H)(a, t)$

$$235 \int_0^A \int_0^A e^{-\int_0^t \mu_H(\alpha \tau - \alpha t + a) d\tau} \times$$

$$236 B_H(\alpha s + a - \alpha t, s) \left(\frac{B_{H2}(s)}{k_H + B_{H2}(s)} |S_2 - S_1| (\alpha s + a - \alpha t, s) \right.$$

$$237 \left. + \frac{S_1(\alpha s + a - \alpha t, s) k_H |B_{H2} - B_{H1}| (s)}{(k_H + B_{H1}(s))(k_H + B_{H2}(s))} \right.$$

$$238 \left. + \theta(\alpha s + a - \alpha t, s) (R_2 - R_1)(\alpha s + a - \alpha t, s) \right| ds da$$

239
 240
 241 Note that we let $s_1 = \alpha(s - t) + a$ and $s_2 = s$, then $0 < -\alpha t + a < \alpha(s - t) + a < a$ or
 242 $0 < (s - t) + a < A$ and $0 \leq s_2 < \Omega$. In addition, the Jacobian for this transformation becomes
 243 finite. Hence, we can now bound the estimate above by

$$\begin{aligned}
& \int_0^T \int_0^A D_3 |S_2 - S_1|(s_1, s_2) + D_4 |R_2 - R_1|(s_1, s_2) ds_1 ds_2 \\
& + D_5 \int_0^T \int_0^A |S_1(s_1, s_2)| ds_1 \{ |B_{H2}(s_2) - B_{H1}(s_2)| ds_2 \} \\
& \leq D_6 \Omega \sup_t \int_0^A (|S_2 - S_1| + |R_2 - R_1|)(a, t) da \\
& + D_7 N \Omega \sup_t [|B_{H2} - B_{H1}|(t)]
\end{aligned}$$

In the above equations, we have substituted S_1 and S_2 by a and t respectively. Again, the constants D_k for $k = 3, \dots, 7$ depend on the bounds of the coefficients. For terms that consist of the fractional parts, we have employed the 2B bound for the terms made up of the Si for $i = 1, 2$ in the second term of 7 for integrals over $(0, A) \times (0, t)$ when $a > \alpha t$ or for integrals over $(0, A) \times (0, a)$ when $a < \alpha t < \alpha T$. We can determine these estimates which leads

$$\begin{aligned}
& \int_0^A |L_1(S_1, I_1, R_1, B_{H1}) - L_1(S_2, I_2, R_2, B_{H2})|(a, t) da \\
& \leq D_8 \Omega \sup_t \int_0^A (|S_2 - S_1| + |R_2 - R_1|)(a, t) da + D_9 N \Omega \sup_t [|B_{H2} - B_{H1}|(t)]
\end{aligned}$$

Similarly we estimate for $j = 2, 3$ and for $j = 4, 5$ we have

$$\begin{aligned}
& |L_j(S_1, I_1, R_1, B_{H1}) - L_j(S_2, I_2, R_2, B_{H2})|(t) \\
& \leq \Omega \sup_t \int_0^A |I_1 - I_2|(a, t) da + D_{10} \Omega \sup_t |B_{H1} - B_{H2}|(t) \\
& |L_j(S_1, I_1, R_1, B_{H1}) - L_j(S_2, I_2, R_2, B_{H2})|(t) \\
& \leq \Omega \sup_t \int_0^A |I_1 - I_2|(a, t) da + D_{10} \Omega \sup_t |B_{H1} - B_{H2}|(t)
\end{aligned}$$

where D_{10} has to do with η and δ .

By putting the work and carefully selecting Ω sufficiently small, we obtain the contraction result and therefore, desire fixed point to the system 2 –2d.

4. Numerical Simulations

We state briefly the numerical method employed in our simulations. The equations for the quantities S , I and R from 2 —2c from hyperbolic system of PDEs; in addition to these, we have one ODE for B_H from 2d. Our choice of numerical method is a forward time/ backward space finite difference [17]. For the convenience of our model, we use the scalar one- way wave equation.

$$\frac{\partial u}{\partial t} + \alpha \frac{\partial u}{\partial a} = f(a, t)$$

where α is a constant (that is the wave speed), and t and x denote time and space, respectively. The forward time/backward space scheme [17] for the above model is expressed as

$$\frac{f_m^{n+1} - f_m^n}{\Delta t} - \alpha \frac{f_m^n - f_{m-1}^n}{\Delta x} = q(x_m, x_n),$$

where n stands for the time index and m the space index in the time and space grid. We note that any explicit scheme is only conditionally stable [17]. The stability of our scheme is achieved by applying **Courant-Friedrich-Levy** (CFL) condition [17] to ensure a necessary and sufficient condition and satisfies that

$$\left| \alpha \frac{\Delta x}{\Delta t} \right| \leq 1$$

For a given spatial discretization Δx , this produces a restriction on the time step as $\Delta t \leq \Delta x / |\alpha|$

5 Computational Experiments and Results

Buruli ulcer disease requires more antibiotic in children than adults. We model the rate of **losing** immunity of humans at age a by

$$\theta(a) = \begin{cases} 1/365 \text{ for } a \leq 15 \text{ year} \\ 1/2.363 \text{ for } a > 15 \text{ year} \end{cases}$$

The rate of waning is important because it influences our choice of initial conditions

6 The reference Simulation with no Infected Population

We assumed a pool of 20, 000 humans distributed uniformly over the age range $0 \leq \alpha \leq A$, for all ages a at $t = 0$. Therefore, all 20, 000 humans are distributed to the susceptible and removed classes. Based on the rate of losing immunity conditions for children and adult, it requires a year for a newborn baby to lose his or her immunity and become susceptible to Buruli ulcer. In this regard, we initialize everyone with age less than or equal to one year old in the removed section and everyone older than one year old in the susceptible section. This leads to the initial conditions

$$S(a, 0) = \begin{cases} 0, & \text{if } 0 \leq a \leq 40, \text{ weeks} \\ d, & \text{if } a > 40, \text{ weeks} \end{cases}$$

$$R(a, 0) = \begin{cases} 0, & \text{if } 0 \leq a \leq 40 \text{ weeks} \\ d, & \text{if } a > 40 \text{ weeks} \end{cases}$$

for the susceptible and removed population, respectively. The numerical value of the age density d in the initial conditions depends on the number of humans and the numerical resolution of the age variable.

By applying numerical and having age resolution in weeks, we will then have to have a fixed density d for each age for $0 \leq \alpha \leq 40$, given by

$$d = \frac{20,000(\text{humans})}{50(\text{weeks} / \text{year}) \times 60(\text{year})} \approx 8.33 \text{ humans} / \text{weeks}$$

Parameter	Value/Range	Sources
$\Lambda(a, t)$	0	Estimated
$g(a, t)$	0.8	Estimated
B_H	1.5/7	[2]
k_H	10^5	Estimated
β_H	0.00065	[2]
$\mu_H(a)$	0.45	[2]
ρ_1	1/5	Estimated
ρ_2	1/3	Estimated
η	0.04	Estimated
δ_V	1/5	Estimated

Table 2: These are the values of the model parameters in the simulation.

This provides the values of d in the initial conditions for $S(a, 0)$ and $R(a, 0)$. Given the age resolution of 1 week, that at the initial time with constant density d , this leads 40 to 333 humans of each age a . In other words, we are saying that 20, 000 total humans are distributed to the ages 0 to 60 uniformly as $20,000 / 60 \approx 333$ humans

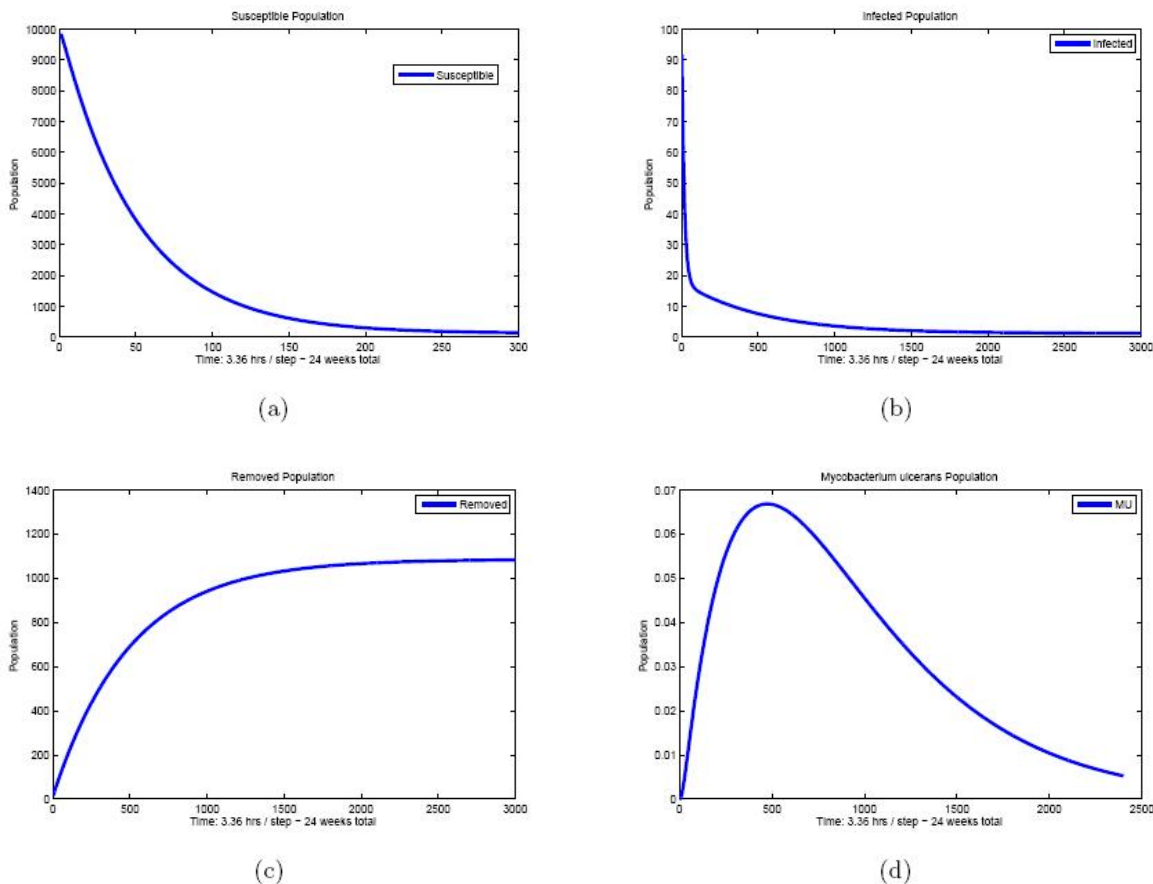
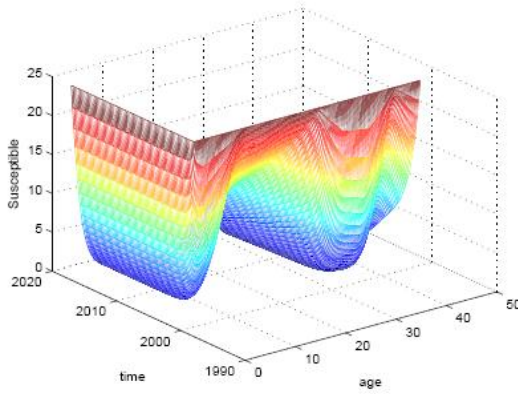


Figure 2: Shows simulations of BU with susceptible, infected population and recovered population dynamics over time.

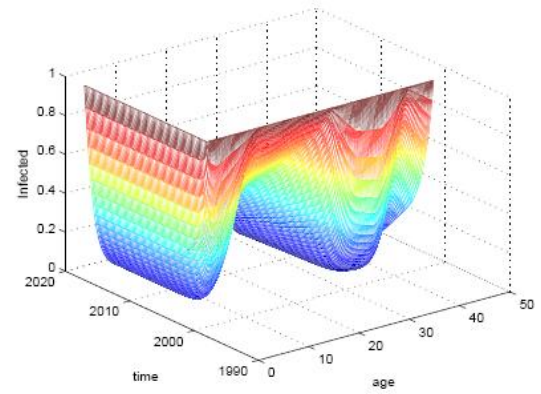
In Figure 2 above, we show the dynamics in the total population, susceptible population, infected population, and recovered population over time. We note here, the decrease in the susceptible population, which is attributed to humans who died of natural causes during the period-line of the simulation. Furthermore, we notice an increase in recovered population, which is partly due to antibiotic and partly due to natural recovery of MU by humans.

This however, takes sometime for human to lose immunity to get back to susceptible class and is governed by the rate of waning of immunity. In Figure 2b we see that the infection reduced with respect to time and this could be inferred from people getting awareness of MU and antibiotic medications which are now available to BU patients. Even though there is no epidemic in this simulation, our model indicates more than just the population dynamics. Our three-dimensional surface plots in Figure3 depict the advantages of this age-structured model even in this basic simulation. Each plot in Figure3 indicates the number of humans at an age a in years at time t in weeks; the color provides the same information as the height of surface. The number of humans at a particular age is calculated by integrating each density. For instance $S(a, t)$ from a years to

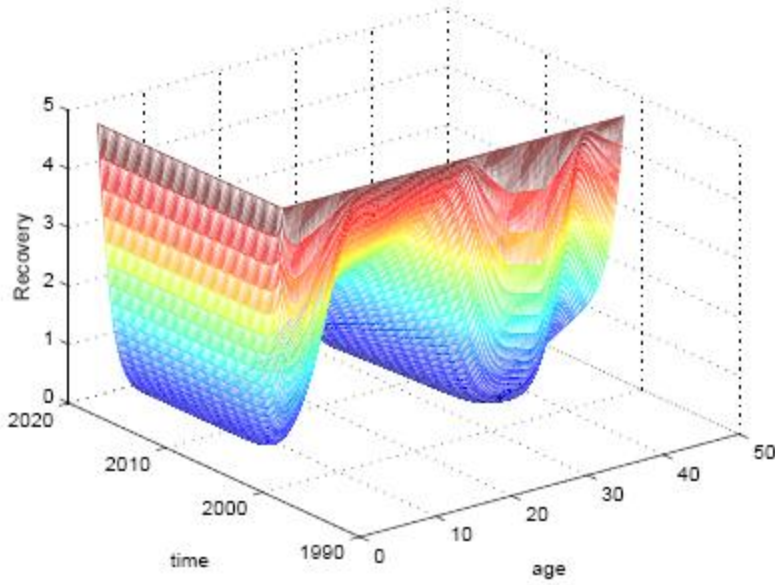
$a + 1$ years by $\int_a^{a+1} S(\bar{a}, t) d\bar{a}$ constituting the basic apprehension that humans from age a to $a + 1$



(a)



(b)



(c)

Figure 3: Shows simulation of BU with susceptible, infected population and recovered population dynamics as function of age and time

are taken to be a years old. Notice that we use a resolution of 1 week in age, thus at the initial time with constant density d . This leads $52 \approx 120$ humans of each age a . We also examined the dynamics of B_H over time which is shown in Figures 2(d). It depicts a peak within few days of the spread of BU and this is due to the fact that initially people do not pay attention to the environment. Hence a greater accumulation in the entire area in the curve was observed.

To make excessive use of our PDE model, we can observe at the model quantities in Figure3 which indicate how the quantities vary over time across different age groups. For instance, in Figure 3, in the surface plot of the susceptible, infected and recovered population, the height (the vertical coordinate) at point (a, t) is the number of susceptible, infected and recovered people of age a at time t as the height of surface respectively. Since the susceptible and infected populations decline, as anticipated, the recovered rise over time and age. We note that owing natural recovery and antibiotic given, the recovered increase. There is a decrease in both Figure 3(a) and 3(b) as assumed to crop up as a result of medication and long duration for humans to who have recovered to wane their immunity. We note a rise in the Figure 3(c) as a result of high recovery rate based on natural and antibiotic medications.

7. Conclusion

An age-structured model can model the infection pathway of Buruli ulcer more accurately since the risk for contracting the disease has something to do with the age of a human being [1]. We observe that introducing age as another independent variable encompasses solving a system of partial differential equations instead of simpler ordinary differential equation systems and this brings in new challenges for the existence of a solution of the system, and for the numerical method. We also present our existence result for the PDE system applying a fixed point argument. We present time dependent S, I, R simulation. We also present numerical simulation on both age and time the dynamics of BU disease. We also observe that *Mycobacterium ulcerans* spread is facilitated by the behaviour of humans. The inclusion of treatment control strategies in an age-structured Buruli ulcer model will help in further explanation of the dynamics of BU.

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