



SDI FINAL EVALUATION FORM 1.1

PART 1:

Table with 2 columns: Field (Journal Name, Manuscript Number, Title of the Manuscript) and Value (British Journal of Mathematics & Computer Science, 2014_BJMCS_10040, An Age- Structured Model for the spread of Buruli ulcer : Analysis and Simulation in Ghana)

PART 2:

Table with 2 columns: FINAL EVALUATOR'S comments on revised paper (if any) and Authors' response to final evaluator's comments. The table contains detailed feedback and responses regarding mathematical models, assumptions, and the abstract Cauchy problem.



SDI FINAL EVALUATION FORM 1.1

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

space between mathematical expression (...), “if” and the inequalities with a .

153- “ $B_H(0) = B_H 0$.” Should be written as in line No 190: $0 \leq B_{H0} \leq B$

200-201-202 The presentation/form of the expression of L on characteristics should be improved.

205: “The fixed point of the map L was derived, meeting the conditions” (without “.”) **WHICH CONDITIONS?**

210: There is a notational problem with notation Ω : it is a number, the size of a set or a set itself? **YOU MAY CORRECT IT BEFORE ANY PUBLICATION.**

PLEASE: NUMBERING YOUR RESULT LIKE THIS THEOREM.

219- Li : write with “i” indexed.

225- it is “sup” instead of “max” in $|L_j(S, I, R, B_H)| \leq \max\{B_{H0}\} + D_2 B \Omega \leq 2B$

242: In addition, the Jacobian for this transformation...” *Please define clearly the transformation.*

250: “the terms made up of the Si...” index I in S_i .

264: $\theta(a) = \begin{cases} 1/365 \text{ for } a \leq 15 \text{ year} \\ 1/2.363 \text{ for } a > 15 \text{ year} \end{cases}$ “, year(s)”

277-278: $\left| \alpha \frac{\Delta x}{\Delta t} \right| \leq 1$

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

I had already ask (check from expression 277 !) to permute Delta t and Delta x in $\Delta t \leq \Delta x / |\alpha|$

It will have bad effect on the stability of your numerical scheme: correct please that error. You get instead a restriction in space step.

295-296: $S(a, 0) = \begin{cases} 0, & \text{if } 0 \leq a \leq 40, \text{ weeks} \\ d, & \text{if } a > 40, \text{ weeks} \end{cases}$

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

$$D(A) = \left\{ \phi = (\phi_1, \phi_2, \phi_3) \in W^{1,1}(0, a^+, \mathbb{R}^3) \text{ and } \begin{pmatrix} \phi_1(0) \\ \phi_2(0) \\ \phi_3(0) \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ \int_0^{a^+} |f(a)[\phi_1(a) + \phi_2(a) + \phi_3(a)] da \end{pmatrix} \right\}$$

The function $F: \overline{DA} \rightarrow Y$ defined by

$$F_1 \begin{pmatrix} \phi_1 \\ \phi_2 \\ \phi_3 \end{pmatrix} = \begin{pmatrix} \Lambda - \beta_H \frac{B_H}{k_H + B_H} \phi_1 - \mu_H \phi_1 + \theta \phi_3 \\ \beta_H \frac{B_H}{k_H + B_H} \phi_1 - \mu_H \phi_2 - \rho_1(1-g)\phi_2 - \rho_2 g \phi_2 \\ \rho_1(1-g)\phi_2 + \rho_2 g \phi_2 - (\mu_H + \theta)\phi_3 \end{pmatrix}$$

$$F_2 = \int_0^{+\infty} \eta \phi_1 da$$

As well as the nonlinear map $F: Y_0 \rightarrow Y$ defined by

Let us consider that

$$\overline{DA} = X_0.$$

Now by carefully observing $(S(t, \cdot), I(t, \cdot), R(t, \cdot), B_H(t))$ in (2a-d) together with

$$u(t) = (0, 0, 0, S(t, \cdot), I(t, \cdot), R(t, \cdot), B_H(t))^T,$$

One obtains that $u(t)$ satisfies the following abstract Cauchy problem

$$\frac{du}{dt} = Au(t) + F(ut), \quad t > 1, \quad (2.21a)$$

together with the initial data $u(0) = y = (0, 0, 0, 0, S_0, I_0, R_0, B_{H0})^T \in Y_0$.

We also take into account the positive cones

$$Y_+ = [\mathbb{R}^+]^3 \times [L_+^1(0, \infty)]^3, \quad Y_{0+} = Y_0 \cap Y_+.$$

Theorem 1 : *There exists a continuous semiflow $\{U(t)\}_{t \geq 0}$ on Y_{0+} into itself such that for each $y \in Y_{0+}$, the map $t \rightarrow U(t)y$ is the unique integrated solution of (2.21a) with initial data y , namely $t \rightarrow U(t)y$ satisfies*

$$(i) \quad \int_0^t U(s)y ds \in D(A), \quad \forall t \geq 0,$$

$$(ii) \quad \int_0^t U(s)y ds = x + A \int_0^t U(s)y ds + F \int_0^t U(s)y ds$$

Moreover we have for each $y \in Y_{0+}$.



SDI FINAL EVALUATION FORM 1.1

“if0” “ifa”
302: space between mathematical expression and units,
$$d = \frac{20,000(\text{humans})}{50(\text{weeks / year}) \times 60(\text{year})} \approx 8.33 \text{humans / weeks}$$

332-334: Why the three figures a-b-c are quite similar?

362-363: “We also observe that Mycobacterium ulcerans spread is facilitated by the behaviour of humans”. Where are the justifications of this proposition in your study? I rather see it as a perspective. But you could also support your statement by showing the importance of the rates ρ_1 and ρ_2 .

”M.(2005).” What is M?

384:

392 (ref. 8) is similar to 432 (ref. 22): **Webb, G. 1985. Theory of Non-linear Age-Dependent Population Dynamics, Marcel Dekker, New York.** AND **Webb, G. 1985. Theory of Nonlinear Age-Dependent Population Dynamics, Marcel Dekker, New York.** Be careful with references.

395-396: Bonyah, E ., Owusu-Sekyere E . 2012. Modelling of Buruli Ulcer Prevalence in Amansie West District, Ghana. International Journal of Sciences (ISSN 2305-3925), please the volume, the Number of the series/Journal?

410-411: [14] World Health Organization. Buruli ulcer: Number of new cases of Buruli ulcer reported (per year). Assessed WHEN and WHERE?

424- [19] World Health Organization. Buruli Ulcer (2001). Diagnosis of Mycobacterium ulcerans **Dis- ease**. (please correct)

434: “Poc. Edinburgh Math...” Proc.

-
GENERAL COMMENTS: in any study like this, there is a parameter named “reproduction number” or “basic reproduction rate”: where are yours in this manuscript? This parameter is important when an author want to present stability of steady states (Disease Free Equilibrium/DFE or Endemic Equilibrium/EE) and say in which state is the population where the data has been taken.
(see for example: <http://www.math.u-bordeaux1.fr/%7Eaducro100p/pdf/DM-nonlinearity.pdf> or H. W. Hethcote, The Mathematics of Infectious Diseases, SIAM Review, 42:2 (2000), 599 - 653.)

$$\limsup_{t \rightarrow \infty} \|U(t)y\| y \leq \frac{\Lambda}{\mu_H}$$

Proof:

Let us take into consideration that for each N centered at 0 .One gets the existence of maximal positive semiflow for (2.21a) on Y_{0+} into itself. It remains to prove that this semiflow is globally defined. In order to achieve this, let $y \in Y_{0+}$ be given and recall that

$$U(t)y = (0, 0, 0, S(t, \cdot), I(\cdot, \cdot), R(\cdot, \cdot))^T$$

Also let us consider the quantity

$$Q(t) = \|U(t)y\| y = \int_0^\infty S(t, a) da + \int_0^\infty I(t, a) da + \int_0^\infty R(t, a) da, \quad B_H(t) \leq \frac{\bar{\eta}\Lambda}{\mu_H \delta_V}$$

the total population at time t . Then it satisfies the differential inequality

$$\limsup_{t \rightarrow \infty} \|U(t)y\| y \leq \frac{\Lambda}{\mu_H}, \quad \forall y \in Y_{0+} - \mu_H Q(t)$$

Thus the map $t \rightarrow Q(t)$ cannot blow up in finite time and the global existence result follows. Let us in addition, notice that, from this inequality one gets

$$\limsup_{t \rightarrow \infty} \|U(t)y\| y \leq \frac{\Lambda}{\mu_H}, \quad \forall y \in Y_{0+}$$

One the other hand one has

$$\begin{aligned} \frac{dQ(t)}{dt} &= \Lambda - \mu_H Q(t) \\ &\geq \Lambda - \mu_H \end{aligned}$$

So that

$$\liminf_{t \rightarrow \infty} \|U(t)y\| y \leq \frac{\Lambda}{\mu_H}, \quad \forall y \in Y_{0+}, \quad B_H(t) \leq \frac{\bar{\eta}\Lambda}{\mu_H \delta_V}$$

This completes the proof of the result.

2.23 Equilibria and their stabilities

Let $\bar{\eta} = \max\{\bar{\eta}\}, \bar{\eta} = \text{ess sup}_{[0, \infty)} |\bar{\eta}|$. It is easy to demonstrate the following set is positively invariant for the system (2a-d)

$$W = (S, I, R, B_H) \left| \left(\int_0^\infty S(a, t) + \int_0^\infty I(a, t) + \int_0^\infty R(a, t) \right) da \leq \frac{\Lambda}{\mu_H}, \quad B_H(t) \leq \frac{\bar{\eta}\Lambda}{\mu_H \delta_V} \right. \\ (2.23a)$$

System of equation (2a-d) always has the disease free equilibrium $E_0(\Lambda e^{\mu_H a}, 0, 0, 0)$.

To simplify expressions, we introduce the following notations

$$\pi(a) = e^{-u(a)} e^{-\int_0^a (\rho_1(v) + g(v)) dv}$$

Let $(S^*(a), I^*(a), R^*(a), B_H^*)$ represent any arbitrary endemic equilibrium of the model (2a-d). This equilibrium satisfies the following equations

$$\frac{dS^*(a)}{da} = \Lambda(a, t) - \beta_H(a) \frac{B_H^*}{k_H(a) + B_H^*} S^*(a) - \mu_H(a) S^*(a) + \theta(a) R^*(a),$$



SDI FINAL EVALUATION FORM 1.1

(2.4a)

$$\frac{dI^*(a)}{da} = \beta_H(a) \frac{B_H^*}{k_H(a) + B_H^*} S^*(a) - \mu_H(a) I^*(a) - \rho_1(1-g(a)) I^*(a) - \rho_2 g(a) I^*(a)$$

(2.4b)

$$\frac{dR^*(a)}{da} = \rho_1(1-g(a)) I^*(a) + \rho_2 g(a, t) I^*(a) - \mu_H(a) R^*(a) - \theta(a) R^*(a)$$

(2.4c)

$$\int_0^\infty \eta I^*(a) da - \delta_V B_H^* = 0,$$

(2.4d)

Solving the second and fourth equation of (2.4b-d) respectively, leads

$$I^*(a) = I^*(0) \pi(a)$$

$$B_H^* = \frac{1}{\delta_V} \int_0^{+\infty} \eta I^*(a) da$$

Let

$$R_0 = \frac{\beta_H \Lambda}{\mu_H \delta_V} \int_0^\infty [\eta_1(a) \pi(a)] da$$

(2.4e)

According to Diekmann et al., (1990) R_0 in (2.4e) can be regarded as the basic reproduction number of the disease and explained as follows. Since the total infectivity at time t is the sum of the infectivity in the compartment and the Mycobacterium ulcerans compartment, we define $R_0 = R_I + R_B$ where

$$R_I = \int_0^\infty S_0 \beta_H(a) \pi(a) da$$

Is the number of secondary cases generated by individual in the infective

compartment, and $S_0 = \frac{\Lambda}{\mu_H}$ is the number of susceptible individuals in the absence of

the disease. The term $\pi(a) = e^{-\int_0^a (\mu_H(v) + \rho_1(1-g(v)) + \rho_2 g(v)) dv}$ is the survival probability as a function of age a in the infected class.

The reproduction number of the infectious caused by the free Mycobacterium ulcerans is

$$RB_H = \frac{\beta_H}{\delta_V} S_0 \int_0^\infty \eta(a) \pi(a) da$$

Now we consider the existence of the endemic equilibria. From (2.4b) and (2.4d), we obtain that the equilibrium level of susceptible individual S^* satisfies the following



SDI FINAL EVALUATION FORM 1.1

	equations $S^* = \frac{k_H + \frac{1}{\delta_V} \int_0^{+\infty} (\eta \pi(a))}{\frac{\beta_H}{\delta_V} \int_0^{+\infty} (\eta \pi(a))} (\mu_H(a) + \rho_1(1 - g(a) + \rho_2 g(a)) \pi(a))$ We also observe that Mycobacterium ulcrans spread is facilitated by the behaviour of humans as the rate of recovery untreated Buruli ulcer depend on the immunity. Treatment of Buruli ulcer at early stages reduces the epidemiology of BU disease.
--	--