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Mathematical modeling of the migration's effect and analysis of the spreading of a cholera epidemic

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Abstract. We propound a mathematical modeling of the migration's effect on the size of any population dynamic from a site of a heterogeneous space $\Omega \subset \mathbf{R}^d$, $d = 1, 2, \ldots$. The obtained model is afterwards added at SIR model including the dynamics of the bacteria and some control parameters to model the spreading of a cholera epidemic which occurs in Ω. The formulated model is given by a system of four parabolic partial differential equations. Existence and stability of equilibria, Turing's instability and optimal control problem of this model are studied. We finish with a real-world application in which we apply the model specifically to the cholera epidemic that took place in Cameroon in 2011.

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1 Introduction

The cholera is an acute intestinal infection which is the result of the absorption, by ingestion, of the vibrio choleraic finding oneself in water or in

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food, but can also be the result of a contamination of a person to an another starting from the pathological products (excrements, vomiting, sweat). The experiences show that the vibrios ingested in food are most liable to be the cause of an infection than those ingested in water. The infectious dose determined experimentally is of the order of 10^8 to 10^{11} bacteria. The gastric acidity is little propitious to the survival of the bacterium in the stomach. After the crossing of the gastric barrier, the vibrios settle down in the nearness part of the small intestine, going through the mucus layer and secrete the choleraic toxin. This toxin modifies the exchanges of water and of the electrolytes by preventing the penetration of the sodium inside the cell. This induces a crossing in the light of the digestive tract of a big quantity of water being able to reach 15 l per day, causing a severe dehydration of the ill individual [6].

The cholera is an extremely virulent disease which affects the children as the adults. In the absence of the treatment, one can die in few hours. About 75 percent of infected individuals by the vibrio choleraic doesn't manifest any symptom, though the bacillus be present into their excrements during 7 to 14 days after the infection and be eliminated in the environment, where it can infected potentially another persons. For those whom manifest symptoms, these symptoms remain slight in 80 percent of cases, whereas about 20 percent of cases, an acute watery diarrhoea, coming with severe dehydration, the vomiting but without temperature increasing is developing. The excrements become rapidly watery, taking the water rice color. This important leak of the water induces intense cramps spreading in all the human body, pushing the eyes in the orbits, contracting the orbicular muscles of the lips, leading then to give a cyanosis look to the face of the sick. The individuals having a weak immunity, the children suffering of malnutrition or the persons living with the H.I.V. for example, are more exposed at risk of death in case of infection [8].

The transmission of the cholera is tightly tied up to a bad management of the environment and the number of cases of the cholera notified to WHO continues to increase (World Health Organization, Cholera fact sheets, August 2011. Available from: www.who.int). In spite of about a hundred years of studies on the disease, the cholera remains endemic and epidemic in several countries of Africa, Asia and Latin America. The epidemiology is dominated by hydrous transmission. It is then few probable that extensive epidemics occur in the countries where bacteriological waters control is strictly applied, even if localized sources started up. The overpopulation, the lack of corporeal and nutritious hygiene, can also contribute at spreading of the disease.

The mathematical model commonly used to describe the spreading of an infectious disease is the SIR model, the name resulting of the fact that the population is divided into three disjoint groups: susceptible (S), infected (I) and recovered (R) (see [5,10,15]). With the intention of building mathematically the dynamics of the bacteria in water or bacterial abundance, Emvudu and Kokomo (see [11]) proposed a model which inserts bacterial abundance. This allowed us to obtain a SIRB model formed of a system of four ordinary differential equations.

The goal of this paper is to build a mathematical model which considers the migration of individuals and the control methods of the disease necessary to the eradication of the epidemic.

This paper is organized as follows. With Section 2, we formulate a mathematical model describing the effect of the migration on the dynamic of the size of a given population. In Section 3, we propound a controlled model of spreading of the cholera. With Section 4, we carry out the mathematical analysis of the proposed model in 3. The optimal control problem is formulated and studied in section 5. We finish, in Section 6, by a real-world problem where we apply our model to the study of the epidemic of the cholera having took place at Cameroon in 2011.

2 Mathematical modeling of the effect of the migration in the dynamic of a population

2.1 Assumptions of modeling

Assumption 1: The individuals are assigned to a topographic space $\Omega \subset \mathbb{R}^d$ $(d = 1, 2, 3)$, continuous, heterogeneous, stable, of boundary $\partial\Omega \in C^2$ and can move inside Ω.

Assumption 2: The individuals can be transported to a constant speed v via a known transport's mean in Ω.

Assumption 3: The population of a site of Ω is homogeneous and only the movements in large scale between the various sites are constrained in the space, the moving of an individual being independent of his social status.

Assumption 4: The migration is solely function of the distance and symmetric, that is, the rate of individuals who migrate from a site i towards a site j is the same than this which allows us to quit the site j for the site i $(i \neq j)$.

2.2 Formulation of the model

Assumption 1 shows that the spatiotemporal model to build is an explicit model. Thus, the time being continuous, we will begin by construct a model of the migration's effect in a discrete space, which will allow us to obtain the searched model in the continuous space Ω.

Model of the effect of the migration in a discrete space

The space being discrete, we can used the metapopulation model of Levin (see [17]). For that, let us divide the space Ω (assumed here to be discrete) in n sub-populations rallied in n sites ($n = 2, 3, \ldots$), the sites being joined by the migrations. The population of a site of Ω being homogeneous (assumption 3), let us denote by: $X(i,t)$ the density of the individuals of the site i at time t. $K(i,j)$ the transition rate per unit of time of individuals migrating to the site i towards the site j $(i \neq j)$. We thus have:

$$X(i,t+\Delta t) = X(i,t) + \sum_{j=1}^{n} X(j,t)K(j,i)\Delta t - \sum_{j=1}^{n} X(i,t)K(i,j)\Delta t.$$

The first sum corresponds at immigrations and the second at emigrations. The assumption 4 allows us to write $K(i,j) = K(j,i)$ and $K(i,j) = \Phi(\|i - j\|_\Omega)$.

When Δt tends towards 0, we have:

$$\begin{aligned}
\lim_{\Delta t \to 0} \frac{X(i,t+\Delta t) - X(i,t)}{\Delta t} &= \frac{\partial X(i,t)}{\partial t} \\
&= \sum_{j=1, j\neq i}^{n} X(j,t)K(j,i) - \sum_{j=1, j\neq i}^{n} X(i,t)K(i,j) \\
&= \sum_{j=1, j\neq i}^{n} X(j,t)K(j,i) - X(i,t) \sum_{j=1, j\neq i}^{n} K(i,j) \\
&= \sum_{j=1, j\neq i}^{n} X(j,t)K(i,j) - X(i,t) \sum_{j=1, j\neq i}^{n} K(i,j).
\end{aligned}$$

Thus, for each site i, $i = 1, 2, \ldots n$, the model of migration's effect (in the discrete space Ω) is given by:

$$\frac{\partial X(i,t)}{\partial t} = \sum_{j=1, j\neq i}^{n} X(j,t)K(i,j) - X(i,t) \sum_{j=1, j\neq i}^{n} K(i,j). \tag{1}$$

Model of the effect of the migration in a continuous space

We assume now that the space $\Omega \subset \mathbf{R}^d$ is continuous. Let us denote by $X(x,t)$ the density of the individuals inhabiting the position x at time t. Taking Assumption 3 into account, and then by setting $\epsilon = x - y \in \Omega$ the model (1) becomes

$$\begin{aligned}\frac{\partial X(x,t)}{\partial t} &= \int_{\Omega\setminus\{x\}} X(x-\epsilon,t)\Phi(\|\epsilon\|_\Omega)d\epsilon - X(x,t)\int_{\Omega\setminus\{x\}} \Phi(\|\epsilon\|_\Omega)d\epsilon,\\ &= \int_{\Omega\setminus\{x\}} X(y,t)\Phi(\|x-y\|_\Omega)dy - X(x,t)\int_{\Omega\setminus\{x\}} \Phi(\|\epsilon\|_\Omega)d\epsilon,\end{aligned}$$

that is,

$$\frac{\partial X(x,t)}{\partial t} = \left(X(.,t) * \Phi\right)(x) - X(x,t)\int_{\Omega\setminus\{x\}} \Phi(\|\epsilon\|_\Omega)d\epsilon, \tag{2}$$

where $X(.,t) * \Phi$ being the product of convolution of $X(.,t)$ and Φ.

Since the Dirac delta allows us to convey in transit to the discrete towards the continuous, we choose Φ so that (see [19]) :

$$\Phi = \delta - v \text{ div } \delta + \frac{\sigma^2}{2}D^2\delta, \tag{3}$$

where δ is the (multidimensional) Dirac delta distribution, $\frac{\sigma^2}{2}$ the diffusion coefficient, div $= \sum_{i=1}^{d} \frac{\partial}{\partial x_i}$ and $D^2 = \sum_{i,j=1}^{d} \frac{\partial^2}{\partial x_i \partial x_j}$ operators defined in the meaning of distributions' theory (see [23]).

Taking the linearity of the product of convolution into account and the fact that we have for all test function f (see [9], [23]):

$$f(x) * \partial^n\delta(x) = \partial^n f(x) \tag{4}$$

where $\partial^n = \frac{\partial^n}{(\partial x_1)^{\alpha_1}(\partial x_2)^{\alpha_2}\ldots(\partial x_d)^{\alpha_d}}$ $(n = 0, 1, \ldots$ and $\alpha_1 + \alpha_2 + \cdots + \alpha_d = n)$ is the partial derivative operator of order n with $\partial^0 f = f$, we have:

Theorem 1. *In the heterogeneous continuous space Ω, the model of the effect of the migration is given by:*

$$\frac{\partial X(x,t)}{\partial t} = -v \text{ div } X(x,t) + \frac{\sigma^2}{2}\sum_{i,j=1}^{d} \frac{\partial^2 X(x,t)}{\partial x_i \partial x_j}, \tag{5}$$

with $x = (x_1, x_2, \ldots, x_d)^T \in \Omega$.

Proof. It suffices to transfer (3) and (4) in (2) and carry out the calculations. □

Approximation of the model of the effect of the migration in a continuous space

Let us set $H = \sum_{i=1}^{d} \epsilon_i \frac{\partial}{\partial x_i}$. By applying truncated Taylor's expansion at order n at $X(x-\epsilon,t)$ with $\epsilon = (\epsilon_i)_{1\le i\le d}$, we obtain according to (2):

$$\frac{\partial X(x,t)}{\partial t} \simeq \Big[\int_{\Omega\setminus\{x\}} \Big(X(x,t) - HX(x,t) + \frac{1}{2}H^2X(x,t) + \cdots + \frac{(-1)^n}{n!}H^nX(x,t)\Big)\Big]\Phi(\|\epsilon\|_\Omega)d\epsilon - X(x,t)\int_{\Omega\setminus\{x\}}\Phi(\|\epsilon\|_\Omega)d\epsilon, \quad (6)$$

where the power term $(p, n-p)$ corresponds to the n- derivative $\frac{\partial^n}{\partial x_1^p \partial x_2^{n-p}}$ with $(x_1,x_2) = (x_i)_{1\le i\le d}$. In addition (see [9]) we have:

$$\delta(\epsilon) = \partial^n\delta(\epsilon) = 0 \quad \text{when} \quad x \neq y. \quad (7)$$

$$\int_\Omega \delta(\epsilon)d\epsilon = 1, \quad \int_\Omega f(\epsilon)\partial^{(n)}\delta(\epsilon)d\epsilon = (-1)^n\partial^{(n)}f(0), \quad (8)$$

and consequently by transferring (7), (8) and (3) into (6), we obtain after calculations:

$$\frac{\partial X(x,t)}{\partial t} \simeq \frac{\sigma^2}{2}\triangle X(x,t) - v\ \text{div}\ X(x,t), \quad (9)$$

which is the diffusion classical equation, constituting thus an approximation of the model of the migration's effect in a heterogenous continuous space.

Remark 1. *The models (9) and (5) are equivalent only when* $d = 1$.

3 Controlled model of the spreading of the cholera

In this section, we formulate a controlled model of the spreading of the cholera under the conditions where all the assumptions of the subsection 2.1 are verified.

We consider a population subdivided in three disjoint groups representing the great stages of the disease: the Susceptible (S), Infected (I) and Recovered (R). The population of each subgroup is homogeneous and we denote by $S = S(x,t)$, $I = I(x,t)$, $R = R(x,t)$, the respective densities of Susceptible, Infected and Recovered inhabiting the place $x \in \Omega$ at time $t \in \mathbb{R}_+$. In accordance with Emvudu and Kokomo model (see [11]), the population of bacilli (vibrio choleraic) is homogeneous and transported via a running water crossing the different sites of the space Ω. Its density is $B = B(x,t)$.

The newborns are neither susceptible, nor be struck down by the cholera, all the births being protected. The only voice of the infection of a susceptible individual (S) is the consumption of a water coming from a contaminated source (B). The infected individuals of cholera, cure at rate γ_1 for the non treated infected individuals, γ_2 for the treated infected individuals and die as the result of the cholera at rate μ_1. All the time that he remains infected, the individual contributes to the increasing of the bacteria population through its excrements at rate e. The bacteria population (B) decreases by the natural mortality at rate γ and can also increases at rate determined by some environmental factors (the temperature for example). The effects of seasonality are described by a periodic variation of the contact parameter β between bacteria and the hosts. The parameter β can be function of the time and of the space.

In order to fight efficiently against the disease, three fighting strategies $\theta_1(x,t)$, $\theta_2(x,t)$ and $\theta_3(x,t)$ representing respectively the proportion of people who receive antibiotic cure, the proportion of people who receive the hydration therapy, and, the proportion of the contaminated water treated, are introduced into the model. The antibiotic cure lessens the contribution of an infected individual to the increasing of the vibrio choleraic in the environment, whereas, the hydration therapy allows to save the life of an infected individual without limit his contribution to the increasing of the vibrio choleraic in the environment. Let us note that in the reality, the antibiotic cure can not be administer without the hydration therapy (see [1]).

We choose $\theta_i(.,0) = 0$ with $\theta = (\theta_1, \theta_2, \theta_3)^T$ belonging to $\Gamma = \{\theta \in (L^1(0,T,L^\infty(\Omega))^3 | 0 \le \theta_1(x,t) \le N_1; 0 \le \theta_2(x,t) \le N_2;\ 0 \le \theta_3(x,t) \le N_3 \quad p.s.\}$, where $0 < T \le \infty$, with $N_1 < 1$, $N_2 < 1$ and $N_3 < 1$ which represent the intervention's maximal proportions. The following controlled model, which is constituted of four parabolic partial differential equations is then obtained:

$$\left\{ \begin{array}{rcl} \frac{\partial S(x,t)}{\partial t} &=& -\mu S - \beta(x,t)\frac{B}{K+B}S + r_1 R + \frac{\sigma^2}{2}\sum_{i,j=1}^{d}\frac{\partial^2 S}{\partial x_i \partial x_j}, \\ \frac{\partial I(x,t)}{\partial t} &=& \beta(x,t)\frac{B}{K+B}S - \mu I - (1-\theta_2(x,t))\mu_1 I \\ && -\gamma_1(1-\theta_1(x,t))I - \gamma_2\theta_1(x,t)I + \frac{\sigma^2}{2}\sum_{i,j=1}^{d}\frac{\partial^2 I}{\partial x_i \partial x_j}, \\ \frac{\partial R(x,t)}{\partial t} &=& -(r_1+\mu)R + \frac{\sigma^2}{2}\sum_{i,j=1}^{d}\frac{\partial^2 R}{\partial x_i \partial x_j} + \gamma_1(1-\theta_1(x,t))I \\ && +\gamma_2\theta_1(x,t)I, \\ \frac{\partial B(x,t)}{\partial t} &=& eI - (\gamma + \theta_3(x,t))B - v \operatorname{div} B + \frac{\sigma_B^2}{2}\sum_{i,j=1}^{d}\frac{\partial^2 B}{\partial x_i \partial x_j}. \end{array} \right. \tag{10}$$

$D = \frac{\sigma^2}{2}$ and $D_B = \frac{\sigma_B^2}{2}$ respectively represent the diffusion coefficients of the individuals and bacteria. v represents the constant speed of bacteria in running water. div and $\triangle$ respectively represent divergence and Laplacian operators. The initial conditions are given by $S(x,0) = S(x)$, $I(x,0) = I(x)$, $R(x,0) = R(x)$ and $B(x,0) = B(x)$. Whereas boundaries conditions are given by $S(x,t) = I(x,t) = R(x,t) = B(x,t) = 0$ on $\partial\Omega$ $\forall (x,t) \in \Omega \times \mathbb{R}_+$.

4 Mathematical analysis of the controlled model

4.1 Existence of a flow of the model

Let us consider the Banach spaces $E = L^2(\Omega)$ and $X = \left[W^{2,2}(\Omega) \bigcap W_0^{1,2}(\Omega)\right]^4$. Let us consider the unknown function $\Phi : \left[0, T\right[\to X$ defined by

$$\Phi(t) = (S(.,t), I(.,t), R(.,t), B(.,t))^T \in X \;\; (0 < T \leq \infty).$$

Let us consider the operator $\mathcal{A} : D(\mathcal{A}) = X \to X$ defined for all $t \in \left[0, T\right[$ by

$$\mathcal{A}\Phi(t) = \begin{pmatrix} -\mu S + r_1 R + \frac{\sigma^2}{2} \sum_{i,j=1}^{d} \frac{\partial^2 S}{\partial x_i \partial x_j} \\ -(\mu_1 + \mu) I + \frac{\sigma^2}{2} \sum_{i,j=1}^{d} \frac{\partial^2 I}{\partial x_i \partial x_j} - \gamma_1 I \\ -(r_1 + \mu) R + \frac{\sigma^2}{2} \sum_{i,j=1}^{d} \frac{\partial^2 R}{\partial x_i \partial x_j} + \gamma_1 I \\ eI - \gamma B - v \text{ div } B + \frac{\sigma_B^2}{2} \sum_{i,j=1}^{d} \frac{\partial^2 B}{\partial x_i \partial x_j} \end{pmatrix}.$$

Clearly then $\mathcal{A}$ is an unbounded linear operator on E (see [12]). Let us consider the operators $\mathcal{B} : \Gamma \to C(0, T, X)$ and $f : \left[0, T\right[\to X$ defined for all $\theta \in \Gamma$ and all $t \in \left[0, T\right[$ by:

$$(\mathcal{B}\theta)(t) = \begin{pmatrix} 0 \\ -\theta_2(.,t)\mu_1 I(.,t) + (\gamma_1 - \gamma_2)\theta_1(.,t) I(.,t) \\ (\gamma_2 \theta_2(.,t) - \gamma_1 \theta_1(.,t)) I(.,t) \\ -\theta_3(.,t) B(.,t) \end{pmatrix},$$

and

$$f(t) = (-\beta'(t) \frac{B(.,t)}{K + B(.,t)} S(.,t), \beta'(t) \frac{B(.,t)}{K + B(.,t)} S(.,t), 0, 0)^T,$$

where $\beta'(t) = \beta(.,t)$ is such that $\beta'(0) = 0$.

Then, the system (10) can be rewritten like the following Cauchy problem on the Banach space X:

$$\begin{cases} \dfrac{d\Phi}{dt}(t) = \mathcal{A}\Phi(t) + (\mathcal{B}\theta)(t) + f(t), \quad 0 < t < T, \\ \Phi(0) \;\; \in D(\mathcal{A}). \end{cases} \tag{11}$$

We have the following lemma:

Lemma 1. *(i) The operator $\mathcal{A}$ generates a contraction semigroup $\mathcal{T}(t)$, $t \geq 0$ on E.*
(ii) The nonlinear operator $g = (\mathcal{B}\theta) + f : \left[0, T\right[\longrightarrow X$ is a continuous and lipschitzian function from $\left[0, T\right[$ towards X.

Proof. (i) This comes from [12] (see [12], theorem 5, chapter 7).
(ii) It is obvious that $g = (\mathcal{B}\theta) + f$ is continuous in t $\forall t \in \left[0, T\right[$. In addition, $\|g(t_1) - g(t_2)\|_X = \| (\mathcal{B}\theta)(t_1) - (\mathcal{B}\theta)(t_2) + f(t_1) - f(t_2) \|_X \leq D\|t_1 - t_2\|$ with $D = \sup_{\Phi \in X}(\| (\mathcal{B}\theta) \|_{\mathcal{L}(\Gamma, C(0,T,X))} + 2\sup_{\Phi \in X}(\beta'(t_1), \beta'(t_2)).\ \| S(\Phi, t_1) - S(\Phi, t_2) \|_X)$. We conclude thus that $g = (\mathcal{B}\theta) + f$ is a continuous and lipschitzian function from $\left[0, T\right[$ towards X. □

The main result of this subsection is the following:

Theorem 2. *The Cauchy problem (11) admits on $\left[0, T\right[$, $T > 0$ a unique classical solution given by:*

$$\Phi(t) = \mathcal{T}(t)\Phi(0) + \int_0^t \mathcal{T}(t - \tau)g(\tau)d\tau. \tag{12}$$

Proof. This is due to Songmu, 2004 (see [25], Corollary 2.4.3) □

Remark 2. *The solution given by (12) shows that the problem (10) is well-posed in the Hadamard's meaning (see [13]).*

4.2 Equilibria and stability

4.2.1 Equilibria

For a contact rate $\beta(x,t) \equiv \beta(x) \equiv \beta$ for all $t \geq 0$ and the intervention strategies $(\theta_1(x,t), \theta_2(x,t), \theta_3(x,t)) \equiv (\theta_1(x), \theta_2(x), \theta_3(x))$, an equilibrium $(S^*(x), I^*(x), R^*(x), B^*(x))$ of the system (10) is a solution of the system

$$\frac{\partial S(x,t)}{\partial t} = \frac{\partial I(x,t)}{\partial t} = \frac{\partial R(x,t)}{\partial t} = \frac{\partial B(x,t)}{\partial t} = 0. \tag{13}$$

Let us consider the spaces $E = \{\Phi | \Phi_i \in C^1(\overline{\Omega}), \Phi_i = 0 \quad \text{on} \quad \partial\Omega\}$, and $Y = \{\Phi | \Phi_i \in C^2(\overline{\Omega}), \Phi_i = 0 \quad \text{on} \quad \partial\Omega\}$, $(i = 1, \ldots, 4)$, respectively equipped with the norms $\| \Phi \|_E = \max\{\| \Phi_i \|_{C^1(\overline{\Omega})}\}$ and $\| \Phi \|_Y = \max\{\| \Phi_i \|_{C^2(\overline{\Omega})}\}$. $D_1 = D^2$ and $D_2 = -v\,\mathrm{div} + \frac{\sigma_B^2}{2}\sum_{i,j=1}^{d} \frac{\partial^2}{\partial x_i \partial x_j}$ and let us consider the

operators $L : Y \to (C^1(\overline{\Omega}))^4$ and $F : Y \to (C^1(\overline{\Omega}))^4$ defined by:
$L := diag(-D_1, -D_1, -D_1, -D_2)$ and

$$F[\Phi] = \begin{pmatrix} -\mu S - \beta \frac{B}{K+B} S + r_1 R \\ \beta \frac{B}{K+B} S - (r' + \mu) I \\ rI - (r_1 + \mu) R \\ eI - \gamma' B \end{pmatrix},$$

with $r = \gamma_1(1-\theta_1) + \gamma_2\theta_1$, $r' = r + (1-\theta_2)\mu_1$, $\gamma' = \gamma + \theta_3$. Thus, the system (13) can be rewritten in the form

$$L[\Phi^*] = F[\Phi^*], \quad \Phi^* \in Y. \tag{14}$$

With the aim to study efficiently this nonlinear problem, we consider the following auxiliary problem

$$L[\Phi^*] = \lambda F[\Phi^*], \quad \Phi^* \in Y, \tag{15}$$

where $\lambda \in \mathbb{R}^+$ is a parameter. Let us note that $\mathcal{P} = \{\Phi \in E | \Phi_i \geq 0 \text{ in } \overline{\Omega}\}$ and let us consider the operator $Q : \mathbb{R}^+ \times \mathcal{P} \to \mathcal{P}$ defined by

$$Q(\lambda, \Phi) = \Phi - \lambda L^{-1} F[\Phi], \quad (\lambda, \Phi) \in \mathbb{R}^+ \times \mathcal{P}. \tag{16}$$

The problem (15) is then equivalent to:

$$Q(\lambda, \Phi^*) = 0, \quad (\lambda, \Phi^*) \in \mathbb{R}^+ \times \mathcal{P}. \tag{17}$$

It is obvious that $Q(\lambda, 0) = 0$ for all $\lambda \in \mathbb{R}^+$. Thus, $(\lambda, 0)$ is a trivial solution of (17). Let us consider the set $\sum = \{(\lambda, \Phi^*) \in \mathbb{R}^+ \times (\mathcal{P} \setminus \{0\}) : Q(\lambda, \Phi^*) = 0\}$ of the nontrivial solutions of (17). The closure of the $\sum$ ($\overline{\sum}$) may contain the trivial solutions only if those solutions are the limits of the nontrivial solutions i.e. the bifurcation points of (17) (see for example [21]). We have the following lemma.

Lemma 2. *There exists $\lambda_0 > 0$ such that $\overline{\sum}$ contains an unbounded continuum C with $(\lambda_0, 0)$ belonging to C.*

Proof. Let us consider the operators $L_i : C^2(\overline{\Omega}) \to C(\overline{\Omega})$ $(i = 1, 2)$ defined by $L_1 := -D_1$, $L_2 := -D_2$ and the following linear eigenvalue problems:

$$L_i u(x) = \lambda u(x) \quad x \in \overline{\Omega}; \quad u(x) = 0 \quad \forall x \in \partial\overline{\Omega}. \tag{18}$$

It is known (see for example [18]) that (18) admits respectively an infinite number of eigenvalues $0 < \lambda_1 \leq \lambda_2 \leq \cdots$ and $0 < \rho_1 \leq \rho_2 \leq \cdots$. It is then sufficing to take $\lambda_0 = \min(\lambda_1, \rho_1)$ and apply Theorem 1.2 given in [21] (see [21], Page 216, Theorem 1.2). □

The main result of this part is the following:

Theorem 3. *The model (10) admits two equilibria: a trivial equilibrium $E^0 = (0, 0, 0, 0)$ and a nontrivial equilibrium $E^1 = (S^*, I^*, R^*, B^*)$ obtained by a bifurcation point $\lambda_0 > 0$ of (17).*

Proof. It is enough to notice that if $(\lambda, \Phi^*) \in \mathbb{R}^+ \times \mathcal{P}$ is a solution of (17) then Φ^* is a solution of (13) (see [2]) and take Lemma 2 into account. □

Remark 3. *$E^0 = (0, 0, 0, 0)$ is the equilibrium at boundary $\partial\Omega$ of Ω, whereas, $E^1 = (S^*, I^*, R^*, B^*)$ is the equilibrium inside Ω. Moreover, Lemma 2 shows that E^0 and E^1 have distinct neighborhoods.*

4.2.2 Stability

The linearized of the model (10) at the equilibrium $\Phi^* = (S^*, I^*, R^*, B^*)$ is given by:

$$\frac{\partial \Phi}{\partial t} = \mathbf{L}(\Phi) = D(\triangle \Phi) - vE(\text{div } \Phi) + J(\Phi), \tag{19}$$

with $D = diag(\frac{\sigma^2}{2}, \frac{\sigma^2}{2}, \frac{\sigma^2}{2}, \frac{\sigma_B^2}{2})$, $E = diag(0, 0, 0, 1)$ and

$$J = \begin{pmatrix} -\mu - \beta\frac{B^*}{K+B^*} & 0 & r_1 & -\beta\frac{K}{(K+B^*)^2}S^* \\ \beta\frac{B^*}{K+B^*} & -r' - \mu & 0 & \beta\frac{K}{(K+B^*)^2}S^* \\ 0 & r & -r_1 - \mu & 0 \\ 0 & e & 0 & -\gamma' \end{pmatrix}.$$

According to the standard linear operators theory, it is known that if all the eigenvalues of $\mathbf{L}$ have a negative real part, then Φ^* is locally asymptotically stable, and if at least one eigenvalue of $\mathbf{L}$ has a positive real part, the equilibrium Φ^* is unstable. The characteristic equation of the operator $\mathbf{L}$ is:

$$\mathbf{L}(\psi) = \xi\psi. \tag{20}$$

Let $\psi = (\psi_1(x), \psi_2(x), \psi_3(x), \psi_4(x))^T$ an eigenvector of $\mathbf{L}$ corresponding to the eigenvalue ξ, and let $\psi = \sum_{k=0}^{\infty} \vartheta_k x^k$, with $\vartheta_k = (a_k, b_k, c_k, d_k)^T$, where a_k, b_k, c_k and d_k are real coefficients (see [16]), we have according to (20):

$$k(k-1)D\big[\sum_{k=2}^{\infty} \vartheta_k x^{k-2}\big] - kvE\big[\sum_{k=1}^{\infty} \vartheta_k x^{k-1}\big] + J\big[\sum_{k=0}^{\infty} \vartheta_k x^k\big] = \xi \sum_{k=0}^{\infty} \vartheta_k x^k,$$

that leads to

$$(k+1)(k+2)D\big[\sum_{k=0}^{\infty} \vartheta_k x^k\big] - (k+1)vE\big[\sum_{k=0}^{\infty} \vartheta_k x^k\big] + J\big[\sum_{k=0}^{\infty} \vartheta_k x^k\big] = \xi \sum_{k=0}^{\infty} \vartheta_k x^k.$$

We thus have

$$J_k(\psi) = \xi\psi, \quad k = 0, 1, 2, 3, \ldots, \tag{21}$$

with $J_k = J + (k+2)(k+1)D - (k+1)vE$, $u = \frac{(k+2)(k+1)}{2}\sigma^2$ and $t = (k+1)v + \frac{(k+2)(k+1)}{2}\sigma_B^2$, for $k = 0, 1, 2, 3, \ldots$. It follows from this that the eigenvalues of $\mathbf{L}$ are those of J_k, $k = 0, 1, 2, 3, \ldots$.

For the stability of the trivial equilibrium $E^0 = (0, 0, 0, 0)$, we have the following result:

Theorem 4. *The trivial equilibrium $E^0 = (0,0,0,0)$ of the model (10) is locally asymptotically stable when* $\max(-\mu + \sigma^2, -\gamma' + \sigma_B^2) < 0$.

Proof. At point E^0, it is easy to show that the spectrum of J_k is given by $Sp(J_k) = \{-\mu + u, -r' - \mu + u, -r_1 - \mu + u, -\gamma' + t\}$. □

For the stability of the nontrivial equilibrium $E^1 = (S^*, I^*, R^*, B^*)$ of the model (10), let us set

$$R_0 = \left[\frac{(-r' - \mu + \sigma^2)(-\mu - \beta\frac{B^*}{K+B^*} + \sigma^2)(-r_1 - \mu + \sigma^2)(\gamma' + \sigma_B^2 - v)}{\frac{e\beta S^* K(-r_1-\mu+\sigma^2)(-\mu+\sigma^2)}{(K+B^*)^2} + r' r_1 \beta\frac{B^*}{K+B^*}(\gamma' - v + \sigma_B^2)}\right]^{-1}. \tag{22}$$

We have the following result:

Theorem 5. *The nontrivial equilibrium $E^1 = (S^*, I^*, R^*, B^*)$ of the model (10) is unstable if $R_0 > 1$ and locally asymptotically stable if $R_0 < 1$.*

Proof. The characteristic polynomial of J_k at point E^1 is given by:

$$P_k(X) = X^4 + a_1(k)X^3 + a_2(k)X^2 + a_3X + a_4(k)$$

with

$$\begin{aligned}
a_1(k) &= r' + 3\mu + 3u + \beta\frac{B^*}{K+B^*} + r_1 + \gamma' + t,\\
a_2(k) &= (r' + \mu + u)(\mu + \beta\frac{B^*}{K+B^*} + u) + (r_1 + \mu + u)(\gamma' + t)\\
&\quad +(r' + 2\mu + 2u + \beta\frac{B^*}{K+B^*})(r_1 + \mu + u + \gamma' + t),\\
a_3(k) &= (r' + \mu + u)(\mu + \beta\frac{B^*}{K+B^*} + u)(r_1 + \mu + u + \gamma' + t)\\
&\quad +(r_1 + \mu + u)(\gamma' + t)(r + 2\mu + 2u + \beta\frac{B^*}{K+B^*})\\
&\quad -e\beta(r_1 + 2\mu + 2u)\beta\frac{KS^*}{K+B^*} - r' r_1\beta\frac{B^*}{K+B^*},\\
a_4(k) &= (r' + \mu + u)(\mu + \beta\frac{B^*}{K+B^*} + u)(r_1 + \mu + u)(\gamma' + t)\\
&\quad -e(\mu + u)(r_1 + \mu + u)\beta\frac{KS^*}{(K+B^*)^2} - r' r_1(\gamma' + t)\beta\frac{B^*}{K+B^*}.
\end{aligned}$$

Thus, the necessary and sufficient conditions of stability are given according to Routh - Hurwitz criteria by: $a_1(k) > 0$, $a_1(k)a_2(k) - a_3(k) > 0$, $a_4(k) > 0$ and $a_1(k)a_2(k)a_3(k) - (a_1(k))^2 a_3(k) - (a_3(k))^2 + a_3(k)a_4(k) > 0$. Clearly, $a_4(0) < 0$ leads to $R_0 > 1$, what induces that P_k admits at least one root having a positive real part. Thus, we deduce that E^1 is unstable.

When $R_0 < 1$, it is obvious that $a_4(0) > 0$ and by induction, $a_4(k) > 0$ $\forall k \in \mathbb{N}$. Moreover, clearly, $a_1(k) > 0$, $a_2(k) > 0$,$a_2(k)a_3(k) - a_1(k)a_3(k) > 0$, $a_1(k)a_2(k) - a_3(k) > 0$ and $a_1(k)(a_2(k)a_3(k) - a_1(k)a_3(k)) - a_3(k)(a_3(k) - a_4(k)) > 0$. □

4.3 Analysis of Turing's instability

In this subsection, we look into the effect of the migration on the positive equilibrium of the model (10) in the absence of migration (local model). In actual fact, the Turing's theory (see [24]) shows that the interaction between a chemical reaction (which here represents the local model) and a diffusion (migration here) can allow that a stable equilibrium of the local model becomes unstable for the reaction-diffusion model (here, the model with migration) and thus lead to the spontaneous formation of a stationary spatial and periodic structure. This type of instability is known under the name of Turing's instability or the diffusion driven instability.

In the absence of migration, the model (10) becomes:

$$\begin{cases} \frac{dS}{dt} = -\mu S - \beta(t)\frac{B}{K+B}S + r_1 R, \\ \frac{dI}{dt} = \beta(t)\frac{B}{K+B}S - (r' + \mu)I, \\ \frac{dR}{dt} = rI - (r_1 + \mu)R, \\ \frac{dB}{dt} = eI - \gamma' B, \\ S(t) = I(t) = R(t) = B(t) = 0 \quad \text{on} \quad \partial\Omega \quad \forall t \geq 0. \end{cases} \tag{23}$$

The model (23) has two equilibria: A trivial equilibrium $E^0 = (0,0,0,0)$ and a positive nontrivial equilibrium $E^1 = (S^*, I^*, R^*, B^*)$ with

$$I^* = \frac{K\gamma'(r' + \mu)}{e(\beta A - r' - \mu)}, \quad S^* = AI^*, \quad R^* = \frac{r}{r_1 + \mu}I^* \quad \text{and} \quad B^* = \frac{e}{\gamma'}I^*,$$

where

$$A = \frac{r' r_1 (K\gamma' + e)}{(r_1 + \mu)[e\beta + \mu(K\gamma' + e)]}.$$

It is easy to establish that E^0 is locally asymptotically stable on $\partial\Omega$. The equilibrium E^1 of the model (23) (see [11] for the methodology) is locally asymptotically stable inside Ω if $R_c > 1$ and unstable if $R_c < 1$ with

$$R_c = \frac{\gamma'(r' + \mu)}{\beta e S^* K}(K + B^*)^2.$$

The main result of this subsection is the following:

Theorem 6. *If $R_c > 1$ and $R_0 > 1$ where R_0 is given by (22), then the model (10) presents a Turing instability.*

Proof. It is obvious that if $R_c > 1$ and $R_0 > 1$, then the stable positive nontrivial equilibrium E^1 of the model (23) becomes unstable for the model (10). □

5 Optimal control problem

In this section, we proceed at the formulation and the study of solutions of the optimal control problem in order to eradicate the epidemic.

5.1 Optimal control problem formulation

A successful mitigation scheme is one which reduces cholera related deaths with minimal cost. A control scheme is assumed to be optimal if it minimizes the objective functional:

$$J(\Phi, \theta) = \int_0^T \big(L(t, \Phi(t), \theta(t))\big)dt + l(\Phi(0), \Phi(T)), \tag{24}$$

with $L : [0, T[\times X \times (L^\infty(\Omega))^3 \to] - \infty, +\infty]$ and $l : X \times X \to] - \infty, +\infty]$ functions given by

$$\begin{aligned} L(t, \Phi(t), \theta(t)) &= A(1 - \theta_2(t))\mu_1 I(., t) + B_1\theta_1(t)I(., t) + C_1\theta_1^2(t) + B_2\theta_2(t) \\ &\quad + C_2\theta_2^2(t) + B_3\theta_3(t) + C_3\theta_3^2(t), \end{aligned} \tag{25}$$

$$l(h_1, h_2) = \begin{cases} 0, & \text{if } h_1 = \Phi(0) \text{ and } h_2 = \Phi(T) \text{ ;} \\ +\infty, & \text{elsewhere,} \end{cases} \tag{26}$$

where $A, B_1, B_2, B_3, C_1, C_2, C_3$ are balancing coefficients transforming the integral into dollars expended over a finite time period T. In the expression of $L(t, \Phi(t), \theta(t))$, the first sum multiplied by A represents the cost of the deceases due at cholera and the another expressions are the costs of implementation of the three control strategies (see [22]). The quadratic expressions of control indicate the nonlinear costs which can arise to a high level of treatment. The optimal control problem is then formulated as follows.

Problem (P) *Find a pair* $(\Phi^*, \theta^*) \in C([0,T[, X) \times \Gamma$ *which minimizes the functional* (24) *in the set of all the functions* $(\Phi, \theta) \in C([0,T[, X) \times \Gamma$ *which satisfy (11).*

5.2 Existence of an optimal pair

Here, we study the existence of an optimal pair of the problem (P). Let us consider firstly the following lemma :

Lemma 3. *(i) Operator* $\mathcal{B} : \Gamma \to C(0,T,X)$ *is linear continuous and "causal".*
(ii) The functions l *and* $L(t,.,.)$, $0 \leq t \leq T$ *are lower semi-continuous and convex on* $X \times X$ *(resp.* $X \times (L^\infty(\Omega))^3$*) with values in* $\big(-\infty, +\infty\big)$*.*
(iii) For every strongly measurable function $\Phi : [0,T[\to X$ *and* $\theta : \big[0,T\big[\to (L^\infty(\Omega))^3)$*, the Hamiltonian function associated with* L*,* $H(., \Phi(.), 0)$ *is Lebesgue measurable function.*
(iv) $L(t,\Phi,\theta) \geq f(\| \theta \|_{L^1(0,T,(L^\infty(\Omega))^3)}) - g(\| \Phi \|_{C(0,T,X)})$
$\forall (t,\Phi,\theta) \in \big[0,T\big[\times X \times L^\infty(\Omega))^3$ *where:*
(a) f *is a convex nonnegative function on* $\big[0,T\big[$ *such that* $f(0) = 0$*;*
(b) g *is a nonnegative nondecreasing function on* $\big[0,T\big[$ *which is bounded on bounded sets;*
(c) $\frac{f(\tau)}{\tau} \to +\infty$ *as* $\tau \to +\infty$*;*
(d) $T[f(\frac{\tau}{T}) - g(K + c\lambda)]) - \eta c\lambda \to +\infty$ *as* $\lambda \to +\infty$*, with*

$$K = \| \mathcal{T}\Phi \|_{C(0,T,X)} + \| m \|_{C(0,T,X)},$$

and

$$c = \| \Gamma \|_{\mathcal{L}(L^1(0,T,(L^\infty(\Omega))^3),C(0,T,X))} .$$

Proof. (i) It is obvious that $\mathcal{B}$ is linear and continuous. In addition, by posing

$$(E^t(\mathcal{B}\theta))(s) = \begin{cases} (\mathcal{B}\theta)(s), & ifs \leq t; \\ 0, & \text{if } s > t, \end{cases}$$

it is easy to verify that

$$E^t(\mathcal{B}\theta) = E^t(\mathcal{B}\theta'),$$

for all $\theta, \theta' \in L^1(0,T,\Gamma)$ such that $E^t\theta = E^t\theta'$, from which it results that $\mathcal{B}$ is causal.

(ii) It is obvious that the functions l and $L(t,.,.)$, $0 \leq t \leq T$ are respectively continuous on $X \times X$ and $X \times (L^{\infty}(\Omega))^3$. For the convexity, let us consider the epigraphs of l and $L(t,.,.)$ given by:

$$\begin{aligned} epil &= \{(h_1,h_2,\alpha),(h_1,h_2) \in X \times X, \alpha \in \mathbb{R}, l(h_1,h_2) \leq \alpha\}, \\ epiL &= \{(\Phi_1,\theta_1,\alpha),(\Phi_1,\theta_1) \in X \times (L^{\infty}(\Omega))^3, \alpha \in \mathbb{R}, L(t,\Phi_1,\theta_1) \leq \alpha\}, \end{aligned}$$

Thus (see [4]), it suffices to show that $epil$ and $epiL$ are convex sets of $X \times X \times \mathbb{R}$ and $X \times (L^{\infty}(\Omega))^3 \times \mathbb{R}$, respectively. The relation (26) allows to obtain $epil = \{(\Phi(0),\Phi(T),\alpha)\}$, thus l is convex. Let (Φ_1,θ_1,α), $(\Phi_2,\theta_2,\alpha') \in epiL$ and $\lambda \in [0,1]$. A simple calculation allows to obtain

$$\begin{aligned} L(t,\lambda\Phi_1+(1-\lambda)\Phi_2,\lambda\theta_1+(1-\lambda)\theta_2) &\leq \lambda L(t,\Phi_1,\theta_1)+(1-\lambda)L(t,\Phi_2,\theta_2)+M \\ &\leq \lambda\alpha+(1-\lambda)\alpha'+M, \end{aligned}$$

with

$$M = -\lambda C_1\theta_{22}^2 + 2C_1\lambda\theta_{11}\theta_{21} - \lambda C_2\theta_{22}^2 + C_2\lambda\theta_{12}\theta_{22} - \lambda C_3\theta_{23}^2 + 2C_3\lambda\theta_{13}\theta_{23},$$

where $\theta_i = (\theta_{i1},\theta_{i2},\theta_{i3})^T, i = 1,2$. Thus,

$$\lambda(\Phi_1,\theta_1,\alpha)+(1-\lambda)(\Phi_2,\theta_2,\alpha') \in epiL,$$

i.e., $L(t,.,.)$ is convex.

(iii) It suffices to take account of the definition of the associated hamiltonian of the system (11) and (24) (see [4]).

(iv) We have

$$L(t,\Phi,\theta) \geq \min(C_1,C_2,C_3) \parallel \theta \parallel_{L^1(0,T,(L^{\infty}(\Omega))^3)} - A\mu_1 \parallel \Phi \parallel_{C(0,T,X)},$$

for all $(t,\Phi,\theta) \in [0,T[\times X \times L^{\infty}(\Omega))^3$. It suffices thus to take $g(t) = A\mu_1 t$ and $f(t) = \min(C_1,C_2,C_3)t^2$. □

The main result of this subsection is the following:

Theorem 7. ***Problem (P)*** *admits at least one solution.*

Proof. This comes from Lemma 3, which taking account of Popescu 1979 (see [20] theorem 5.1), gives of the sufficient conditions of the existence of a solution of the problem (P). □

6 Real-world application

In this section, we proceed to a real-world application in order to confirm our theoretical results. Table 1 gives the new cases of the cholera registered per region at Cameroon from January 3rd to October 2nd, 2011.

Table 1: New cases of cholera per region. Source : Department of disease control, Ministry of public health, Cameroon.

Region	Adamawa(1)	Centre (2)	East (3)	Far North (4)	Littoral (5)
Month	New cases	Nc	Nc	Nc	Nc
1	0	0	0	0	0
2	0	0	0	0	0
3	3	525	0	0	150
4	30	5	0	22	110
5	2	488	0	180	20
6	0	300	0	310	4
7	53	100	0	313	80
8	3	101	0	17	157
9	27	100	8	440	420
10	1	165	44	426	900

Region	North (6)	Northwest(7)	West (8)	South (9)	Southwest (10)
Month	New cases	Nc	Nc	Nc	Nc
1	5	0	0	0	500
2	15	4	0	25	635
3	10	0	11	7	909
4	0	0	100	25	973
5	6	105	492	25	114
6	40	3	500	0	1117
7	150	30	140	0	101
8	58	0	30	0	1759
9	775	0	27	65	1093
10	150	0	0	65	346

6.1 Numerical simulations of the state variables of the model

In this subsection, we conduct the numerical simulations of the state variables of the model (10) in the presence and in the absence of the control mechanisms, this, in taking account of the results obtained in Section 4. The new cases of the cholera per region of Table 1 correspond at term

$$f(x,t) = \beta(x,t)\frac{B(x,t)}{K + B(x,t)}S(x,t),$$

of the second equation of the model (10). The parameters values are given by: $\mu = 1/(51.5 \times 12)$ (National Institute of Statistics value), $\gamma_1 = 1.8/month$ (see [22]), $\gamma_2 = 3.6/month$ (see [22], $K = 10^6$ (see [14]), $r_1 = 1/30$ (see [14]), $\gamma = 1 month^{-1}$ (see [14]), $e = 15$ (see [7]), $\sigma = 0.001$, $\sigma_B = 0.01$, $v = 2$km/day, $\mu_1 = 0.02/month$ (see [22]), $\theta_1 = 0.6$ (see [22]), $\theta_2 = 0.9$ (see [1]), $\theta_3 = 0.01$ (see [22]). The initial and boundaries conditions are given by:

$$\begin{aligned} S(x,0) &= 1000000e^{-\frac{\sqrt{2\mu}}{\sigma}x}, \\ I(x,0) &= 0, \\ R(x,0) &= e^{-\frac{\sqrt{2(r_1+\mu)}}{\sigma}x}, \\ B(x,0) &= e^{v-\frac{\sqrt{v^2+2\gamma\sigma_B^2}}{\sigma_B^2}x} + e^{v+\frac{\sqrt{v^2+2\gamma\sigma_B^2}}{\sigma_B^2}x}, \end{aligned}$$

and $S(x,t) = I(x,t) = R(x,t) = B(x,t) = 0$ for all $(x,t) \in \partial\Omega$. It is easy starting from the parameters values to establish that the endemic equilibrium of the local model (23) is given by

$$E^1 = (150450; 141.2981; 7276.9; 2119.5)^T.$$

Thus, (22) and the expression of Rc allow to obtain: $Rc = 1.0021 > 1$ and $R0 = 0.6490 < 1$. Consequently (see Theorem 6), there is not a Turing instability. This situation is confirmed by Figures 1 which presents the evolution of the state variables in presence $((a)-(d))$ and in absence $((e)-(h))$ of the control mechanisms. Figure 1 also confirms our theoretical result on the stability of the trivial equilibrium at the boundary $\partial\Omega$ of Ω, like the existence of a nontrivial equilibrium, which here is unstable inside Ω. We can remark according to Figure 1(f), that, in absence of the control mechanisms, the infected individuals are present in all the regions, whereas in presence of the control mechanisms, Figures 1(b) and 1(c) show that the densities of the infected and of the recovery individuals are less than 1, this proves the eradication of the cholera inside the population and confirms the efficiency of the control strategies adopted.

7 Conclusion

In this paper, we have propounded a mathematical scheme permitting to model under clear assumptions, the dispersion of the individuals in a discrete or a continuous heterogeneous space. We have applied afterwards the obtained result (in the continuous case) to the study of the optimal control problem of the cholera epidemic in a heterogeneous environment with migrations. The regarded environment here is a space Ω with a boundary $\partial\Omega$ such that the individuals can move only inside Ω. In the mathematical analysis of the obtained diffusive epidemiological model, after to have showed that the solution of the proposed model is observable in the reality, we have established the existence of two equilibria belonging to a same

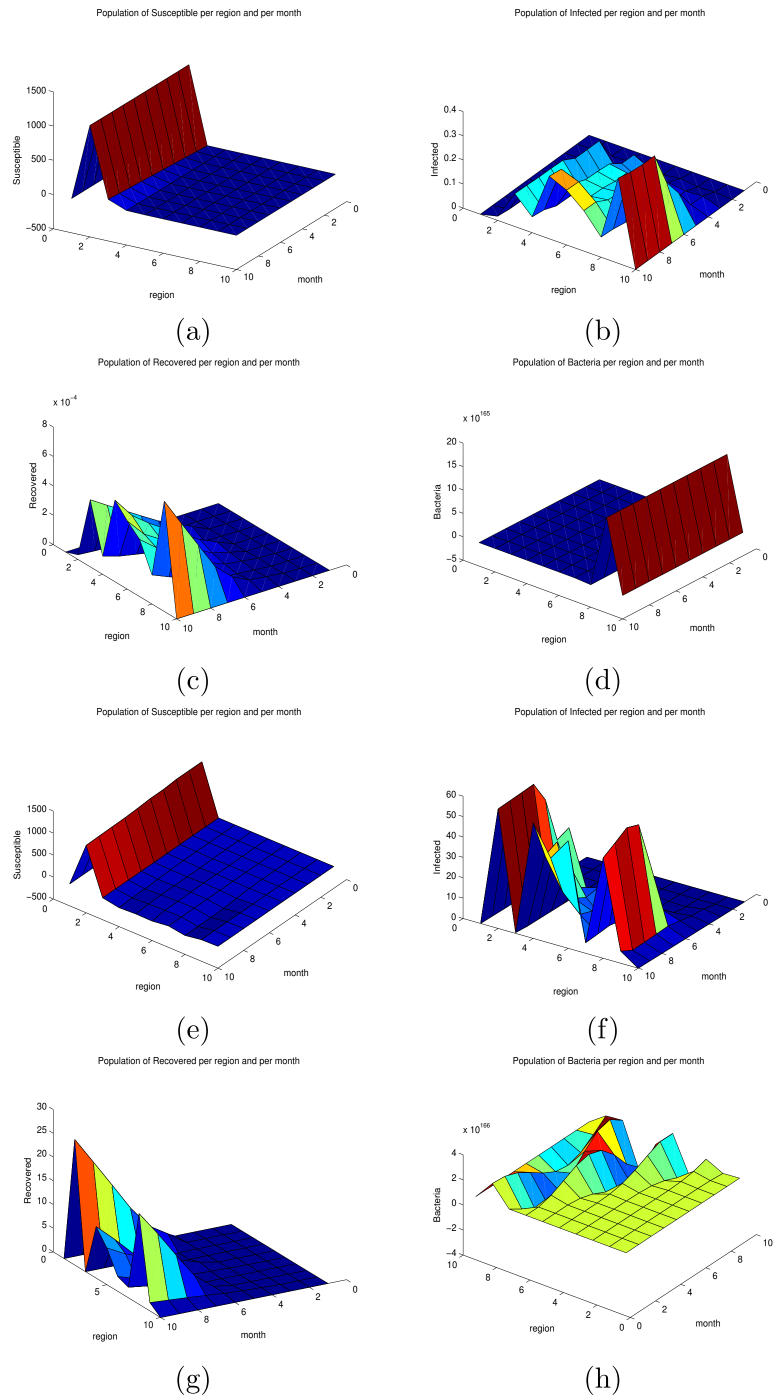

Figure 1: Dynamic of the Susceptible, Infected, Recovery and Bacteria per region and per month in presence ((a)-(d)) and in absence ((e)-(h)) of the control mechanisms.

continuum: a trivial equilibrium at boundary $\partial\Omega$ and a nontrivial equilibrium inside Ω. We have determined a threshold parameter R_0 which allows to a certain extent to show how the implementation of the controls would help alleviate the epidemic problem inside Ω. We have also determined a threshold parameter R_c, which joints to R_0, permits us to analyze Turing's instability. The mathematical optimal control problem has been formulated in order to reduce the cholera related deaths with a minimal cost, and, sufficient conditions of the existence of a solution of this problem have been given. We have applied our model to a real-world problem, by specifically applying it to the cholera epidemic that took place in Cameroon in 2011. In the real-world problem treated, we have showed that the proposed model is effective to control and to prevent a real epidemic, and, we have also justified its validity.

References

[1] A. Alexanderian, M.K. Gobberty, K. Renee Fisterz, H. Gaff, S. Lenhart and E. Schaeferk, *An age-structured model for the spread of epidemic cholera: analysis and simulation*, Nonlinear Anal. Real World Appl. **12** (2011) 3483–3498.

[2] A. Ambrosetti and A. Malchiodi, *Nonlinear analysis and semilinear elliptic problems*, Cambridge University Press, 2007.

[3] B. Aulbach and N. Van Minh, *Nonlinear semigroups and the existence and stability of solutions of semilinear nonautonomous evolution equations*, Abstr. Appl. Anal. **4** (1996) 350–380.

[4] V. Barbu and T. Precupanu, *Convexity and optimization in Banach spaces*, Springer Science+Business Media B.V., Fourth Edition, 2012.

[5] F. Brauer, *Mathematical epidemiology is not an oxymoron*, BMC Public Health **9** (Suppl. 1) (2009), S2.

[6] R.A. Cash, S.I. Music, J.P. Libonati, A.R. Schwartz and R.B. Hornick *Reponse of men to infection with vibrio cholerae*, Infect. Immun. **10** (1974) 762.

[7] C.T. Codeo, *Endemic and epidemic dynamics of cholera: the role of the aquatic reservoir,* BMC Infect. Dis. **1** (2001) 1.

[8] R.R. Colwell, *Global climate and infectious disease: the cholera paradigm*, Sci. **214** (1996) 2025–2031.

[9] J.J. Duistermaat and J.A.C. Kolk, *Distributions: theory and applications,* Springer, 2006.

[10] Y. Emvudu and E. Kokomo, *Stability analysis of cholera epidemic model of a closed population*, J. Appl. Math. Bioin. **2** (2012) 69–97.

[11] Y. Emvudu and E. Kokomo, *Mathematical analysis of cholera epidemic model with seasonality,* J. Nonlinear Syst. Appl. **4** (2013) 11–29.

[12] L.C. Evans, *Partial differential equations*, Amer. Math. Soc. **19** (1998).

[13] J. Hadamard, *Lectures on Cauchy's problem in linear partial differential equations*, Yale University Press, 1923.

[14] D.M. Hartley, J.G. Morris and D.L. Smith, *Hyperinfectivity: a critical element in the ability of V. cholerae to cause epidemics?* PLoS Med. **3** (2006).

[15] E. Kokomo and Y. Emvudu. *Mathematical modeling: proposal of a general methodology and application of this methodology to epidemiology*, Acad. J. Appl. Math. Sci. **2** (2016) 147–156.

[16] E. Kokomo and Y. Emvudu. *Mathematical analysis and numerical simulation of an age-structured model of cholera with vaccination and demographic movements,* Nonlinear Anal. Real World Appl. **45** (2019) 142–156.

[17] R. Levins, *Some demographic and genetic consequences of environmental heterogeneity for biological control,* Bull. Entomological Soc. Amer. **15** (1969) 237–240.

[18] A.W. Leung, *Nonlinear systems of partial differential equations: applications to life and physical sciences*, World Scientific Publishing Co. Pte. Ltd, 2009.

[19] J. Medlock and M. Kot, *Spreading disease: integro-differential equations old and new,* Math. Biosci. **184** (2003) 201–222.

[20] V. Popescu *Existence for an abstract control problem in banach spaces,* Numer. Funct. Anal. Optim. **1** (1979) 475–497.

[21] G. Prodi, *Eigenvalues of non-linear problems*, Springer Heidelberg Dordrecht London New York, 1974.

[22] R.L.M. Neilan, E. Schaefer, H. Gaff, K.R. Fister and S. Lenhart *Modeling optimal intervention strategies for cholera*, Bull. Math. Biol. **72** (2010) 2004–2018.

[23] L. Schwartz, *Théorie des distributions*, Herman diteurs des Sciences et des arts, 1961.

[24] A.M. Turing, *The chemical basis of morphogenesis,* Philos. Trans. R. Soc. Lond. B. **237** (1952) 37–72.

[25] S. Zheng, Nonlinear Evolution Equations, Chapman & Hall/CRC Series Monographs and Surveys in Pure and Applied Mathematics Vol. 133 (CRC, Roca Raton, 2004).