Dynamic of S-I-R-S cholera model with an Allee Effect on bacterial population

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Abstract

We formulated a generic S-I-R-S (Susceptible-Infected-Recovered-Susceptible) epidemic model of cholera that incorporate three key features: an Allee Effect on bacteria dynamic, the loss of immunity of recovered individuals and infection force to cholera regulated by the contact and logistic dose-reponse of bacteria. These assumptions are built into a simple model which yields surprisingly rich dynamics. Having three different disease-free equilibriums Q_0, Q_ρ and Q_θ, the dynamic of the model is essentially characterized by a threshold quantity $\mathscr{R}_0^0$ which represents the basic reproduction number of the disease-free equilibrium Q_0. The model supports the possibility of bi-stability, backward bifurcation and forward bifurcation. The sensibility analysis of the model and theoretical results supported by numerical simulations suggest that an efficient control strategy would be to increase the value of θ (Allee threshold bacterial population) which is equivalent to increasing unfavorable conditions for bacteria growth. These conditions are generally: regular environmental consolidation measures, compliance with hygiene rules and unfavorable climatic factors.

Key words: Cholera, Effect Allee, Disease-free equilibrium, Basic reproduction number, bi-stability.

1 Introduction

Limited access to safe water and sanitation resources is common in developing countries, leaving them vulnerable to cholera outbreaks. Cholera is an intestinal infection caused by ingesting food or water contaminated with the bacterium *V. cholerae*. If left untreated, an infected individual may become severely dehydrated and die within several days. In addition to prompt rehydration and medical treatment, proper sanitation facilities are needed to prevent infected individuals from shedding the bacteria back into the environment further fuelling the pathogen concentration and the persistence of the disease. According to the World Health

Organization (WHO), researchers have estimated that there are 1.4 to 4.3 million cases, and 28 000 to 142 000 deaths worldwide due to cholera every year [1].

Numerous mathematical models have been published to analyse cholera outbreaks in an effort to better understand the complex disease transmission and determine adequate prevention and effective control strategies [2, 3, 4, 5, 6, 7, 8, 9, 10] and [11]. These studies have certainly produced many useful results and have improved our understanding of cholera dynamics. One limitation of these models, however, is that most of them assumed that bacteria have generally linear or logistic growth. From the mathematical point of view, linear or logistic growth assumption has the advantage of simplifying the models and analysis, and facilitating the use of some well-known theory in dynamical systems.

But recently biological results require to review the dynamic of these bacteria in the mathematical models of cholera. In fact, it has been discovered that environmental aquatic bacteria such as *V. Cholerae O1* and *V. cholerae non-O1* have ability to survive to the stress caused by the variation of some environmental factors, such as temperature, pH or the lack of nutritional resources [12, 13]. The adaptation of these bacteria to their environment will lead to metabolic and phenotypic changes that will condition their survival; what can be compared to a phenomenon of dormancy. Cells are considered " viable but non-culturable " (VNC) because the main effect of this change is the loss of the ability to be cultivated on a bacteriological culture medium [14]. This dormancy state has been considered for many species of bacteria as a survival strategy in the natural environment [15, 12, 13, 16, 17]. The state change to the cultivable state is possible particularly if the factors causing stress become favorable to the development and growth of the bacterial population. This phenomenon implies to reconsider the thinking concerning the survival of pathogenic bacteria scattered into the environment and its dynamics in the aquatic ecosystem. This cell viability (VNC) is considered as a possible hypothesis at the origin of " disappearance " of the bacteria of the aquatic ecosystem during the colder months.

Such filed observations underline the limitation of some current mathematical cholera models and imply that mathematical model of cholera must consider these environmental factors which are responsible of resurgence and propagation of this epidemic. For these reason, we recently suggested a mathematical model of cholera which investigate impacts of environmental factors on the dynamical transmission of cholera within a human community. This model incorporates the virulence of bacteria and the commensalism relationship between bacteria and the aquatic reservoirs of the bacteria [9]. We found that the aquatic reservoirs are playing a significant role among the factors explaining endemicity of these disease. But the model had nine state variables with four state variables for bacteria population.

We suggest to simplify this model by keeping environmental factors. On mathematical view, environmental factors can be considered like extinction force on population of bacteria. This extinction force is able to eliminate a certain maximal value θ of population of bacteria. This value θ, is also considered like the critical concentration bacteria under which population of bacteria will go to the extinction and upper which population of bacteria will grow to the saturation value ρ. A such dynamic is known on the name of "*Allee Effect*". The Allee effect, is a biological phenomenon named after W. C. Allee, describes a positive relation between population density and the per capita growth rate of species. In the presence of the Allee effect, there is a decrease in population growth rate at low population densities. Species under the Allee effect do not thrive at low population densities. However, the effect usually saturates or disappears as populations get larger.

Environmental factors greatly influence the growth of vibrio in nature. They are generally responsible of resurgence, of propagation and disappearance of cholera epidemic. Reason why we will consider a bacterial dynamics with Allee effect coupled with a S-I-R-S model. To identify degree of influence for each model parameters we will make sensibility analysis of

model. We will compute the different disease-free equilibrium points of system. The local stability conditions and attraction domain of these fixed points will be determined. We will analyze the basic reproduction number $\mathscr{R}_0^0$ and $\mathscr{R}_0(\mathrm{Q}_\rho)$ of the disease-free equilibrium point Q_0 and Q_ρ respectively. This analysis will permit us to deduce that the phenomena of backward bifurcation and forward bifurcation could be realized at $\mathscr{R}_0^0 = 1$ at the neighborhood of Q_0. But at the neighborhood of Q_ρ only forward bifurcation is realized at $\mathscr{R}_0^0 = 1$

The rest of the paper is organized as follows. After the formulation of the model in Section 2, we present its quantitative and qualitative analysis supported by numerical simulations in Section 3. The last section is devoted to concluding remarks on how our work fits in the literature and on possible extensions.

2 The model

2.1 Model construction

The proposed model classifies the human population according to their disease status, namely: susceptible individuals S, individuals infected with cholera I and recovered individuals R. Thus, the total human population at time t, $N(t)$ is given by $N(t) = S(t) + I(t) + R(t)$. The population of bacteria is denoted by B. Susceptible individuals are recruited through birth and immigration at rate Λ. Infection is regulated by the contact rate β and depends on the number of bacteria through the logistic dose-response $\frac{B}{K+B}$, where K is the concentration of bacteria that yields 50% chance for a susceptible individual to catch cholera [3]. The source of infection is through oral ingestion of faecal contaminated water or food.

Once infected, individuals can recover from the disease at rate α. As suggested by many studies [18, 19], recovered individuals may only have partial immunity. Then, recovered human can loss their immunity and will return to the class of susceptible individuals at rate γ. The parameters μ and d are the natural human mortality and cholera induced death rate of infected humans respectively. Infected individuals contribute to the concentration of vibrios at rate δ. For the population of bacteria, we assume that the reproduction from mixing among bacteria that includes the Allee effect, limited resources and natural mortality is:

$$\begin{aligned} f(B) &= -rB^3 + r(\rho+\theta)B^2 - r\rho\theta B, \\ &= rB(B-\theta)(\rho-B), \end{aligned} \tag{1}$$

where $r(\rho+\theta)B^2$ is the reproduction of bacteria, the term $-rB^3$ is intra-specific competition due to limited resource; and the term $-r\rho\theta B$ is the mortality of bacteria.

The structure of the model is depicted in Fig. 1. The dashed arrow from I to B indicates contamination of the environment by humans and the second dashed arrow indicates influence of contaminated environment on infection force.

The dynamics of cholera epidemic can be described by the following system of non autonomous differential equations with the Allee effect:

$$\begin{cases} \dot{S} &= \Lambda - (\lambda+\mu)S + \gamma R, \\ \dot{I} &= \lambda S - (\mu+d+\alpha)I, \\ \dot{R} &= \alpha I - (\mu+\gamma)R, \\ \dot{B} &= rB(B-\theta)(\rho-B) + \delta I, \end{cases} \tag{2}$$

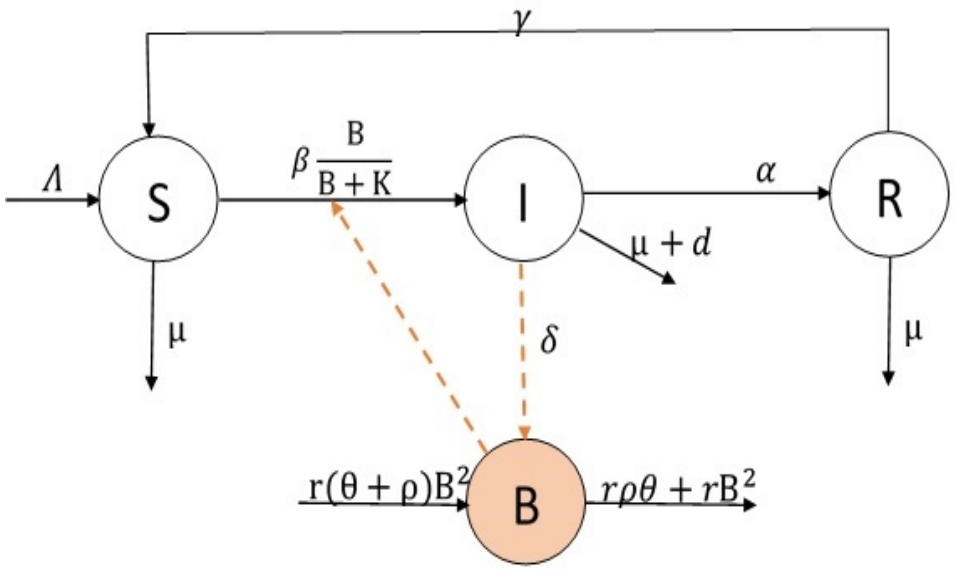


Figure 1: Graphical Representation

where $0 < \theta < \rho$ and

$$\lambda = \beta \frac{B}{K+B}, \tag{3}$$

In all the next, one notes parameter $\omega = \mu + d + \alpha$. The parameter values used for numerical simulation are given in Tab. 1.

Definition	**Symbole**	**Estimated**	**Source**
Recruitment rate	Λ	10 day^{-1}	Assumed
Bacteria ingestion rate	β	0.0001 person^{-1}day^{-1}	Assumed
Human population death rate	μ	0.0104 day^{-1}	[20]
Bacteria shedding rate	δ	70 cells/(ml day)	[21]
Half saturation constant	K	10^7cell/ml	Assumed
Cholera related death	d	0,6 year^{-1}	[22]
Loss of immunity rate	γ	0.01 day^{-1}	[23]
Recovery rate	α	0.045 day^{-1}	[24]
Growth rate of Vibrios	r	1e-18 day^{-1}	Assumed
Carrying capacity bacterial population	ρ	1e+8	Assumed
Allee threshold bacterial population	θ	1e+6	Assumed

Table 1: Numerical values for the parameters of model system (2)

2.2 Sensibility analysis

We carried out the sensitivity analysis to determine the model's robustness to parameter values. That is to help us identifying the parameters that are most influential in determining disease dynamics [25]. A Latin Hypercute Sampling (LHS) scheme [26, 27] samples 1000 values for each input parameter using a uniform distribution over the range of biologically realistic values, listed in Tab. 1 with descriptions and references. Using model system (2) and a time period of 7000 day, 1000 model simulations are performed by randomly pairing sampled values for all LHS parameters. Four outcome measures are calculated for each run:

the maximum and total size of state variable over the model's time span, Partial Rank Correlation Coefficients (PRCC) and corresponding p-values are computed. An output is assumed sensitive to an input if the corresponding PRCC is less than -0.50 or greater than $+0.50$, and the corresponding p-value is less than 5%.

PRCCs and significance					
Parameters	Range	S	I	R	B
Λ	$[1-300]$	0.8970**	0.0968*	0.0171	-0.0332
β	$[0.001-0.999]$	-0.9580*	-0.2359**	0.1221**	-0.1702**
δ	$[1-1000]$	-0.8934**	-0.0545	0.0885	-0.1173*
μ	$[0.001-0.999]$	-0.0718	-0.0255	0.0270	-0.0818
d	$[0.001-0.999]$	0.0290	0.0432	-0.0676	-0.0462
r	$[0.001-0.999]$	-0.0282	-0.0180	0.0395	0.0291
γ	$[0.001-0.999]$	-0.0388	0.0147	0.0577	-0.0106
α	$[0.001-0.999]$	0.1010	0.0680	0.0530	0.0948
K	$[10^4-10^{17}]$	0.0050	0.0335	0.0092	-0.0213
ρ	$[10^5-10^{20}]$	-0.0723	-0.1149*	0.0561	0.6220**
θ	$[10^3-10^{15}]$	0.0210	0.0628	0.0473	0.5029*
*: p-value < 0.01,**: p-value < 0.001					

Table 2: Table of parameters PRCCs with model's variables

The results are presented in Tab. 2. Each row in the table contains the coefficients for the corresponding parameter against the variables in columns. A positive PRCC value indicates a parameter whose increase causes an increase in the corresponding output variable, while on the contrary, a negative PRCC value indicates a parameter whose increase leads to a decrease in the corresponding output variable.nAccording to the result obtained in Tab.2, the parameters Λ, β, δ, θ and ρ should significantly affect state variables of (2). The parameters Λ is not related to transmission of disease. Influence of β suggest to sensitize population to avoid getting in touch with bacteria. Influence θ and ρ suggest to intensify sanitation campaigns of risk areas and reservoirs of *V. Cholera*.

3 Mathematical analysis

3.1 Basic properties

Herein, we study the basic properties of the solutions of model system (2). These basic properties concern generally existence, positivity and boundary of solutions. They are useful to show that model system (2) is well posed mathematically and epidemiologically. They are also very useful in the proofs of stability results.

3.1.1 Positivity and boundedness of solutions

Obviously, model system (2) which is a C^∞ differential system, admits a unique maximal solution for any associated Cauchy problem.

Theorem 3.1 *: The region Ω defined by:*

$$\Omega = \Omega_H \times \Omega_B, \tag{4}$$

where

$$\Omega_H = \left\{ (S,I,R) \in \mathbb{R}^3_+,\ N(t) \leq \frac{\Lambda}{\mu} \right\} \qquad \textit{and} \qquad \Omega_B = \left\{ B \in \mathbb{R}_+,\ B(t) \leq \frac{r\rho^2\mu(\rho-\theta)+\delta\Lambda}{r\rho\mu(\rho-\theta)} \right\},$$

is positively invariant and attracting for model system (2).

Proof: The proof is provided in two steps.

Step 1 We show that for any initial condition $(t_0 = 0,\ X_0 = (S(0), I(0), R(0), B(0)) \in (\mathbb{R}_+^*)^4)$, maximal solution $([0, T[,\ X = (S(t), I(t), R(t), B(t)))$ of the Cauchy problem associated to system (2) is non negative.

Let $\tilde{T} = \sup\left\{\tilde{t} \in [0; T[,\ (S(t),\ I(t),\ R(t),\ B(t)) \in (\mathbb{R}_+^*)^4\right\}$. Now we are going to show that $\tilde{T} = T$. Suppose that $\tilde{T} < T$. At least one of the following conditions is satisfy $S(\tilde{T}) = 0$, $I(\tilde{T}) = 0$, $R(\tilde{T}) = 0$ and $B(\tilde{T}) = 0$. Suppose $S(\tilde{T}) = 0$, then from the first equation of model system (2), one has

$$\frac{d}{dt}\left(Se^{\int_0^t(\lambda(r)+\mu)dr}\right) = (\Lambda + \gamma R)e^{\int_0^t(\lambda(r)+\mu)dr}, \quad \forall t \in [0; \tilde{T}[\tag{5}$$

This implies that

$$\frac{d}{dt}\left(Se^{\int_0^t(\lambda(r)+\mu)dr}\right) > 0, \quad \forall t \in [0; \tilde{T}[\tag{6}$$

Integrating Eq. (6) from 0 to $\tilde{T}$ yields:

$$S(\tilde{T}) \geq S(0)e^{-\int_0^{\tilde{T}}(\lambda(r)+\mu)dr} > 0 \tag{7}$$

Similarly, one can show that $I(\tilde{T}) > 0$, $R(\tilde{T}) > 0$, and $B(\tilde{T}) > 0$. This is a contradiction. Then, $\tilde{T} = T$ and consequently the maximal solution $(S(t), I(t), R(t), B(t))$ of the Cauchy problem associated to model system (2) is non negative.

Step 2 We prove that the total population of humans and bacteria satisfies the boundedness property. We first split model system (2) into two parts, the human population (i.e. $S(t)$, $I(t)$ and $R(t)$) and the pathogen population (i.e. $B(t)$). Let $N = S + I + R$ and using equation of model system (2), one can deduce that

$$\dot{N} = \Lambda - \mu N - dI \leq \Lambda - \mu N.$$

Thus,

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu}\right)e^{-\mu t},$$

where $N(0)$ represents the initial value of $N(t)$. The lower limit comes naturally from the fact that the model variables are non-negative ($t \in [0, T[$) since they monitor human populations. Thus, $0 \leq N(t) \leq \dfrac{\Lambda}{\mu}$ whenever $0 \leq N(0) \leq \dfrac{\Lambda}{\mu}$.

Suppose $0 \leq N(0) \leq \dfrac{\Lambda}{\mu}$, from the last equation of model system (2) and using the fact that $I(t) \leq \Lambda/\mu$ for all $t \geq 0$ one has:

$$\dot{B} \leq f(B) + \frac{\delta\Lambda}{\mu}, \tag{8}$$

where $f(B) = rB(B - \theta)(\rho - B)$. Note that $\lim\limits_{B \to +\infty} f(B) = -\infty$ and $f(B)$ is a decreasing in $[\rho; +\infty[$. The equation of tangent of $f(B)$ at $B = \rho$ is given by $y(B) = -r\rho(\rho - \theta)B + r\rho^2(\rho - \theta)$. It follows that for $B > \rho$ we have:

$$\dot{B} \leq r\rho^2(\rho - \theta) + \frac{\delta\Lambda}{\mu} - r\rho(\rho - \theta)B.$$

Integrating the above differential inequality yields

$$0 \leq B(t) \leq \frac{r\rho^2\mu(\rho-\theta)+\delta\Lambda}{r\rho\mu(\rho-\theta)} + \left(B(0) - \frac{r\rho^2\mu(\rho-\theta)+\delta\Lambda}{r\rho\mu(\rho-\theta)}\right) e^{-r\rho(\rho-\theta)t},$$

where $B(0)$ is the initial condition of $B(t)$. Thus, as $t \to +\infty$, one has

$$B(t) \leq \frac{r\rho^2\mu(\rho-\theta)+\delta\Lambda}{r\rho\mu(\rho-\theta)}.$$

Since each maximal solution of the Cauchy problem associated to (2) is positive and bounded, therefore each solution of (2) is global.,

Combining **Step 1** and **Step 2**, Theorem 3.1 follows from the classical theory of dynamical systems. This completes the proof. □

Thus, model system (2) is mathematically and epidemiologically well-posed and it is sufficient to consider the dynamics of the flow generated by model system (2) in Ω.

3.1.2 Positively invariant set

The study of the dynamics of system (2) requires the introduction of the following important sets.

Let $\varepsilon \in]0;\theta[$ and $B_m = \frac{r\rho^2\mu(\rho-\theta)+\delta\Lambda}{r\rho\mu(\rho-\theta)}$. One notes:

$$\Omega_0 = \{(S,I,R,B) \in \Omega : 0 < B < \theta - \varepsilon\}\ ,\ \Omega_{\theta-\varepsilon} = \{(S,I,R,B) \in \Omega : \theta - \varepsilon < B < B_m\}$$

$$\Omega_\theta = \{(S,I,R,B) \in \Omega :\ \theta \leq B(t) \leq B_m\} \text{ and } \Omega_\rho = \{(S,I,R,B) \in \Omega :\ \rho \leq B(t) \leq B_m\}$$

Herein, we present some results which will be useful for investigation of the dynamics system (2).

Lemma 3.1 *The sets Ω_θ and Ω_ρ are positively invariant for the model system (2).*

Proof: To proof the result of lemma 3.1, we just consider the fact that $\dot{B} \geq \delta I \geq 0$ for all value of $B \in [\theta;\rho]$. This means that every trajectory of B beginning in $[\theta;\rho]$ will grow and cross the value ρ and remain in $[\rho;B_m]$. It would be maintained on the value ρ if $I = 0$.

□

Lemma 3.2 *The set Ω_ρ is a compact attractor for the model system (2).*

Proof: The proof of Lemma 3.2 is essentially based on the fact that Ω_ρ is a invariant set and also on the fact that for every solution $X(t)$ of model system (2) associated to the initial condition $X(0) = (S(0),I(0),R(0),B(0)) \in \Omega_\theta$ we have $\lim_{t \longrightarrow +\infty} dist(X(t),\Omega_\rho) = 0$. Thus, Ω_ρ is a attractor and his attraction domain contains Ω_θ. □

3.2 Existence and stability of equilibrium

3.2.1 Disease-free equilibrium

Model system (2) has tree disease-free equilibriums obtained by setting the right-hand side of equations in model system (2) to zero with $I = 0$.

$$\mathrm{Q}_0 = (S_0, 0, 0, 0), \qquad \mathrm{Q}_\theta = (S_\theta, 0, 0, \theta) \qquad \text{and} \qquad \mathrm{Q}_\rho = (S_\rho, 0, 0, \rho), \tag{9}$$

where

$$S_0 = \frac{\Lambda}{\mu}, \quad S_\theta = \frac{\Lambda(\theta + K)}{\beta\theta + \mu(\theta + K)} \text{ and } S_\rho = \frac{\Lambda(\rho + K)}{\beta\rho + \mu(\rho + K)}$$

Since the vibrio are aboriginal bacteria in the environment [28], it is consequently difficult to entirely eradicate them in environment. So that disease-free equilibrium Q_0, which is ideal state, corresponds in reality to a situation where concentration of bacteria in environment is very low to generate an epidemic. Thus state Q_0 correspond in reality to a disease-free and bacteria-free environment. The states Q_θ and Q_ρ are the disease-free equilibriums associated to Allee threshold and carrying capacity of bacteria respectively.

3.2.2 Stability of equilibrium and Threshold quantities

The local stability of disease-free equilibriums of model system (2) is summarized in the following proposition.

Proposition 3.1 *Let*

$$\mathscr{R}_0^0 = \frac{\beta\Lambda\delta}{Kr\rho\theta\mu(\mu + d + \alpha)}, \tag{10}$$

and

$$\mathscr{R}_0^\rho = \frac{\beta}{[\mu(\rho + K) + \beta\rho](\mu + d + \alpha)} \left[\frac{\alpha\rho\gamma}{\mu + \gamma} + \frac{K\Lambda\delta}{(K + \rho)r\rho(\rho - \theta)}\right]. \tag{11}$$

For the dynamical system (2),

(i) *If $\mathscr{R}_0^0 < 1$, the disease-free equilibrium Q_0 is locally stable.*

(ii) *If $\mathscr{R}_0^\rho < 1$, the disease-free equilibrium Q_ρ is locally stable.*

(iii) *The disease-free equilibrium Q_θ is always unstable.*

To prove Proposition 3.1, we will use the following lemma of Kamgang J.C. and Sallet in ([29]):

Lemma 3.3 *Let M be a square Metzler matrix written in block form $M = \begin{bmatrix} \mathscr{A} & \mathscr{B} \\ \mathscr{C} & \mathscr{D} \end{bmatrix}$ where $\mathscr{A}$ and $\mathscr{D}$ are square matrices. Then, the matrix M is Metzler stable if and only if matrices $\mathscr{A}$ and $\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B}$ (or $\mathscr{D}$ and $\mathscr{A} - \mathscr{B}\mathscr{D}^{-1}\mathscr{C}$) are Metzler stable.*

Let $\mathrm{Q}_x = (S_x, 0, 0, B_x)$ any disease-free equilibrium. The jacobian of system (2) at the point Q_x is denoted by the following matrix $J(\mathrm{Q}_x)$:

$$J(\mathrm{Q}_x) = \begin{bmatrix} -\mu - \frac{\beta B_x}{B_x + K} & 0 & \gamma & -\frac{\beta S_x K}{(K + B_x)^2} \\ \frac{\beta B_x}{B_x + K} & -\omega & 0 & \frac{\beta S_x K}{(K + B_x)^2} \\ 0 & \alpha & -(\mu + \gamma) & 0 \\ 0 & \delta & 0 & -L_x \end{bmatrix}$$

where $L_x = r\theta\rho - 2r(\theta+\rho)B_x + 3rB_x^2$ and $\omega = \mu + d + \alpha$. Using lemma 3.3, matrix $J(\mathrm{Q_x})$ matrix can be express in the form of the matrix M (in lemma 3.3) with:

$$\mathscr{A} = \begin{bmatrix} -\mu - \frac{\beta B_x}{B_x+K} & 0 \\ \frac{\beta B_x}{B_x+K} & -\omega \end{bmatrix}, \ \mathscr{B} = \begin{bmatrix} \gamma & -\frac{\beta S_x K}{(K+B_x)^2} \\ 0 & \frac{\beta S_x K}{(K+B_x)^2} \end{bmatrix}, \ \mathscr{C} = \begin{bmatrix} 0 & \alpha \\ 0 & \delta \end{bmatrix}$$

$$\text{and } \mathscr{D} = \begin{bmatrix} -(\mu+\gamma) & 0 \\ 0 & -L_x \end{bmatrix}.$$

Obviously the matrix $\mathscr{A}$ is Metzler stable matrix. A simple calculation gives:

$$(\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_0} = \begin{bmatrix} -(\mu+\gamma) & \frac{\beta S_0 \alpha}{K\omega} \\ 0 & -r\theta\rho + \frac{\beta S_0 \delta}{K\omega} \end{bmatrix},$$

$$(\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_\rho} = \begin{bmatrix} -(\mu+\gamma) + \frac{\alpha\gamma\beta\rho}{\omega[\beta\rho+\mu(\rho+K)]} & \frac{\beta S_\rho K\alpha\mu}{(K+\rho)\omega[\beta\rho+\mu(\rho+K)]} \\ \frac{\delta\gamma\beta\rho}{\omega[\beta\rho+\mu(\rho+K)]} & -r(\rho-\theta)\rho + \frac{\beta S_\rho K\delta\mu}{(K+\rho)\omega[\beta\rho+\mu(\rho+K)]} \end{bmatrix},$$

and

$$(\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_\theta} = \begin{bmatrix} -(\mu+\gamma) + \frac{\alpha\gamma\beta\theta}{\omega[\beta\theta+\mu(\theta+K)]} & \frac{\beta S_\theta K\alpha\mu}{(K+\theta)\omega[\beta\theta+\mu(\theta+K)]} \\ \frac{\delta\gamma\beta\theta}{\omega[\beta\theta+\mu(\theta+K)]} & r(\rho-\theta)\theta + \frac{\beta S_\theta K\delta\mu}{(K+\theta)\omega[\beta\theta+\mu(\theta+K)]} \end{bmatrix}.$$

Thus, the matrix $(\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_0}$ is stable if and only if:

$$\begin{cases} tr((\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_0}) < 0 & \Longleftrightarrow \frac{\beta S_0 \delta}{K\omega[r\theta\rho+\mu+\gamma]} < 1 \\ Det((\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_0}) > 0 & \Longleftrightarrow \frac{\beta S_0 \delta}{K\omega r\theta\rho} < 1 \end{cases} \tag{12}$$

So that, $(\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_0}$ is Metzler stable matrix when:

$$\mathscr{R}_0^0 = \frac{\beta S_0 \delta}{Kr\theta\rho(\mu+d+\alpha)} < 1 \tag{13}$$

Similarly we can easily prove that the matrix $(\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_\rho}$ is Metzler stable matrix if:

$$\mathscr{R}_0^\rho = \frac{\beta}{[\mu(\rho+K)+\beta\rho](\mu+d+\alpha)}\left[\frac{\alpha\rho\gamma}{\mu+\gamma} + \frac{K\Lambda\delta}{(K+\rho)r\rho(\rho-\theta)}\right] < 1. \tag{14}$$

For the matrix $(\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_\theta}$, the condition $det((\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_\theta}) > 0$ gives

$$\frac{(\mu+\gamma)[\beta\theta+\mu(\theta+K)]}{\alpha\gamma\beta\theta} + \frac{S_\theta K\delta(\mu+\gamma)\mu(\theta+K)}{r\rho(\rho-\theta)\alpha\gamma\theta} < 1. \tag{15}$$

Also, the condition $tr((\mathscr{D} - \mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{\mathrm{Q_x}=\mathrm{Q}_\theta}) < 0$ gives

$$\frac{\alpha\gamma\beta\theta}{(\mu+\gamma)[\beta\theta+\mu(\theta+K)]} + \frac{r\theta(\rho-\theta)}{\mu+\gamma} + \frac{\beta S_\theta K\delta\mu}{(K+\theta)\omega[\beta\theta+\mu(\theta+K)]} < 1, \tag{16}$$

which is a contradictory to the condition $det((\mathscr{D}-\mathscr{C}\mathscr{A}^{-1}\mathscr{B})|_{Q_x=Q_\theta})>0$. This concludes the proof.

□

We are now interested to the globally asymptotically stable of the disease and bacteria free equilibrium point Q_0. Following Kamgang and Sallet [30], we write model system (2) in the following form:

$$\begin{cases} \dot{x}_s = A_1(x)(x_s - x_s^0) + A_{12}(x)x_i, \\ \dot{x}_i = A_2 x_i, \end{cases} \tag{17}$$

where $x_s = (S,R)^T$ represents susceptible and recovered individuals, $x_i = (I,B)^T$ represents the infectious and population of bacteria. $x_s^0 = (S_0,0)$ is the non zero component of the disease-free equilibrium, $x = (x_s,x_i)^T$,

$$A_1(x) = \begin{bmatrix} -(\mu+\lambda) & \gamma \\ 0 & -(\gamma+\mu) \end{bmatrix},\ A_{12}(x) = \begin{bmatrix} 0 & -\frac{\beta S_0}{B+K} \\ \alpha & 0 \end{bmatrix} \text{ and } A_2(x) = \begin{bmatrix} -\omega & \frac{\beta S}{B+K} \\ \delta & r(B-\theta)(\rho-B) \end{bmatrix}.$$

The conditions $H_1 - H_5$ below must be met to guarantee the global asymptotic stability (GAS) of Q_0.

H_1**:** Model system (17) is defined on a positively invariant set $\mathscr{D}$ of the nonnegative orthant. Model system (17) is dissipative on $\mathscr{D}$.

H_2**:** The sub-system $\dot{x}_s = A_1(x_s,0)(x_s - x_s^0)$ is globally asymptotically stable at the equilibrium x_s^0 on the canonical projection of $\mathscr{D}$ on $\mathbb{R}^2_+$.

H_3**:** The matrix $A_2(x)$ is Metzler (A Metzler matrix is a matrix with off-diagonal entries non-negative) and irreducible for any given $x \in \mathscr{D}$.

H_4**:** There exists an upper-bound matrix $\overline{A_2}$ for $\mathscr{M} = \{A_2(x) | x \in \mathscr{D}\}$ with the property that either: $\overline{A_2} \notin \mathscr{M}$ or if $\overline{A_2} \in \mathscr{M}$ then for any $x \in \mathscr{D}$ such that $\overline{A_2} = A_2(x)$, $x \in \mathbb{R}^2_+ \times \{0\}$.

H_5**:** $\rho(\overline{A_2}) < 0$ is satisfied. Where $\rho(\overline{A_2}) < 0$ denotes the largest real part of the eigenvalues of $\overline{A_2}$.

If conditions $H_1 - H_5$ are satisfied, then Q_0 is globally asymptotically stable in $\mathscr{D}$.

The result of Kamgang-Sallet approach [30] uses the algebraic structure of model system (17), namely the fact that $A_1(x)$ and $A_2(x)$ are Metzler matrices. Since in the said approach the matrix $A_2(x)$ is required to be irreducible, we further restrict the domain of the system to:

$$\mathscr{D} = \{(x_s,x_i) \in \Omega, x_s \neq 0\}.$$

The set $\mathscr{D}$ is positively invariant because only the initial point of any trajectory can have $x_s = 0$. Therefore, we restrict the domain of system (17) to $\mathscr{D}$ where $A_2(x)$ irreducible. Thus, one has that

$$A_2(x) \text{ is Metzler and irreducible for all } x \in \mathscr{D}.$$

The sub-system $\dot{x}_s = A_1(x_s,0)(x_s - x_s^0)$ is equivalent to:

$$\begin{cases} \dot{S} = \Lambda + \gamma R - \mu S, \\ \dot{R} = -(\delta+\mu)R. \end{cases} \tag{18}$$

Resolving the above equations and taking the limit of solutions when t go to infinity yields:

$$\lim_{t \longrightarrow +\infty} S(t) = \frac{\Lambda}{\mu} \quad \text{and} \quad \lim_{t \longrightarrow +\infty} R(t) = 0.$$

Therefore, $x_s^0 = (S_0, 0)$ is a globally asymptotically stable equilibrium of the reduced system (18) on the sub-domain $\mathscr{D}$. Then, the hypothesis H_2 is satisfied.

Let $\varepsilon \in]0;\theta[$, since $\max_{B\in[0;\theta-\varepsilon]}\{r(B-\theta)(\rho-B)\} = -r\varepsilon(\rho-\theta) - r\varepsilon^2$ we have the following upper-bound matrix of $A_2(x)$ in $\Omega_0 \subsetneq \Omega$

$$\overline{A_2} = \begin{bmatrix} -\omega & \beta\frac{S_0}{K} \\ \delta & -r\varepsilon(\rho-\theta) - r\varepsilon^2 \end{bmatrix}.$$

Using Kamgang and Sallet's result [30], the sub-matrix $\overline{A_2}$ is a Metzler stable matrix if:

$$\mathscr{R}_0^0 \leq \xi, \tag{19}$$

where

$$\xi = 1 - \frac{\theta\rho - \varepsilon(\rho-\theta)}{\theta\rho} < 1.$$

We can now apply Theorem 4.3 in Kamgang and Sallet [30] and conclude that under the condition (19) the disease-free equilibrium $(x_s^0; 0)$ of model system (2) is globally asymptotically stable in Ω_0. We have established the following result for the global stability of the DFE Q_0.

Theorem 3.2 *Let $\varepsilon \in]0;\theta[$, if $\mathscr{R}_0^0 < \xi < 1$ then the disease-free equilibrium point Q_0 of model system (2) is globally asymptotically stable in the domain Ω_0 and unstable if $\mathscr{R}_0^0 > 1$. However, when $\xi < \mathscr{R}_0^0 < 1$ the backward bifurcation phenomenon may occurs in Ω_0, i.e. the DFE Q_0, may coexists with two endemic equilibrium, one asymptotically stable and one unstable.*

The Fig. 2 is an illustration of Theorem 3.2, showing the stability of the disease-free equilibrium of model system (2) when initial conditions are taken in the basin of attraction of Q_0 and $\mathscr{R}_0^0 < \xi < 1$. So, when $\Lambda = 10$, $\beta = 0.0001$, $\varepsilon = 50000$ (so that $\theta - \varepsilon = 9.5 \times 10^5$) and all other parameters are as in Tab. 1 we have $\mathscr{R}_0^0 = 0.0103$ and $\xi = 0.0495$. Under these conditions, when various initial condition are chosen in attraction domain of Q_0, it is seen on Fig. 2 that the disease disappears.

The backward bifurcation phenomenon is illustrated by the Fig. 3 where are presented time series of model system (2) when $\Lambda = 50$, $\beta = 0.0015$, $\theta = 10^6$ (so that $\theta - \varepsilon = 9.5 \times 10^5$) and $\varepsilon = 50000$ (so $\mathscr{R}_0^0 = 0.7702$ and $\xi = 0.0495$). It clearly appears that $\xi \leq \mathscr{R}_0^0 < 1$. The epidemiological significance of the phenomenon of backward bifurcation is that the classical requirement of $\xi \leq \mathscr{R}_0^0 < 1$ is, although necessary, no longer sufficient for disease eradication when initial condition are taken in attraction domain of Q_0. In such a scenario, disease elimination would depend of various initial sizes of the population (state variables) chosen Ω_0. That is, the presence of backward bifurcation in the cholera transmission (2) suggests that the feasibility of controlling cholera epidemic when $\xi \leq \mathscr{R}_0^0 < 1$ always be dependent on the initial sizes of the population even if the are chosen in Ω_0. To illustrate this situation, model system (2) was simulated for various initial condition $(S(0), I(0), R(0), B(0))$ taken firstly in the domain : $\mathscr{D}_1 =]0;50000]\times]0;10]\times]0;50] \times \{2\times10^5, 3\times10^5, 4\times10^5, 5\times10^5\}$ and secondly for various initial condition $(S(0), I(0), R(0), B(0))$ taken in the domain $\mathscr{D}_2 =]0;50000]\times]0;10]\times]0;50] \times \{7.5\times10^5, 8\times10^5, 9\times10^5, 9.5\times10^5\}$. As is presented in Fig. 3, cholera epidemic disappear in the first case while in the second case disease and bacteria persist in environment.

In order to derive an expression for the region of stability of the boundary equilibrium Q_ρ we measure the capacity of infectious to invade and persist in a human population at the in the neighborhood of Q_ρ. Applying the methods in van den Driessche and Watmough at equilibrium Q_ρ [31], we find the basic reproduction number of infectious in a population model system (2) is (see Appendix A for details):

$$\mathscr{R}_0(Q_\rho) = \frac{\beta\Lambda K\delta}{[\beta\rho + \mu(\rho+K)](K+\rho)\omega r\rho(\rho-\theta)} \tag{20}$$

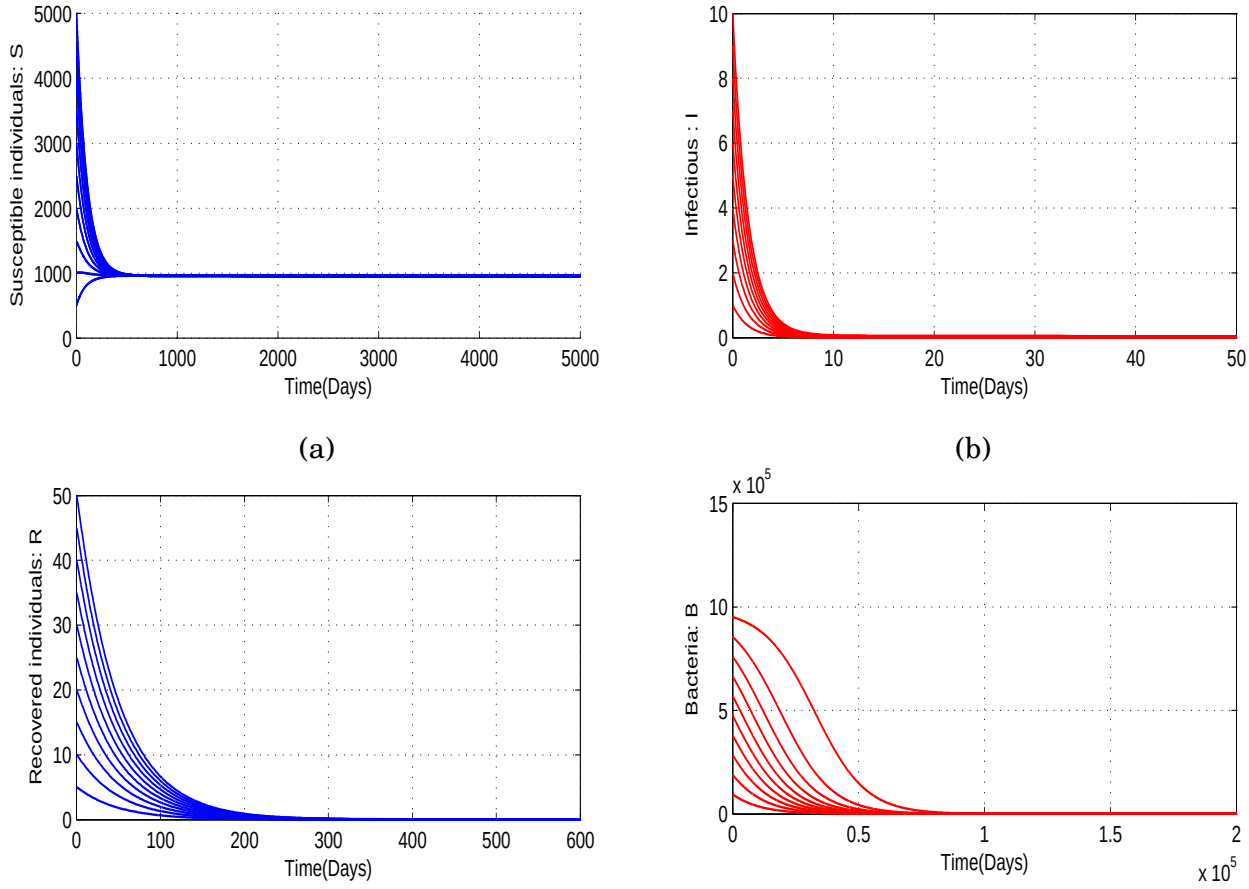


Figure 2: Simulation of model system (2) when $\Lambda = 10$, $\beta = 0.0001$ and $\varepsilon = 50000$ (so that $\theta - \varepsilon = 9.5 \times 10^5$, $\mathscr{R}_0^0 = 0.0103$ and $\xi = 0.0495$) using various initial conditions chosen in attraction domain of Q_0. All other parameters are as in Tab. 1

This formalism permits the derivation of a threshold condition for endemicity of cholera epidemic in population where model system (2) is at equilibrium Q_ρ.

The proposition 3.2 below expresses this result in terms of stability for equilibrium point Q_ρ.

Proposition 3.2 *The equilibrium point* Q_ρ *of model system (2) is stable if* $\mathscr{R}_0(\mathrm{Q}_\rho) < 1$ *and unstable if* $\mathscr{R}_0(\mathrm{Q}_\rho) > 1$.

The following proposition give relationship between stability of Q_0 and of Q_ρ.

Proposition 3.3 *Let* $0 < \varepsilon < \theta$, *if* $\mathscr{R}_0^0 < \xi$ *then* $\mathscr{R}_0(\mathrm{Q}_\rho) < 1$.

Proof: Let $0 < \varepsilon < \theta$,

$$\begin{aligned}
\mathscr{R}_0^0 < \xi &\Longleftrightarrow \mathscr{R}_0^0 < \varepsilon \left(\frac{\rho - \theta}{\rho \theta} \right), \\
&\Longleftrightarrow \mathscr{R}_0(\mathrm{Q}_\rho) < \left(\frac{K}{K+\rho} \right)^2 \frac{S_0}{S_\rho} \frac{\varepsilon}{\rho}, \\
&\Longrightarrow \mathscr{R}_0(\mathrm{Q}_\rho) < 1.
\end{aligned}$$

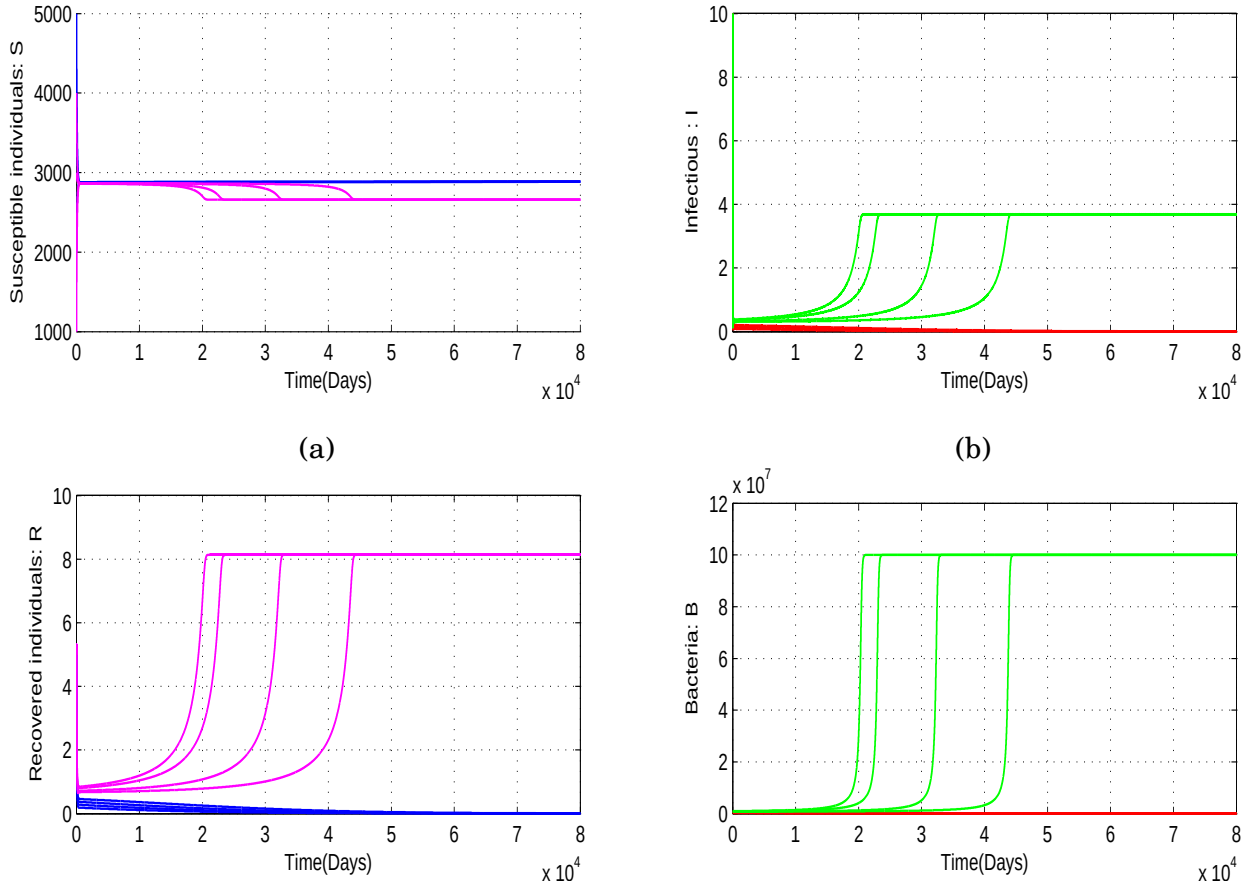


Figure 3: Simulation of model system (2) when $\Lambda = 50$, $\beta = 0.0015$, $\theta = 10^6$ and $\varepsilon = 50000$ (so that $\theta - \varepsilon = 9.5 \times 10^5$, $\xi = 0.0495$ and $\mathscr{R}_0^0 = 0.7702$) using various initial conditions $(S(0), I(0), R(0), B(0))$ chosen in the domains $\mathscr{D}_1 =]0;50000] \times]0;10] \times]0;50] \times \left\{2 \times 10^5, 3 \times 10^5, 4 \times 10^5, 5 \times 10^5\right\}$ and $\mathscr{D}_2 =]0;50000] \times]0;10] \times]0;50] \times \left\{7.5 \times 10^5, 8 \times 10^5, 9 \times 10^5, 9.5 \times 10^5\right\}$. All other parameters values are as in Tab. 1.

□

The restriction of model system (2) on state variable I and B gives the following system:

$$\left\{ \begin{array}{rcl} \dot{I} & = & \lambda S - (\mu + d + \alpha) I, \\ \dot{B} & = & rB(B - \theta)(\rho - B) + \delta I, \end{array} \right. \tag{21}$$

where state variable S is fixed. One notes $X_{(I,B)}(t)$ solution of reduced model system (21) associated to the initial condition $X_{(I,B)}(0) \in \Omega_\theta|_{(I,B)}$ (the restriction of set Ω_θ on the plane (I,B)). Similarly to the proof of Lemma 3.2 it is easy to state that the set $\Omega_\rho|_{(I,B)}$ is a attractor set for model system (21). According to the Poincare-Bendixson theorem, $X_{(I,B)}(t)$ will tend either to a fixed point either to a periodic orbit in $\Omega_\rho|_{(I,B)}$. Now we will use Bendixson-Dulac criteria to state that $\Omega_\rho|_{(I,B)}$ does not contains periodic orbit:

$$\frac{d\dot{I}}{dI} + \frac{d\dot{B}}{dB} = -(\mu + d + \alpha) - 3rB^2 + 2r(\theta + \rho)B - r\theta\rho. \tag{22}$$

Since $\frac{d\dot{I}}{dI} + \frac{d\dot{B}}{dB} < 0$ for all $B \geq \rho$. According to the Bendixson-Dulac criteria, reduced model system (21) does not admits periodic orbit entirely contained in $\Omega_\rho|_{(I,B)}$. The projection on

plane (I,B) of every periodic attractor (different to Q_ρ) of model system (2) contained in Ω_ρ correspond to a limit cycle in $\Omega_\rho|_{(I,B)}$. Since for every value S fixed, model system (21) does not contained cycle limit in $\Omega_\rho|_{(I,B)}$. So that there is not periodic attractor in Ω_ρ for model system (2).

Let $0<\varepsilon<\theta$, if we suppose $\mathscr{R}_0^0<\xi<1$ according to the Proposition 3.3 this imply that $\mathscr{R}_0(Q_\rho)<1$. Thus equilibrium point Q_ρ is a unique asymptotically stable point in Ω_ρ. Consequently every solution of model system (2) associated to initial condition in Ω_θ will converge to Q_ρ.

Theorem 3.3 *Let $\varepsilon\in]0;\theta[$, if $\mathscr{R}_0^0<\xi<1$, equilibrium point Q_ρ of model system (2) is globally asymptotically stable in Ω_θ.*

Remark 3.1 *Considering hypothesis of theorem 3.3, it will be numerically observed that Q_ρ is GAS in $\Omega_{\theta-\varepsilon}$.*

By the Fig. 4 global stability of Q_ρ in $\Omega_{\theta-\varepsilon}$ is also illustrated. Considering $d=0.7$, $\gamma=0.5$, $\alpha=0.45$ and all other parameters are as in Tab. 1 we get $\mathscr{R}_0^0=0.0058$, $\xi=0.0505$ and $\mathscr{R}_0(Q_\rho)=0.0033$. Choosing various initial conditions in $\mathscr{D}_3=]0;50000]\times]0;10]\times]0;50]\times\left[0.9\times10^6,1.2\times10^8\right]$. It is seen on Fig. 4 that solutions of model system (2) converge to Q_ρ.

3.2.3 Endemic equilibrium

Let $Q^*=(S^*,I^*,R^*,B^*)$ be a homogeneous endemic equilibrium of model system (2) with S^*, I^*, R^* and B^* satisfying the following equations:

$$\begin{cases}\Lambda-(\lambda^*+\mu)S^*+\gamma R^*=0,\\ \lambda^*S^*-\omega I^*=0,\\ \alpha I^*-(\mu+\gamma)R^*=0,\\ rB^*(B^*-\theta)(\rho-B^*)+\delta I^*=0.\end{cases}\tag{23}$$

where $\lambda^*=\dfrac{\beta B^*}{K+B^*}$. Expressing endemic states S^* and R^* as a function of I^* and λ^* gives:

$$S^*=\frac{\omega}{\lambda^*}I^* \text{ and } R^*=\frac{\alpha}{\mu+\gamma}I^*.\tag{24}$$

Using Eqs. (24) and the first equation of model system (2), one has

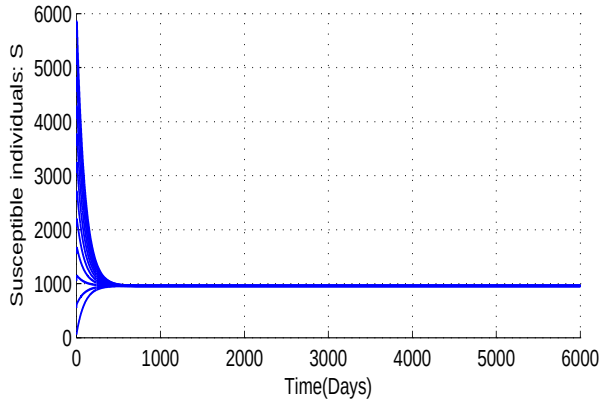
$$I^*=\frac{\lambda^*S^*}{\omega}=\frac{\lambda^*}{\omega}\left[\frac{\Lambda}{\mu}-\frac{\omega}{\mu}I^*+\frac{\gamma\alpha}{\mu(\mu+\gamma)}I^*.\right]\tag{25}$$

Using Eq. (25), one can deduce that

$$I^*=\frac{\Lambda(\mu+\gamma)\lambda^*}{\left[\mu\omega+\gamma(\mu+d)\right]\lambda^*+\omega\mu(\mu+\gamma)}.\tag{26}$$

Using expression $\lambda^*=\dfrac{\beta B^*}{K+B^*}$ in Eq. (26) we get:

$$I^*=\frac{\Lambda(\mu+\gamma)\beta B^*}{\left[(\mu\omega+\gamma(\mu+d))\beta+\omega\mu(\mu+\gamma)\right]B^*+\omega\mu(\mu+\gamma)K}.\tag{27}$$



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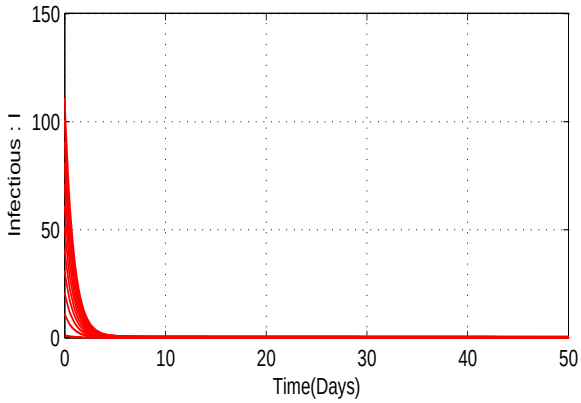

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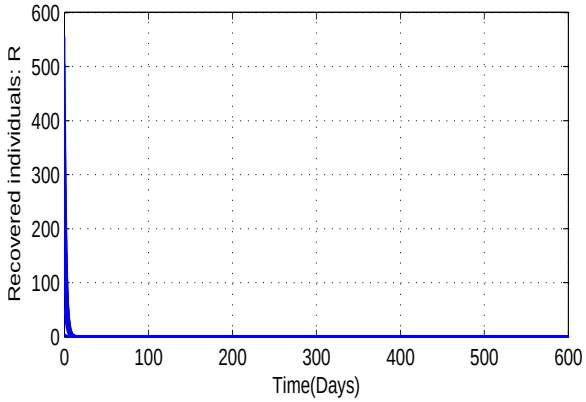

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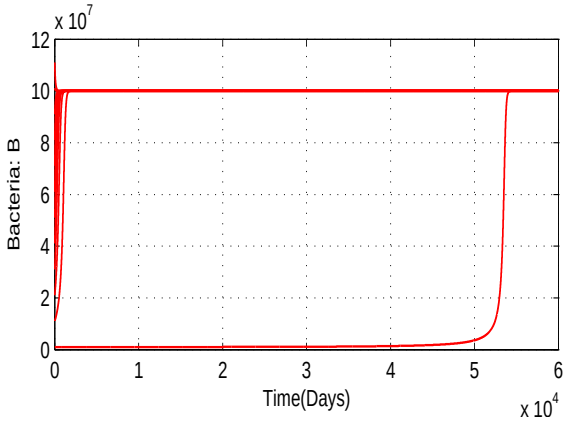

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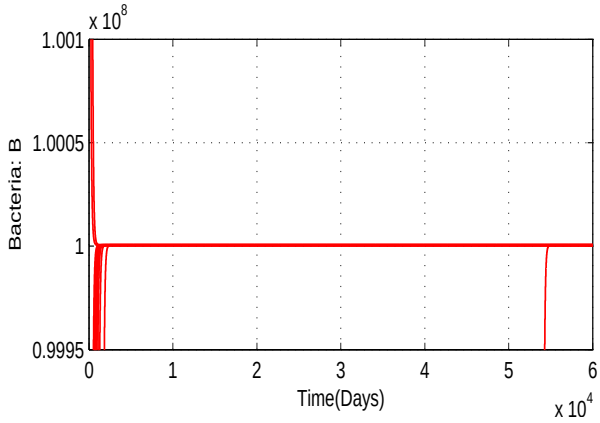


(c)
(Zoom of Bacteria's graph around $\rho = 10^8$)

Figure 4: Simulation of model system (2) when $d = 0.7$, $\gamma = 0.5$, $\alpha = 0.45$ (so that $\mathscr{R}_0^0 = 0.0058$, $\xi = 0.0505$ and $\mathscr{R}_0(\mathrm{Q}_\rho) = 0.0033$) and initial condition are chosen in $\mathscr{D}_3 =]0;50000]\times]0;10]\times]0;50]\times\left[0.9\times10^6, 1.2\times10^8\right]$. All other parameters are as in Tab. 1

Using Eq. (27) in the last equation of (23) we obtain the following three order polynomial equation in B^* :

$$a_3\,(B^*)^3 + a_2\,(B^*)^2 + a_1 B^* + a_0 = 0, \tag{28}$$

where

$$\begin{cases} a_3 &= -r\left[\beta\mu(\mu+d+\alpha)+\beta\gamma(\mu+d)+(\mu+d+\alpha)\mu(\mu+\gamma)\right], \\ a_2 &= r(\theta+\rho)\left[\beta\mu(\mu+d+\alpha)+\beta\gamma(\mu+d)+(\mu+d+\alpha)\mu(\mu+\gamma)\right]-rK(\mu+d+\alpha)\mu(\mu+\gamma), \\ a_1 &= -r\theta\rho\left[\beta\mu(\mu+d+\alpha)+\beta\gamma(\mu+d)+(\mu+d+\alpha)\mu(\mu+\gamma)\right]+rK(\mu+d+\alpha)\mu(\mu+\gamma)(\theta+\rho), \\ a_0 &= r\theta\rho(\mu+d+\alpha)K\mu(\mu+\gamma)(\mathscr{R}_0^0-1). \end{cases}$$

Thus, positive endemic equilibrium Q^* are obtained by solving the cubic equation (28) in B^* and substituting the result (positive values of B^*) into the expression of λ^* and deducing the values of other state variables using relation (24). It is worth noting that the coefficient a_3 is always negative. The coefficient a_0 is positive (negative) if $\mathscr{R}_0^0$ is greater than (less than) unity, respectively. As is demonstrated in Appendix B, System (2) may have none, one, two or three interior equilibriums, depending on parameter values. The various possibilities for the roots of Eq. (28) are summarized in the following lemma.

Lemma 3.4 *: Model system (2) could have*

1. *either one or three interior equilibrium if* $\mathscr{R}_0^0 > 1$.
2. *either none or two endemic equilibrium if* $\mathscr{R}_0^0 < 1$.

Lemma 3.5 *: For every positive solution* B_0^* *of polynomial equation* (28) *we have* $B_0^* \in]0;\theta[\cup]\rho;B_m[$

Proof: The proof of Lemma (3.5) is straightforward and evident. Let B_0^* a solution of polynomial equation (28). Suppose that $B_0^* \in]\theta;\rho[$. Consider $Q_0^* = (S_0^*, I_0^*, R_0^*, B_0^*)$ the endemic equilibrium state deduced from Eq. (26) and (24). Using the last equation of (23) we have:

$$I_0^* = -\frac{r}{\delta}B_0^*(B_0^*-\theta)(\rho-B_0^*) < 0 \text{ which is impossible}$$

□

Now, using the center manifold theory, we are going to show that if $\xi < \mathscr{R}_0^0 < 1$ and for a certain set of model parameters, model system (2) has exactly two endemic equilibrium, with one stable and and another one unstable. To do this, we use the theorem of Castillo-Chavez and Song [32]. We have the following result.

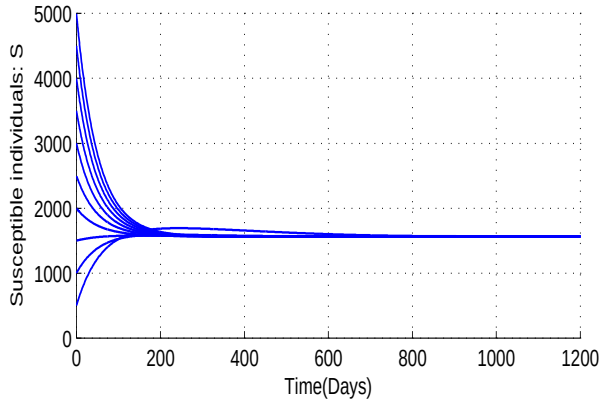
Theorem 3.4 *Model system (3) undergoes a backward bifurcation at* $\mathscr{R}_0^0 = 1$ *if the coefficient a defined as in Eq. (36) is positive, otherwise* $a < 0$ *there exists an endemic equilibrium* Q^* *which is locally asymptotically stable for* $\mathscr{R}_0^0 > 1$ *but close to 1.*

The proof of Theorem (3.4) is given in the Appendix C.

The Fig. 5 shows time series of model system (2) when $\Lambda = 30, \beta = 0.01$ (so that $\mathscr{R}_0^0 = 3.0809 > 1$) and all other parameters are as in Tab. 1. Various initial condition have been taken in $\mathscr{D}_3 =]0;7.5\times10^6]\times]0;1.5\times10^3]\times]0;7.5\times10^3]\times\left[10^5, 1.5\times10^8\right]$. It clearly appears on Fig. 5 that the trajectories of model converge to an unique endemic equilibrium belonging to Ω_ρ. This means that cholera persists within the community and the disease is uncontrollable.

To derive the stability region of any endemic equilibrium when $\mathscr{R}_0^0 \geq 1$, we applied the methods in van den Driessche and Watmough [31] once again. We found the basic reproduction number of infectious in a population where endemic equilibrium $Q^* = (S^*, I^*, R^*, B^*)$ is fixed (see Appendix D for details):

$$\mathscr{R}_0(Q^*) = \frac{\beta K\delta S^*}{(K+B^*)^2\omega(r\theta\rho-2r(\theta+\rho)B^*+3r(B^*)^2)}, \tag{29}$$



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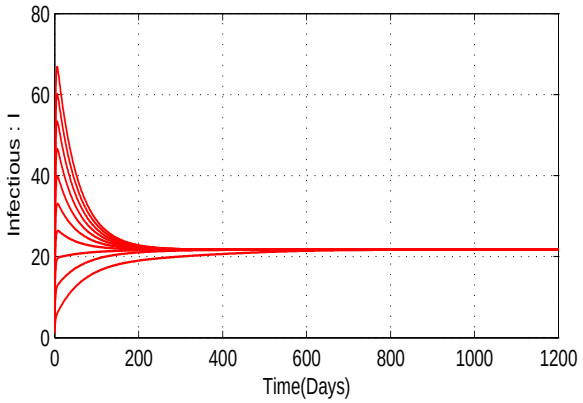

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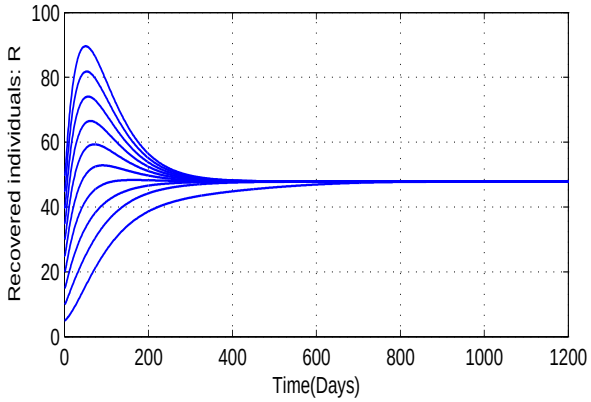

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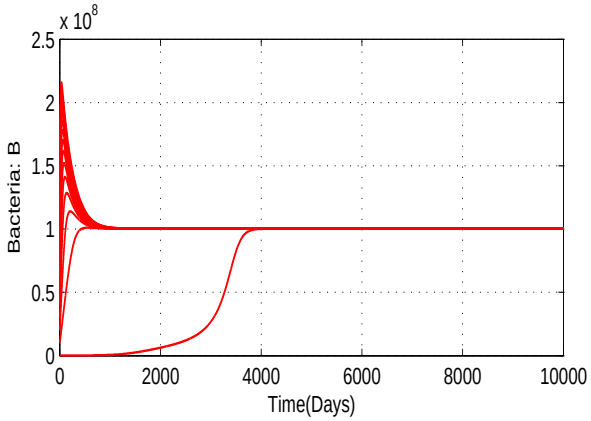

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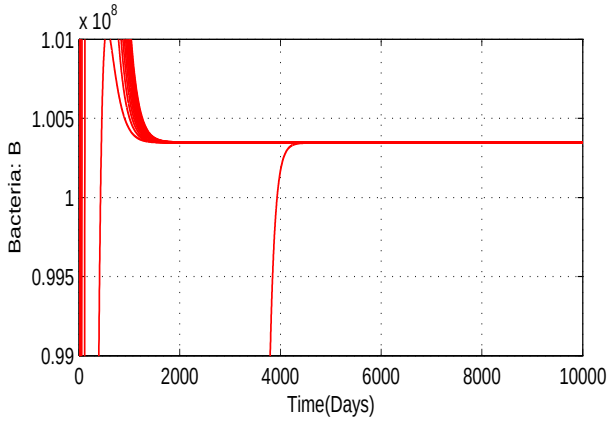


(c)
(Zoom of Bacteria's graph around $\rho = 10^8$)

Figure 5: Simulation of model system (2) when $\Lambda = 30$, $\beta = 0.01$ (so that $\mathscr{R}_0^0 = 3.0809 > 1$) and various initial conditions have been taken in $\mathscr{D}_3 =]0; 7.5 \times 10^6] \times]0; 1.5 \times 10^3] \times]0; 7.5 \times 10^3] \times [0, 1.5 \times 10^8]$. All other parameters are as in Tab. 1.

According to the van den Driessche and Watmough [31] methods, this endemic equilibrium is locally asymptotically stable when $\mathscr{R}_0(Q^*) < 1$.

Now,

$$\mathscr{R}_0(Q^*) < 1 \Longleftrightarrow \mathscr{R}_0^0 \frac{S^*}{S_0} \left(\frac{K}{K+B^*} \right)^2 r\theta\rho < r\theta\rho - 2r(\theta+\rho)B^* + 3r(B^*)^2 \tag{30}$$

Thus,

$$\begin{aligned} \mathscr{R}_0(Q^*) < 1 &\Longleftarrow \mathscr{R}_0^0 r\theta\rho < r\theta\rho - 2r(\theta+\rho)B^* + 3r(B^*)^2 \\ &\Longleftrightarrow 0 < 3r(B^*)^2 - 2r(\theta+\rho)B^* - r\theta\rho(\mathscr{R}_0^0 - 1) \\ &\Longleftrightarrow B^* \in]0; B_1^*[\cup]B_2^*; B_m[\end{aligned}$$

where,

$$B_1^* = \frac{1}{3}\left[\theta+\rho-\sqrt{(\rho-\theta)^2+\theta\rho+3\theta\rho\mathscr{R}_0^0}\right] \text{ and } B_2^* = \frac{1}{3}\left[\theta+\rho+\sqrt{(\rho-\theta)^2+\theta\rho+3\theta\rho\mathscr{R}_0^0}\right]$$

Considering $B_1^* > 0$ we get $\mathscr{R}_0^0 < 1$. Since we have assumed that $\mathscr{R}_0^0 \geq 1$ this imply that $B_1^* \leq 0$ and consequently $B^* \in]B_2^*; B_m[$.
One has,

$$\begin{aligned} B_2^* &= \frac{1}{3}\left[\theta+\rho+\sqrt{(\rho-\theta)^2+\theta\rho+3\theta\rho\mathscr{R}_0^0}\right] \\ &> \frac{1}{3}\left[2\theta+\sqrt{\theta^2+\rho(\rho-\theta)+3\theta\rho\mathscr{R}_0^0}\right] \\ &> \theta \end{aligned}$$

Considering the lemma (3.5) we get $B^* \in]\rho; B_m[$. We have the following result:

Proposition 3.4 *If $\mathscr{R}_0^0 \geq 1$ then any stable endemic equilibrium $Q^* = (S^*, I^*, R^*, B^*)$ of model system (2) verifies $B^* \in]\rho; B_m[$.*

Now we are interested to know what would goes if $\mathscr{R}_0(\mathrm{Q}_\rho) \geq 1$? The contrapositive of Proposition 3.3 gives:

$$\text{If} \quad \mathscr{R}_0(\mathrm{Q}_\rho) \geq 1 \quad \text{then} \quad \forall \varepsilon \in]0; \theta[, \quad \mathscr{R}_0^0 \geq \xi$$

This imply existence of one stable endemic equilibrium for model system (2) in Ω.

Theorem 3.5 *There exists an endemic equilibrium Q^* which is locally asymptotically stable when $\mathscr{R}_0(\mathrm{Q}_\rho) > 1$ but close to 1.*

The proof of Theorem 3.5 is given in the Appendix E.

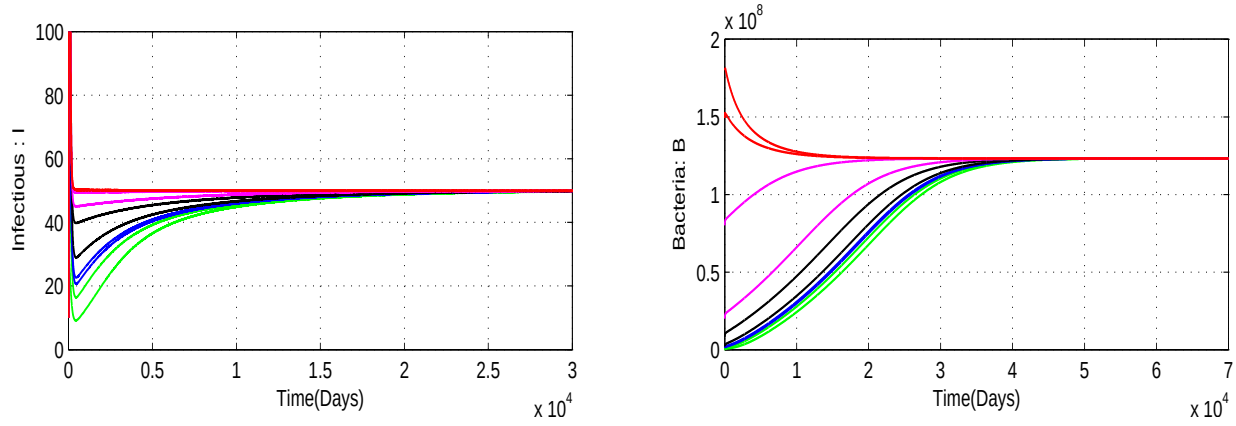
It is important to have a global view of dynamic on model system (2) when various initial conditions are taken in $\mathbb{R}_+^4$ and when threshold quantity $\mathscr{R}_0^0$ and $\mathscr{R}_0(\mathrm{Q}_\rho)$ are varying around critical values (unity and value of ξ). So that, four cases will be examined through graphs of bacteria and infected population.

Case 1: $\mathscr{R}_0(\mathrm{Q}_\rho) < 1 < \mathscr{R}_0^0$

To get this situation, we just have to take $\Lambda = 50$, $\beta = 0.02$ and $r = 10^{-20}$ (so that $\mathscr{R}_0(\mathrm{Q}_\rho) = 0.0526$ and $\mathscr{R}_0^0 = 1.7594 \times 10^3$) and all other parameters are as in Tab. 1. The numerical simulations obtained in Fig. 6 show that all the solutions of model system (2) converges to an endemic equilibrium. It is therefore numerically observed that the instability of Q_0 also imply instability of Q_ρ.

Case 2: $\mathscr{R}_0(\mathrm{Q}_\rho) < \mathscr{R}_0^0 < \xi < 1$

According to theorem 3.2 and theorem 3.3, this case expect convergence to Q_0 or Q_ρ of every solution of model (2) when initial conditions are taken in their attraction domain respectively.



(a) (b)

Figure 6: Simulation of model system (2) when $\Lambda = 50$, $\beta = 0.02$ and $r = 10^{-20}$ (so that $\mathscr{R}_0(\mathrm{Q}_\rho) = 0.0526$ and $\mathscr{R}_0^0 = 1.7594 \times 10^3$) and various initial conditions in $\mathbb{R}^4_+$. All other parameters are as in Tab. 1.

The Fig. 7 is obtained by considering parameter values in Tab. 1 with $\varepsilon = 50000$. For these values we have $\mathscr{R}_0(\mathrm{Q}_\rho) = 0.0023$, $\mathscr{R}_0^0 = 0.0045$ and $\xi = 0.0495$. Extinction of infectious does not depend on the initial conditions. Extinction of population of bacteria is obtained when initial values are chosen in $\mathscr{D}_3 =]0;50000] \times]0;10] \times]0;50] \times \left[10^5, 9.9 \times 10^5\right]$. Saturation of the bacterial population is obtained for initial conditions chosen in $\mathscr{D}_4 =]0;50000] \times]0;10] \times]0;50] \times \left[10^6, 2 \times 10^8\right]$.

Case 3: $\xi < \mathscr{R}_0(\mathrm{Q}_\rho) < \mathscr{R}_0^0 < 1$

The phenomenon of backward bifurcation occurs. But the fact that an stable equilibrium endemic exists in Ω_ρ imply consequently instability of Q_ρ even if $\mathscr{R}_0(\mathrm{Q}_\rho) < 1$. The simulations of Fig. 8 are obtained when $\Lambda = 30$, $\beta = 0.001$ and $\varepsilon = 1000$ (so that $\xi = 0.0010, \mathscr{R}_0(\mathrm{Q}_\rho) = 0.027$ and $\mathscr{R}_0^0 = 0.308$). Extinction of epidemic and population of bacteria is obtained for initial values chosen in $\mathscr{D}_5 =]0;50000] \times]0;10] \times]0;50] \times \left[0, 5 \times 10^5\right]$. Endemicity situation is observed for initial values chosen in $\mathscr{D}_6 =]0;50000] \times]0;10] \times]0;50] \times \left[7 \times 10^5, 2 \times 10^8\right]$.

Case 4: $\xi < \mathscr{R}_0^0 < 1 < \mathscr{R}_0(\mathrm{Q}_\rho)$

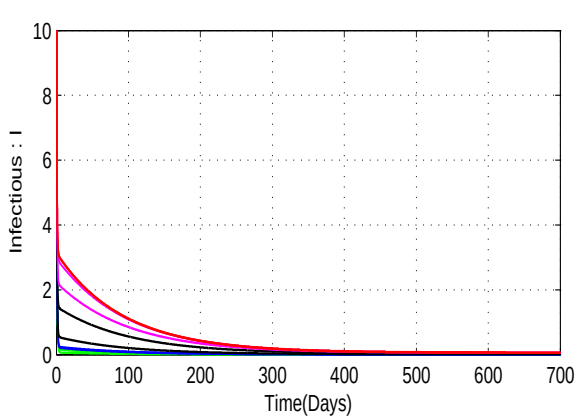
The following parameters are modified $\beta = 0.1$, $\mu = 1.04 \times 10^{-3}$, $\theta = 0.999 \times 10^8$ and $\varepsilon = 50000$ (so that $\xi = 5.005 \times 10^{-8}, \mathscr{R}_0^0 = 0.0104$ and $\mathscr{R}_0(\mathrm{Q}_\rho) = 4.5370$). The previously situation is obtained one again.

From these different cases, it is easy to project dynamic of model system (2) in other situations.

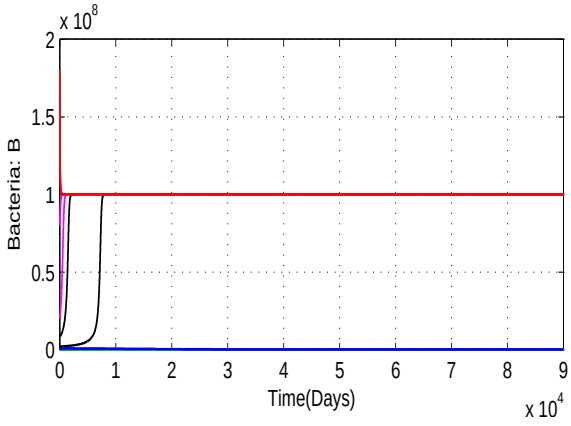
3.3 Numerical simulations of threshold quantities and bifurcations.

The theoretical results in section 3.2 really confirm the biological and epidemiological results on cholera which establish that bacterial growth is a substantial factor for cholera process emergence [33, 34, 35, 36]. That growth is mathematically modelized in model system (2) by a dynamic with Allee effect. This dynamic allows us to represent the different phases of bacterial growth fluctuations due to variations of environmental conjunctures. These different growth phases are materialized by the parameters θ and ρ which represent Allee threshold and carrying capacity of bacteria respectively. The fact that these parameters determine the bacterial growth in the environment involves importance to do a deep simulation of their impact on extinction and persistence of cholera.

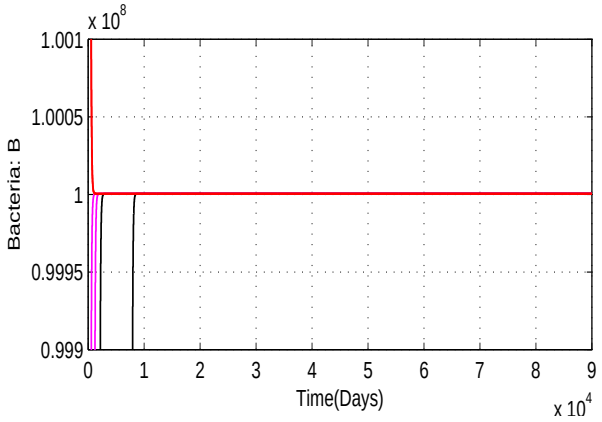
A three-dimensional simulation of $\mathscr{R}_0^0$ in terms of θ and ρ is given in Fig. 10.



(a)



(b)



(c)
(Zoom of Bacteria's graph around $\rho = 10^8$)

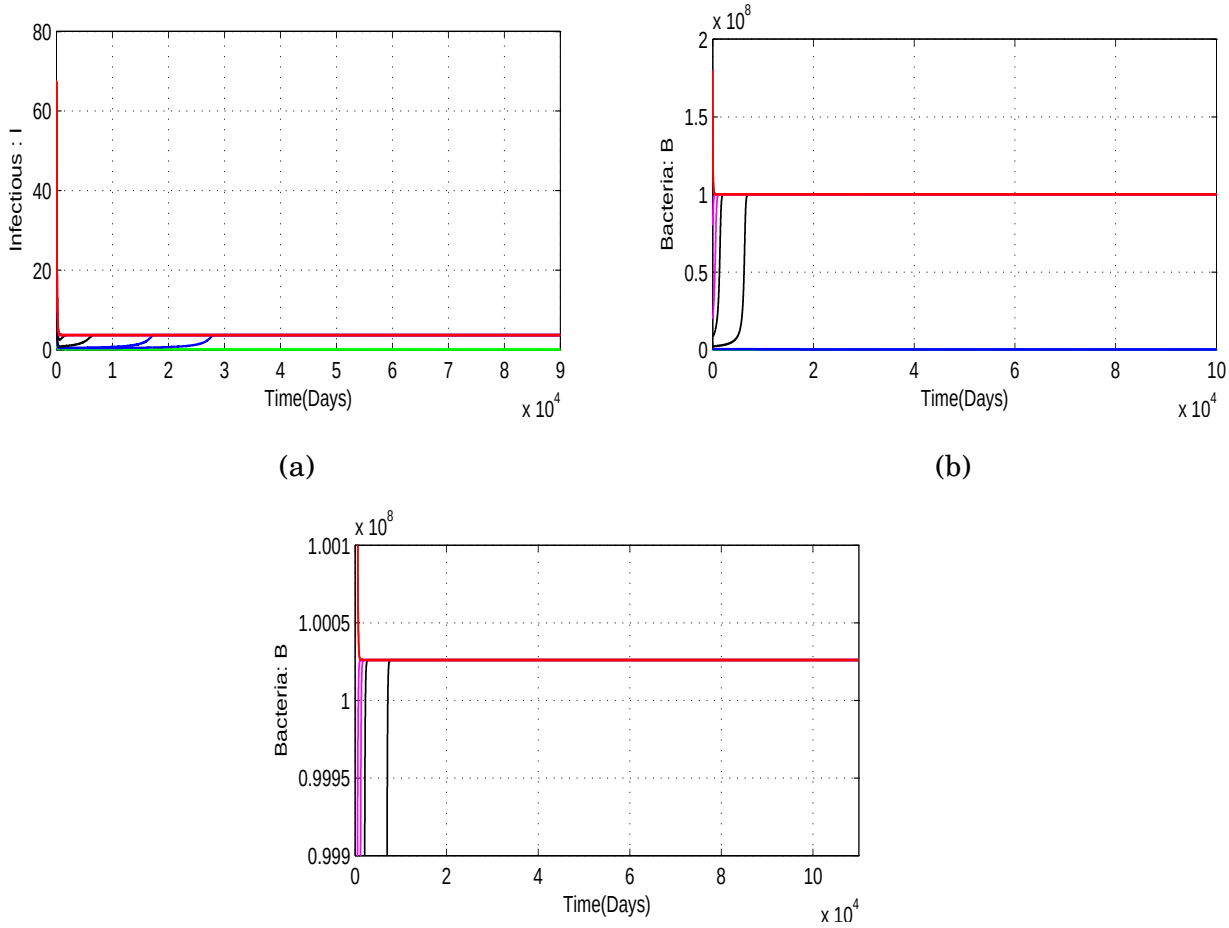
Figure 7: Simulation of model system (2) when all parameters values are as in Tab. 1 (so that $\mathscr{R}_0(\mathrm{Q}_\rho) = 0.0023$, $\mathscr{R}_0^0 = 0.0045$, $\varepsilon = 50000$ and $\xi = 0.0495$) and various initial conditions chosen in $\mathscr{D}_3 =]0;50000]\times]0;10]\times]0;50]\times\left[10^5, 9.5\times10^5\right]$ and in $\mathscr{D}_4 =]0;50000]\times]0;10]\times]0;50]\times\left[10^6, 2\times10^8\right]$.

It is obvious to notice that the basic reproductive number $\mathscr{R}_0^0$ is very closed to zero for θ values greater than 10^5. This would mean that the risk of outbreaks are very small when the Allee threshold is higher that 10^5 in this situation.

On the Fig. 11, we present variations of $\mathscr{R}_0(\mathrm{Q}_\rho)$ for some values of θ and ρ. The curves obtained on Fig. 11 reveal importance to point out the fact that risk of disease outbreaks are not negligible for all values of θ. Furthermore, epidemic outbreaks are increasingly likely for θ values close to ρ

The Fig. 12 present the various combination values of θ and ρ for which we have $\mathscr{R}_0^0 = \xi$ (ε will be fixed) and $\mathscr{R}_0(\mathrm{Q}_\rho) = 1$. The Fig. 12-(a) and the Fig. 12-(b) are obtained for $\varepsilon = 1$ and $\varepsilon = 50000$ respectively. Taking several values of $\varepsilon \in]0;\theta[$, it quickly notice that the conditions $\mathscr{R}_0^0 < \xi$ and $\mathscr{R}_0(\mathrm{Q}_\rho) < 1$ become nearly equivalent when $\varepsilon > 50$. Numerical results on Fig. 12 confirm the theoretical result obtained on proposition 3.3 which states that stability condition of Q_0 imply that of Q_ρ.

It was stated in theorem 3.4 that model system undergoes a bifurcation at $\mathscr{R}_0^0 = 1$. When we vary parameter value $\mathscr{R}_0^0$ around unity through parameter β (all other parameters values are fixed) of model system (2) we get for each value of β different solutions of polynomial

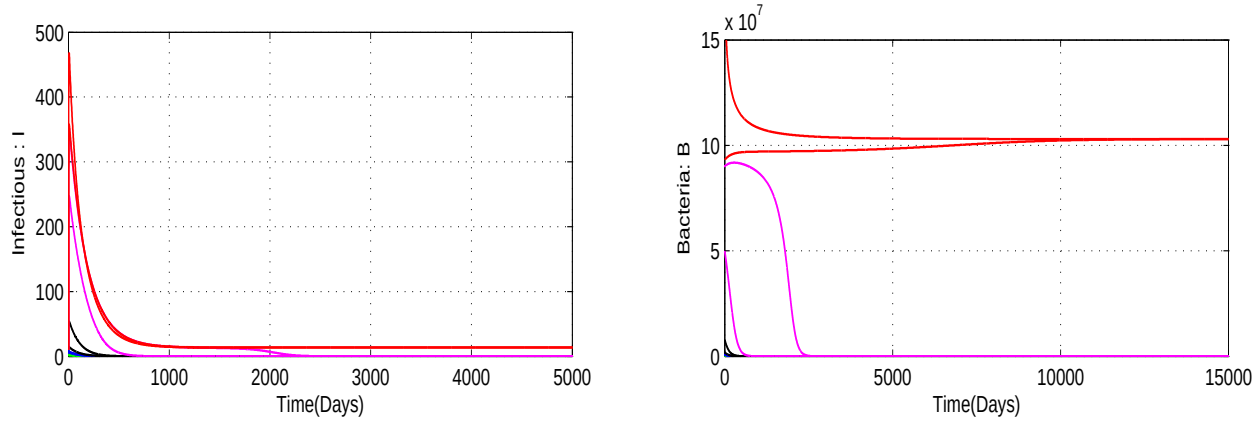


(a) (b)

(c)
(Zoom of Bacteria's graph around $\rho = 10^8$)

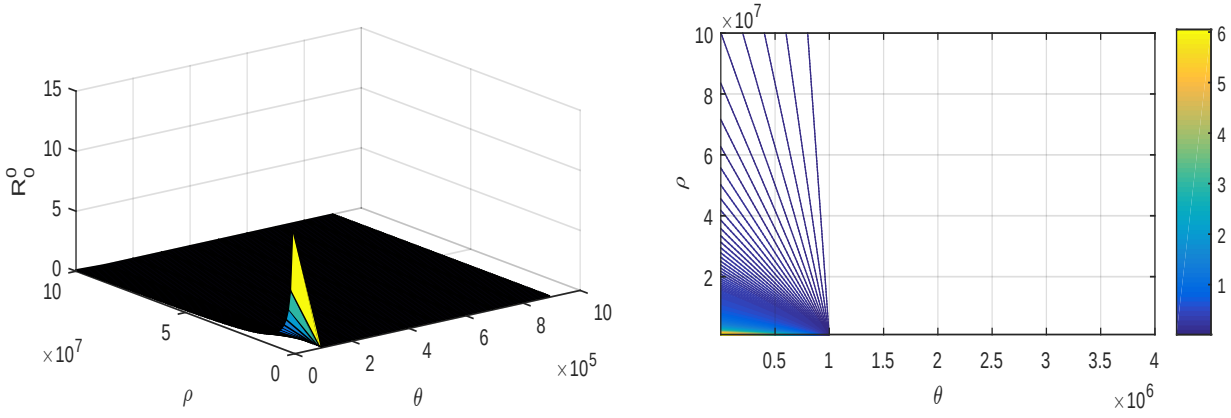
Figure 8: Simulation of model system (2) when $\Lambda = 30$, $\beta = 0.001$ and $\varepsilon = 1000$ (so that $\xi = 0.0010, \mathscr{R}_0(\mathsf{Q}_\rho) = 0.027$ and $\mathscr{R}_0^0 = 0.308$) all other parameters values are as in Tab. 1. Various initial conditions chosen in $\mathscr{D}_5 =]0;50000]\times]0;10]\times]0;50] \times \left[10^5, 5\times 10^5\right]$ and $\mathscr{D}_6 =]0;50000]\times]0;10]\times]0;50] \times \left[7\times 10^5, 2\times 10^8\right]$

equation (28) which permit us to deduce different persistent infection forces. The Figures below illustrate and confirm the discussion on lemma 3.4.



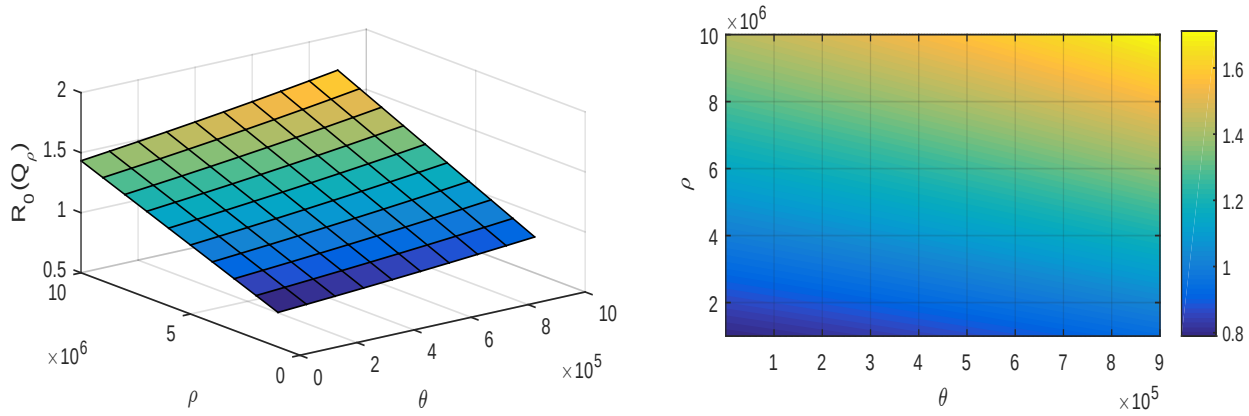
(a) (b)

Figure 9: Simulation of model system (2) when $\beta = 0.1$, $\mu = 1.04 \times 10^{-3}$, $\theta = 0.999 \times 10^8$ and $\varepsilon = 50000$ (so that $\xi = 5.005 \times 10^{-8}, \mathscr{R}_0^0 = 0.0104$ and $\mathscr{R}_0(\mathrm{Q}_\rho) = 4.5370$) all other parameters values are as in Tab. 1. Various initial conditions chosen in $\mathscr{D}_7 =]0;50000] \times]0;10] \times]0;50] \times \left[10^5, 2 \times 10^8\right]$.



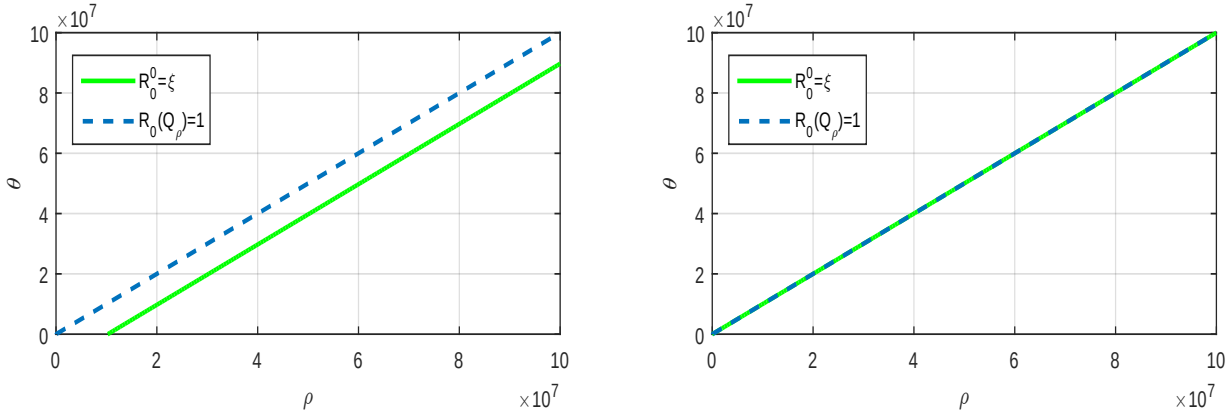
(a) (b)

Figure 10: Simulation of $\mathscr{R}_0^0$ for various values of $\theta \in [0;10^6]$ and $\rho \in [10^6;10^8]$ when $r = 10^{-13}$ and all other parameters values are as in Tab. 1. (a) The curve in 3 dimensions. (b) The contour lines.



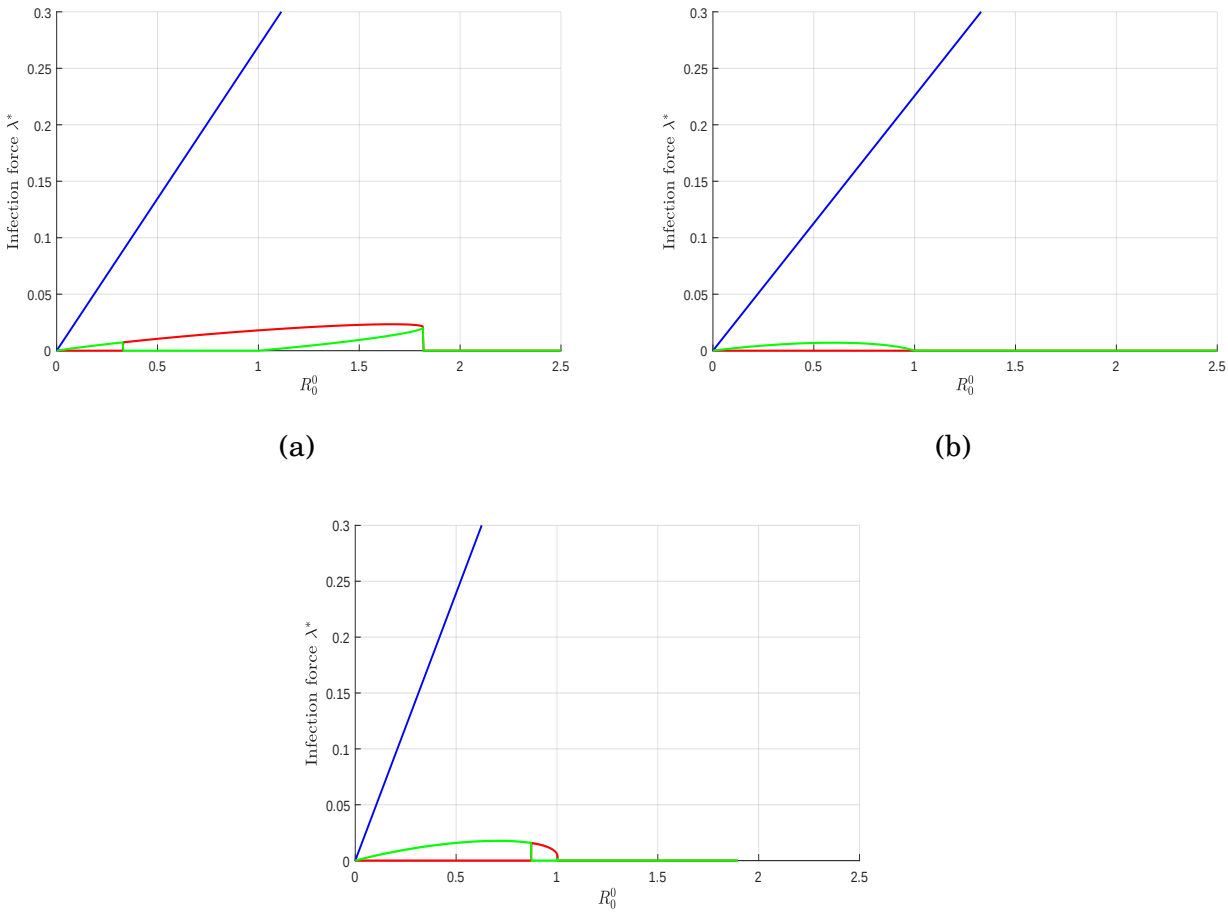
(a) (b)

Figure 11: Simulation of $\mathscr{R}_0(Q_\rho)$ for various values of $\theta \in [0; 10^6]$ and $\rho \in [10^6; 10^7]$ when $\Lambda = 70$, $\beta = 0.001$ and all other parameters values are as in Tab. 1. (a) The curve in 3 dimensions. (b) The contour lines.



(a) (b)

Figure 12: Region of plan (ρ, θ) on which Q_0 and Q_ρ are stable when $r = 10^{-13}$ and all other parameters values are as in Tab. 1. (a) For $\varepsilon = 1$, (b) For $\varepsilon = 50000$



(a) (b)

(c)

Figure 13: Bifurcation Diagram of $\mathscr{R}_0^0$ when (a) $\delta = 23$ (b) $\lambda = 20$ and $\mu = 0.05$ (c) $\lambda = 20$, $\mu = 0.05$ and $\delta = 33$

4 Conclusion

The point of departure of this work is to acknowledge the complexity of taking into account in model of cholera a bacteria reproduction rate incorporating an Allee Effect. In some of the existing models in the literature, the difficulty is neglected through unrealistic assumptions such as bacteria have linear or logistic growth [2, 3, 4, 5, 6, 7, 8]. In this work, we have formulated a generic S-I-R-S epidemic model for the dynamical transmission of cholera disease in which the following factors are incorporated: (i) the bacteria net reproduction rate incorporate an Allee Effect, (ii) the loss of immunity of recovered individuals (iii) infection force to cholera regulated by the contact and logistic dose-reponse of bacteria. The model have three disease-free equilibriums which each corresponds to the real situation. Equilibrium Q_0 is a desirable situation. Concretely this is a situation where there is no infected individual and bacteria concentration is very negligible because the *V. cholerae* cannot be absolutely absent in environment, but its concentration can be so low to generate a disease. Many European countries living that context. The disease-free equilibrium Q_θ is the critical situation under which the disease and bacteria may disappear if $\mathscr{R}_0^0 < \xi$ and initial condition owns in attraction domain of Q_0. But when bacteria concentration cross the value θ solutions of model system (2) will converge either to Q_ρ if $\mathscr{R}_0^0 < \xi$ or to an endemic situation. The context of Q_ρ where bacteria are saturated in environment without infected individual is a common situation to endemic regions in Africa (Cameroon for example). Because when the *V cholerae* is densely present in environment, cholera epidemics are common in these areas. Through sensitivity analysis of the system (2), we found that parameters relative to human-bacteria contact and bacteria dynamic should significantly affect global dynamic of model. This means that in an epidemic situation it is urgent to make an intense awareness campaigns of the population about compliance with hygiene rules and to start sanitation campaigns of areas at risk. The numerical results presented illustrate and validate theoretical results. Through numerical simulation, we found that; the stability of the three disease-free equilibriums of model, the existence and the stability of endemic equilibrium is essentially determined by threshold quantity $\mathscr{R}_0^0$. Different improvements and extensions of the model on which we are still working include: extension to 2 patches; introducing time-dependent parameters in order to integrate fluctuation of environmental factors du to periodic variations of climate. More precisely, we will consider periodic values for parameters β, θ, ρ and δ.

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Appendix A: Calculation of Persistence Threshold for Disease Free Equilibrium Q_ρ.

Considering the disease-free equilibrium $\mathrm{Q}_\rho = (S_\rho, 0, 0, \rho)$ and using the notations in van den Driessche and Watmough [31] for model system (2) the matrices F and V for the new infection terms and the remaining transfer terms are, respectively, given by:

$$F = \begin{bmatrix} 0 & \dfrac{\beta K \Lambda}{(k+\rho)[\beta\rho + \mu(\rho+K)]} \\ 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} \omega & 0 \\ -\delta & -r\rho(\rho-\theta) \end{bmatrix}$$

Following van den Driessche and Watmough [31], the basic reproduction number of infections in population where Q_ρ is fixed is then the spectral radius of the next generation matrix FV^{-1},

$$\mathscr{R}_0(\mathrm{Q}_\rho) = \frac{\beta K \delta \Lambda}{[\beta\rho + \mu(\rho+K)](K+\rho)\omega r\rho(\rho-\theta)}, \tag{31}$$

Appendix B: Proof of Lemma 3.4

The number of positive roots of (28) determines the number of endemic equilibrium of system (2). In order to identify the number of endemic equilibriums, we require the partial derivative of function $P : B^* \longmapsto a_3 (B^*)^3 + a_2 (B^*)^2 + a_1 B^* + a_0$ with respect to B^* which is given by:

$$\frac{dP(B^*)}{dB^*} = 3a_3(B^*)^3 + 2a_2(B^*)^2 + a_1$$

Thus, when $\Delta = 4a_2^2 - 12a_1a_3 > 0$, equation $\dfrac{dP(B^*)}{dB^*} = 0$ has two real roots $v_i, i = 1,2$ given by:

$$v_1 = \frac{-2a_2 - \sqrt{4a_2^2 - 12a_1a_3}}{6a_3} \text{ and } v_2 = \frac{-2a_2 + \sqrt{4a_2^2 - 12a_1a_3}}{6a_3}$$

Therefore we conclude that:

if $\mathscr{R}_0^0 > 1$ model system (2) has:

- one endemic equilibrium if ($v_1 < v_2 < 0$, $P(v_2) > 0$) or if ($v_1 < 0 < v_2$, $P(v_2) > 0$) or if ($v_2 > v_1 > 0$, $P(v_1) < 0$, $P(v_2) < 0$) or if ($v_2 > v_1 > 0$, $P(v_1) > 0$, $P(v_2) > 0$).
- three endemic equilibriums if ($v_2 > v_1 > 0$, $P(v_1) < 0$, $P(v_2) > 0$).

if $\mathscr{R}_0^0 < 1$ model system (2) has:

- no endemic equilibrium if ($0 < v_1 < v_2$, $P(v_1) < 0$, $P(v_2) < 0$) or if ($v_1 < v_2 < 0$, $P(v_1) < 0$) or if ($v_1 < v_2 < 0$, $P(v_1) > 0$, $P(v_2) > 0$) or if ($v_1 < 0 < v_2$, $P(v_1) < 0$, $P(v_2) < 0$).
- two endemic equilibriums if ($v_1 < 0 < v_2$, $P(v_1) < 0$, $P(v_2) > 0$) or if ($0 < v_1 < v_2$, $P(v_1) < 0$, $P(v_2) > 0$).

Appendix C: Proof of Theorem 3.4

We present the proof of Theorem 3.4 on the local stability of the endemic equilibrium point of system (2) when $\mathscr{R}_0^0 > 1$. To do so, the following simplification and change of variables are made first to all. Let $x_1 = S$, $x_2 = I$, $x_3 = R$, $x_4 = B$. Further, by using the vector notation

$x=(x_1,x_2,x_3,x_4)$. The model (2) can be written in the form $\dot{x}=f(x)$ with $f=(f_1,f_2,f_3,f_4)$ as follows:

$$\begin{cases} \dot{x_1} &= \Lambda-(\lambda+\mu)x_1+\gamma x_3, \\ \dot{x_2} &= \lambda x_1-\omega x_2, \\ \dot{x_3} &= \alpha x_2-(\gamma+\mu)x_3, \\ \dot{x_4} &= rx_4(x_4-\theta)(\rho-x_4)+\delta x_2, \end{cases} \tag{32}$$

where $\lambda=\beta\frac{x_4}{x_4+K}$. System (32) has a DFE given by $\mathrm{Q}_0=(S_0,0,0,0)$ where $S_0=\frac{\Lambda}{\mu}$. The Jacobian of system (2) at the DFE Q_0 is

$$J(\mathrm{Q}_0)=\begin{bmatrix} -\mu & 0 & \gamma & -\beta^*\frac{S_0}{K} \\ 0 & -\omega & 0 & \beta^*\frac{S_0}{K} \\ 0 & \alpha & -(\mu+\gamma) & 0 \\ 0 & \delta & 0 & -r\rho\theta \end{bmatrix}.$$

The basic reproduction number of the transformed (linearized) model system (32) is the same as that of the original model given by Eq. (2). Therefore, choosing β as a bifurcation parameter. Solving for β from $\mathscr{R}_0^0=1$, we obtain:

$$\beta^*=\frac{Kr\rho\theta\mu\omega}{\Lambda\delta} \tag{33}$$

It follows that the Jacobian $J(\mathrm{Q}_0)$ of system (32) at the DFE Q_0, with $\beta=\beta^*$, denoted by J_{β^*} has a simple zero eigenvalue (with all other eigenvalues having negative real parts). Hence, the Centre Manifold theory [37] can be used to analyze the dynamics of system (32). In particular, the theorem in Castillo and Song [32], reproduced below for convenience, will be used to show that when $\mathscr{R}_0^0>1$ there exists an endemic equilibrium of system (32) which is locally asymptotically stable for $\mathscr{R}_0^0$ near 1 under certain conditions.

Theorem 4.1 *(Castillo-Chavez and Song [32]). Consider the following general system of ordinary differential equations with a parameter Φ:*

$$\frac{dz}{dt}=f(x,\Phi)\,, \qquad f:\mathbb{R}^n\times\mathbb{R}\longrightarrow\mathbb{R} \qquad \textit{and} \qquad f\in C^2(\mathbb{R}^n\times\mathbb{R}) \tag{34}$$

where 0 is an equilibrium point of the system (that is, $f(0,\Phi)\equiv 0$ for all Φ) and assume

1. *$A=D_zf(0,0)=\left(\frac{\partial f_i}{\partial z_j}(0,0)\right)$ is the linearization matrix of system (34) around the equilibrium 0 with Φ evaluated at 0. Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts;*

2. *Matrix A has a right eigenvector u and a left eigenvector v (each corresponding to the zero eigenvalue). Let f_k be the k^{th} component of f and*

$$a=\sum_{k,i,j=1}^{n}v_ku_iu_j\frac{\partial^2 f_k}{\partial x_i\partial x_j}(0,0) \qquad \textit{and} \qquad b=\sum_{k,i=1}^{n}v_ku_i\frac{\partial^2 f_k}{\partial x_i\partial\Phi}(0,0),$$

then, the local dynamics of the system around the equilibrium point 0 is totally determined by the signs of a and b.

1. *$a>0$, $b>0$. When $\Phi<0$ with $|\Phi|\ll 1$, 0 is locally asymptotically stable and there exists a positive unstable equilibrium; when $0<\Phi\ll 1$, 0 is unstable and there exists a negative, locally asymptotically stable equilibrium;*

2. $a<0,\ b<0$. *When* $\Phi<0$ *with* $|\Phi|\ll 1$, *0 is unstable; when* $0<\Phi\ll 1$, *0, is locally asymptotically stable equilibrium, and there exists a positive unstable equilibrium;*

3. $a>0,\ b<0$. *When* $\Phi<0$ *with* $|\Phi|\ll 1$, *0 is unstable and there exists a locally asymptotically stable negative equilibrium; when* $0<\Phi\ll 1$, *0 is stable, and a positive unstable equilibrium appears;*

4. $a<0,\ b>0$. *When* Φ *changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.*

In order to apply the above theorem, the following computations are necessary (it should be noted that we are used β^* as the bifurcation parameter, in place of Φ in Theorem 4.1).

Eigenvectors of J_{β^*} . For the case when $\mathscr{R}_0^0=1$, it can be shown that the Jacobian of system (32) has a right eigenvector (corresponding to the zero eigenvalue), given by $U=(u_1,u_2,u_3,u_4)^T$, where

$$u_1=-\left[\frac{\gamma\alpha}{\mu(\mu+\gamma)}-\frac{\omega}{\mu}\right]u_2,\ \ u_2=u_2>0,\ \ u_3=\frac{\alpha}{\mu+\gamma}u_2,\ \text{and}\ u_4=\frac{\delta}{r\rho\theta}u_2 \tag{35}$$

Similarly, the components of the left eigenvectors of J_{β^*} (corresponding to the zero eigenvalue), denoted by $V=(v_1,v_2,v_3,v_4)^T$, are given by:

$$v_1=0,\ \ v_2=v_2>0,\ \ v_3=0,\ \text{and}\ v_4=\frac{\beta S_0}{Kr\rho\theta}v_2$$

Computation of b For the sign of **b**, it can be shown that the associated non-vanishing partial derivatives of f are:

$$\frac{\partial^2 f_1}{\partial x_4\partial\beta^*}(0,0)=-\frac{S_0}{K}\qquad\text{and}\qquad\frac{\partial^2 f_2}{\partial x_4\partial\beta^*}(0,0)=\frac{S_0}{K}.$$

It follows that

$$b=\frac{\omega}{\beta^*}v_2u_2>0$$

Computation of a: For system (32), the associated non-zero partial derivatives of f (at the DFE Q_0) are given by:

$$\frac{\partial^2 f_1}{\partial x_1x_4}(0,0)=-\frac{\beta^*}{K},\ \ \frac{\partial^2 f_1}{\partial x_4^2}(0,0)=\frac{2\beta^*S_0}{K},\ \ \frac{\partial^2 f_2}{\partial x_1\partial x_4}(0,0)=\frac{\beta^*}{K},\ \ \frac{\partial^2 f_2}{\partial x_4^2}(0,0)=-\frac{2\beta^*S_0}{K}$$

$$\text{and}\ \frac{\partial^2 f_4}{\partial x_4^2}(0,0)=2r(\rho+\theta).$$

Then, it follows that

$$\begin{aligned}a&=v_2\sum_{i,j=1}^{4}u_iu_j\frac{\partial^2 f_2}{\partial x_i\partial x_j}(0,0)+v_4\sum_{i,j=1}^{4}u_iu_j\frac{\partial^2 f_4}{\partial x_i\partial x_j}(0,0),\\&=v_2u_2^2\left[\frac{\alpha\gamma\omega}{(\mu+\gamma)S_0}+2\left(\frac{\omega K}{\beta^*S_0}\right)^2\frac{\omega}{\delta}r(\rho+\theta)-\frac{\omega}{S_0}\left(\frac{1}{\mu}+\frac{2K}{\beta^*}\right)\right]\end{aligned} \tag{36}$$

Thus, depending on the values of the parameters of the model system (2), the value of **a** can be positive or negative. So, if $\mathbf{b}>0$, if $\mathbf{a}>0$, model system (2) undergoes the phenomenon of backward bifurcation (see Theorem 4.1, item (1)). Also, if $\mathbf{a}<0$ (by Theorem 4.1, item (4)), we have established the result about the local stability of the endemic equilibrium Q^* of model system (2) for $\mathscr{R}_0^0>1$ but close to 1. This concludes the proof of Theorem 3.4

Appendix D: Calculation of Persistence Threshold for Endemicity.

Consider any endemic equilibrium $Q^* = (S^*, I^*, R^*, B^*)$. Suppose cholera is transmissible in population at point Q^*. Using the notations in van den Driessche and Watmough [31] for model system (2), the matrices F and V for the new infection terms and the remaining transfer terms are, respectively, given by:

$$F = \begin{bmatrix} 0 & \frac{\beta K S^*}{(k+B^*)^2} \\ 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} \omega & 0 \\ -\delta & r\theta\rho - 2r(\theta+\rho)B^* + 3r(B^*)^2 \end{bmatrix}$$

Following Van den Driessche and Watmough [31], the basic reproduction number of infections in population where Q^* is fixed is then the spectral radius of the next generation matrix FV^{-1},

$$\mathscr{R}_0(Q^*) = \frac{\beta K \delta S^*}{(K+B^*)^2 \omega (r\theta\rho - 2r(\theta+\rho)B^* + 3r(B^*)^2)} \tag{37}$$

Appendix E: Proof of Theorem 3.5.

The proof will be the same like in Appendix C. Let us made the following simplification and change of variables: Let $y_1 = S$, $y_2 = I$, $y_3 = R$, $y_4 = B$. Further, by using the vector notation $y = (y_1, y_2, y_3, y_4)$. The model (2) can be written in the form $\dot{y} = g(y)$ with $g = (g_1, g_2, g_3, g_4)$ as follows:

$$\begin{cases} \dot{y_1} &= \Lambda - (\lambda+\mu)y_1 + \gamma y_3, \\ \dot{y_2} &= \lambda y_1 - \omega y_2, \\ \dot{y_3} &= \alpha y_2 - (\gamma+\mu)y_3, \\ \dot{y_4} &= r y_4(y_4-\theta)(\rho - y_4) + \delta y_2, \end{cases} \tag{38}$$

where $\lambda = \beta \frac{y_4}{y_4+K}$. System (38) has a DFE given by $\mathrm{Q}_\rho = (S_0, 0, 0, \rho)$ where $S_\rho = \frac{\Lambda(\rho+K)}{\beta\rho+\mu(\rho+K)}$. The Jacobian of system (2) at the DFE Q_ρ is

$$J(\mathrm{Q}_\rho) = \begin{bmatrix} -\mu - \frac{\beta\rho}{\rho+K} & 0 & \gamma & -\frac{\beta K \Lambda}{(k+\rho)[\beta\rho+\mu(\rho+K)]} \\ \frac{\beta\rho}{\rho+K} & -\omega & 0 & \frac{\beta K \Lambda}{(k+\rho)[\beta\rho+\mu(\rho+K)]} \\ 0 & \alpha & -(\mu+\gamma) & 0 \\ 0 & \delta & 0 & -r\rho(\rho-\theta) \end{bmatrix}.$$

Therefore, choosing β as a bifurcation parameter. Solving for β from $\mathscr{R}_0(\mathrm{Q}_\rho) = 1$, we obtain:

$$\beta = \beta^* = \frac{(K+\rho)\omega r\rho(\rho-\theta)[\beta\rho+\mu(\rho+K)]}{\Lambda K \delta}$$

It follows that the Jacobian $J(\mathrm{Q}_\rho)$ of system (2) at the DFE Q_ρ, denoted by simple J_{β^*} has a simple zero eigenvalue (with all other eigenvalue having negative real parts).

Eigenvectors of J_{β^*} . For the case when $\mathscr{R}_0(\mathrm{Q}_\rho) = 1$, it can be shown that the Jacobian of system (38) has a right eigenvector (corresponding to the zero eigenvalue), given by $U = (u_1, u_2, u_3, u_4)^T$, where

$$u_1 = 0, \;\; u_2 = u_2 > 0, \;\; u_3 = \frac{\alpha}{\mu+\gamma}u_2, \text{ and } u_4 = \frac{\delta}{r\rho(\rho-\theta)}u_2 \tag{39}$$

Similarly, the components of the left eigenvectors of J_{β^*} (corresponding to the zero eigenvalue), denoted by $V=(v_1,v_2,v_3,v_4)^T$, are given by:

$$v_1=v_1>0,\ \ v_2=\frac{[\beta\rho+\mu(\rho+K)]}{\beta\rho}v_1,\ \ v_3=\frac{\gamma}{\gamma+\mu}v_1,\ \text{and}\ v_4=\left[\frac{\omega[\beta\rho+\mu(\rho+K)]}{\beta\rho}-\frac{\alpha\gamma}{\gamma+\mu}\right]\frac{v_1}{\delta}$$

Computation of b For the sign of **b**, it can be shown that the associated non-vanishing partial derivatives of f are:

$$\frac{\partial^2 g_1}{\partial y_1\partial\beta^*}(0,0)=-\frac{\rho}{K+\rho},\ \frac{\partial^2 g_1}{\partial y_1\partial\beta^*}(0,0)=-\frac{K\Lambda}{(k+\rho)[\beta\rho+\mu(\rho+K)]},\ \frac{\partial^2 g_2}{\partial y_1\partial\beta^*}(0,0)=\frac{\rho}{K+\rho}$$

$$\text{and}\ \frac{\partial^2 g_2}{\partial y_1\partial\beta^*}(0,0)=\frac{K\Lambda}{(k+\rho)[\beta\rho+\mu(\rho+K)]}$$

It follows that

$$b=\frac{\mu(K+\rho)\omega}{\beta^*\rho}u_2>0$$

Computation of a: For system (38), the associated non-zero partial derivatives of g (at the DFE Q_ρ) are given by:

$$\frac{\partial^2 g_1}{\partial x_1x_4}(0,0)=-\frac{\beta^*K}{(K+\rho)^2},\ \frac{\partial^2 g_1}{\partial^2 x_4}(0,0)=\frac{2\beta^*K\Lambda}{(K+\rho)^2[\beta\rho+\mu(\rho+K)]},\ \frac{\partial^2 g_2}{\partial x_1x_4}(0,0)=\frac{\beta^*K}{(K+\rho)^2}$$

$$\text{and}\ \frac{\partial^2 g_1}{\partial^2 x_4}(0,0)=-\frac{2\beta^*K\Lambda}{(K+\rho)^2[\beta\rho+\mu(\rho+K)]}$$

Then, it follows that,

$$a=-\left(\frac{\delta}{r\rho(\rho-\theta)}\right)^2\left[\frac{2\beta^*K\Lambda\mu}{(K+\rho)[\beta\rho+\mu(\rho+K)]\beta^*\rho}+\left(\frac{\omega[\beta\rho+\mu(\rho+K)]}{\beta\rho\delta}-\frac{\alpha\gamma}{(\gamma+\mu)\delta}\right)\right]v_1u_2^2<0$$

Thus, $a<0$ and $b>0$ model system (2) undergoes the phenomenon of forward bifurcation (see Theorem 4.1, item (4)). So we have established the result about the local stability of the endemic equilibrium of cholera disease model when Q_ρ is suppose be a disease-free equilibrium (note that this result holds for $\mathscr{R}_0(Q_\rho)>1$ but close to 1). This concludes the proof of Theorem 3.5.