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Stability analysis of cholera epidemic model of a closed population

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Abstract

We present a mathematical model of cholera epidemics of closed population that comprises seasonality of infection, the loss of immunity and control mechanism related to sanitation, hygiene, water treatment and vaccination. This model exhibits the traditional threshold behavior. There is always a globally asymptotically stable equilibrium state. Depending on the value of the basic reproduction ratio R_0, this state can be either endemic ($R_0 > 1$), or infection - free ($R_0 < 1$). We demonstrate a real-world application of this model by investigating the recent cholera outbreak in Cameroon. Meanwhile, we present numerical results to verify the analytical prediction.

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Keywords: cholera epidemics, dynamical system, Equilibrium, Stability, basic reproduction number

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1 Introduction

The cholera was a long time and continues to be a major question of health in the world. In spite of a hundred years studies on the disease, there is in the world 3 to 5 million cases of cholera with 100.000 to 120.000 deaths per year (memory Assistance WHO N°107, June 2010). The war and environmental unhealthy conditions can contribute to the expansion of the disease within the communities. Thus, because residence with cholera is a threat for the world, it is significant to continue to test to include/understand the dynamics of the disease and how interactions between the environmental man and factors contribute to the behavior of the epidemic.

During centuries, the disease remains unknown in Europe, propagated especially in Asia and Africa. First mention of this disease in Europe is made in 1503 by a Portuguese officer returning from the Indies, telling a disease having made 20.000 deaths. It appeared thereafter in Europe and was the object of a crowd of interpretations and theories on behalf of the medicines. It is at the time of the epidemic of 1854, in London, that comprehension of the disease knew a major projection. One account returned with the disease struck near certain wells, suggesting a contamination by water. But this assumption was not immediately allowed at the time. Vibrio cholerae, the bacterium in charge of the cholera was for the first time isolated like person suffering from cholera by the Italian anatomist Filippo Pacini in 1854. But its discovery will be ignored because of the predominance theory of miasma, charging the responsibility for cholera (and other diseases which one did not know the origin) with one bad quality of the air. Thirty years later, Robert Koch, who does not know about the results of Pacini, publishes the result of its work and means of fighting vibrio cholerae. In 1965, the bacterium is re-elected in vibrio cholorae in homage to Filippo Pacini.

The cholera is an extremely virulent disease. Concerning children like the adults, one can die some in a few hours. Approximately 75 percent of the subjects infected by v. cholorae express any symptom, although the bacillus is present in their saddles during 7 to 14 days after the infection and is eliminated in the environment, where it can potentially infect other people or those which express symptoms, those remain benign with moderate in 80 percent of the cases, while at approximately 20 percent of the cases, an acute aqueous

diarrhoea, accompanying by severe dehydration, vomiting but without developing rise in temperature. Saddles, fecaloides at the beginning, quickly become aqueous, color water of rice. This significant water lead to leakage of intense cramps being propagated in all the body, pushing the eyes in the orbits, contracting orbicular muscles of the lips then resulting in giving one pace cyanosis with the face of the patient. In the absence of treatment, it can lead to death. Subjects having weak immunity, children suffering from malnutrition or people living with the HIV for example, are more exposed to the risk of death in the event of infection.

The cholera results from absorption, by ingestion, of the vibrio choleraic present in water or food, but also can be the result of a contaminated person to another person through pathological products (saddles, vomiting, sweat). Experiments show that the vibrios introduced into food are more likely to cause an infection than those introduced into water. The infectious amount, in experiments given is of the order of 10^8 with 10^{11} bacteria see [8]. Gastric acidity is not very favorable with the survival of the bacterium in the stomach. When the vibrios choleric are included in food or that the gastric acidity was neutralized by one bicarbonate of soda solution, the infectious amount is of the order of 10^4 with 10^8 bacteria only. After passage of gastric barrier, the vibrios are fixed in the proximate part of the small intestine, crosses the layer of mucus and secrete choleraic toxin. This modifies the exchanges of water and electrolytes by preventing the penetration of sodium inside cell. That causes a passage in the light of the tube digestive of a very great quantity of water being able to reach 15 liters per day, and leads to a severe dehydration on the sick individual see [4]. The transmission of the cholera is closely related to a bad management of the environment. One find in the zones with risk typical, the shantytowns peri urban which do not have any basic infrastructure, or them campuses of refugees or moved people, where minimal needs out of clean water and cleansing are not assured. Catastrophes, with the interruption of the systems of supply of water and of cleansing, or moving of populations in the camps badly equipped and over-populated, have as a consequence to increase the risk of transmission of the cholera, if ever its bacillus is present or if it is introduced. there never was epidemics starting from the corpses. Remainder on the scale is that the cholera is a world threat for the public health and it is an indicator key of the insufficiency of the social development. One has

besides observed its reemergence recently, parallel to the increase continual of the vulnerable populations living in the bad ones conditions of hygiene. The number of the cases of the cholera notified to WHO continue to grow. From 2004 to 2008, this increase was of 24 percent compared to period 2000 - 2004. only in 2008, 56 country notified 190.130 cases, including 5.143 mortals. But many of cases are not listed because of the limitations monitoring systems and fear of sanctions limiting voyages and trade.It is estimated that the true assessment of the disease amounts to $3-5$ million cases and $100.000-120.000$ deaths per year.

The bacterium vibrio cholerae (vibrio choleraic or bacillus comma in French) is a bacterium gram negative, in the shape of stick curved, mobile, oxidase positive, belonging to the family of vibrionaceae, with the vibrio kind, the species vibrio cholerae and person in charge of the cholera at the man.

The vibrio choleric lives in water and has a great capacity of environmental survival. It tolerates salinity very well but really does not find itself in sea but rather in the estuaries, the rivers, ground water and all sources of water contaminated by human dejections. Sweat, rich in vibrios, plays a significant role in the contaminations inter - human especially in dry tropical zones. It seems that certain shellfish (in particular shrimps) play a role of vector thanks to receivers located on their dorsal shells. The vibrio choleric is sensitive to the acid and dies in a solution having a PH lower than 6.

All the stocks of the species vibrio choleric are not persons in charge of the cholera. Indeed, stocks belonging to the species vibrio cholerae can be classified according to the structure of the antigen O see [5]. To date, nearly 200 semigroups O are known according to [16], but only the stocks belonging to the semigroups O1 and O139 were associated with major epidemics. Stocks belonging to the other serogroup can cause sporadic diarrheas, of the abscess or of septicaemia see [11]. Among stocks of the serogroup O1, it is made distinction of two biotype, the first known as "traditional" and the second named "El Tor". For each one of these biotype, there are three serotype: Ogawa, Iniba and Hikojima.

Production of choleraic toxin by the epidemic stocks and pandemic of vibrio cholerae is responsible of the phenotype of the disease. The pathogenicity of these stocks is the result of the action combined to a whole of factors authorizing the colonization of medium (motility, attachment) and of toxins. The

genome of filamentous bacteriophage lysogene CTXΦ contains genes ctxAB which codes the toxin choleric [21]. CTXΦ by its capacity to lyse the bacterial wall, integrates sound genome in that of the choleraic vibrio and thus allows production of the toxin [12]. This transduction is a very good example of horizontal transfer of genes which code the choleraic toxin, as well as transfer of the genes which constitute the small island of pathogenicity of vibrio cholerae [13]. Another significant factor implied in virulence pathogenic stocks of vibrio cholerae is a hair Co - controlled TCP (toxin Co - regulated pili). Its role was initially identified in colonization by vibrio cholerae of the intestinal wall, but proved to be in reality , more directly related to the development of pathogenic capacity by being used as receiver for the CTXΦ bacteriophage.

The various stocks of vibrio cholerae release thereafter from new bacteriophages on the one hand in the digestive tract of the host human and in addition in the watery environment.

Epidemiology is dominated by the hydrous transmission, like it is the case in other enteric diseases. It is thus little probable that wide epidemics can occur in the countries where the bacteriological control of water is strictly applied, even if localized hearths burst. Overpopulation, lack of personal hygiene and food can also contribute to the propagation of the disease. The flies also play a considerable role in the spread of the vibrios.

In the sections above, we present and proceed to analysis of the stability of a model of dynamics of infection of the cholera which takes into account intrinsic and extrinsic factors.

2 The model

The mathematical model described here is a modified version of a model developed in [18] in which one considers that the population is closed, i.e., one is unaware of immigration and emigration and focus only on births and deaths.

One considers a closed population of nonconstant size N divided into three groups : the Susceptible, $\mathbf{S}$, Infected, $\mathbf{I}$ and Recovered, $\mathbf{R}$ such as $N = S+I+R$.

One indicates by $\mathbf{B}$ the concentration of the pathogenic stocks of vibrio choleric in water or bacterial abundance.

It is supposed that all the individuals of population N are born susceptible. The only voice of infection of the susceptible individuals (S) is the ingestion

of a water coming from an untreated source, in other terms, the susceptible individuals (S) are infected with contact of contaminated water (is - with - to say B). Infected cure at a rate r. As long as there remains infected, the individual contribute to the increase in the population of the bacterium to through its excretions at a rate e. Bacterial abundance (B) decrease at a rate γ and can also grow at a rate determined by certain environmental factors (the temperature for example).

The effects of the seasonality are described by a periodical variation of the parameter of contact β between the bacteria and the hosts.

Various mechanisms of controls are taken into account here in particular: the reduction of the parameter of contact β by $\theta_1 < \beta$, the cleansing improved (reduction of parameter e by $\theta_2 < e$), water treatment (increase in the parameter γ by θ_3) and vaccination (reduction in the number of susceptible by θ_4).

Remark 2.1. *The parameters β, θ_1, θ_2, θ_3 and θ_4 can depend on time.*

Remark 2.2. *Probability so that a susceptible individual infects himself is governed by an equation of Michaelis - Menten in [14], since the probability of catching the cholera depend on the concentration of the vibrio choleric in consumed water (relation proportions - answer) [1]. Here, this probability is given by $\lambda(B) = \frac{B}{K+B}$.*

The compartmental model can be described by the following set of five differential equation for the closed population, N, susceptible, S, infected, I, recovered, R, and bacterial abundance, B :

$$\begin{cases} \frac{dN}{dt} = & \Pi - \mu N - dI, \\ \frac{dS}{dt} = & \Pi - \mu S - (\beta(t) - \theta_1(t))\frac{B}{K+B}S + r_1 R - \theta_4(t)S, \\ \frac{dI}{dt} = & (\beta(t) - \theta_1(t))\frac{B}{K+B}S - (r + \mu + d)I, \\ \frac{dR}{dt} = & rI + \theta_4(t)S - (r_1 + \mu)R, \\ \frac{dB}{dt} = & (e - \theta_2(t))I - (\gamma + \theta_3(t))B. \end{cases} \tag{1}$$

Summarily, in the first equation, individuals of closed population at renewed at a rate Π, decrease at rates m and d respectively natural and with

the cholera. In the second equation, susceptible individuals are renewed at a rate Π, infect themselves at a rate $(\beta(t) - \theta_1(t)$ and is transferred by vaccination in the class of cured at a rate of $\theta_4(t)$. Susceptible individuals also increases thanks to the return of people who lose their immunity at a rate r_1 and decreases by natural death with a rate μ.

The third equation describes the temporal evolution of the people infected, which increases by the contact of susceptible with vibrio choleric and decreases by the cure by natural death or the death of people by the disease.

In the four equation, the increases in the immunizing class are due to the individuals lately immunized at a rate r and by a rate θ_4 following vaccination. The number of cured decreases by the loss of immunity and natural death of individuals.

Lastly, the last equation describes the dynamics of the vibrio choleric in the watery tank (supposed to be here the untreated unit and consumed by the population), dynamics who increases by the contribution of the individuals infected by a rate $(e - \theta_2(t))$ and decreases by the mortality of the bacteria $(\gamma + \theta_3(t))$, where γ is the rate of natural mortality.

The rate of contact $\beta(t)$ can be periodic and limited to its seasonal effects (floods, dryness, variations from temperature) [10]. Mathematical analysis of a periodic epidemic model has been study in several authors see [1], [2], [3], [17], [22], [24].

2.1 Symbols used in the model

2.2 specific cases

Before proceeding to the study of the basic properties of the model, let us consider the simple cases of infection at hundred percent in the event of contact of one infected and one not infected ($\lambda(B) = 1$), and probability of null infection ($\lambda(B) = 0$), [6].

Case one. We assume the concentration of V. cholerae in water are much lower than concentration of the pathogenic stocks of the vibrio Choleric in water, i.e., $B << K$. Then the incidence rate in the model $\lambda(B)$ become

$$\lambda(B) = \frac{B}{K + B} \approx 0,$$

Table 1: Description of the parameters of the system (1)

Symbols	Description
Variables of state	
N	Numbers of individuals of population
S	Numbers of susceptible
I	Numbers of infected
R	Numbers of recovered
B	Concentration of the pathogenic stocks of the vibrio Choleric in water (cells/ml)
Parameters	
μ	natural mortality rate
d	death rate of patients with the cholera
β	contact rate between bacterial and susceptible hosts
K	concentration of V. cholerae in water (cells/ml)
r_1	rate at which people lose immunity (day^{-1})
r	rate at which people recover from the disease(day^{-1})
γ	bacterial mortality rate(day^{-1})
e	contribution of each infected person to the population of V cholerae in the aquatic environment (cell/ml $day^{-1}person^{-1}$)

which implies the chance of getting new infection is about 0.

The model (1) in the particular conditions where β constant and in absence of the mechanisms of control in this case is given by :

$$\begin{cases} \frac{dN}{dt} = \Pi - \mu N - dI, \\ \frac{dS}{dt} = \Pi - \mu S + r_1 R, \\ \frac{dI}{dt} = -(r + \mu + d)I, \\ \frac{dR}{dt} = rI - (r_1 + \mu)R, \\ \frac{dB}{dt} = eI - \gamma B. \end{cases} \tag{2}$$

Applying the theory of differential equation see [9], [7], [19], the exact solution of system (2) is

$$\begin{aligned}
N(t) &= c_1 e^{-\mu t} + \frac{\Pi}{\mu} + \frac{rI(0)}{r+d-r_1}(\frac{r_1}{r+d} - 1)e^{-(r+d+\mu)t} + I(0)e^{-(r+d+\mu)t} \\
S(t) &= c_1 e^{-\mu t} + \frac{\Pi}{N} - c_2 e^{-(r_1+\mu)t} + \frac{rr_1 I(0)}{(r+d)(r+d-r_1)}e^{-(r+d+\mu)t} \\
I(t) &= I(0)e^{-(r+d+\mu)t} \\
R(t) &= c_2 e^{-(r_1+\mu)t} - \frac{rI(0)}{r+d-r_1}e^{-(r+d+\mu)t} \\
B(t) &= c_3 e^{-\gamma t} - \frac{eI(0)}{r+\mu+d-\gamma}e^{-(r+d+\mu)t}
\end{aligned}$$

where c_1, c_2 and c_3 are constants.
Thus, it is clear to see that

$$N(t) \to \frac{\Pi}{N}, \;\; S(t) \to \frac{\Pi}{N}, \;\; I(t) \to 0, \;\; R(t) \to 0, \;\; B(t) \to 0 \;\text{ as }\; t \to +\infty.$$

Hence, the point $E^0 = (\frac{\Pi}{\mu}, \frac{\Pi}{\mu}, 0, 0, 0)$ is globally asymptotically stable.

The Figure 1 presents the trajectories of the model (2) for the initial conditions $N(0) = 20.10^6$; $S(0) = 20.10^6$; $I(0) = 0$; $R(0) = 0$; $B(0) = 10^8$ and parameters values given low to Table 4. One clearly notes there the global asymptotic stability of the disease free equilibrium $E^0 = (\frac{\Pi}{\mu}, \frac{\pi}{\mu}, 0, 0, 0)$.

Case two. We now assume concentration of the pathogenic stocks of the vibrio Choleric in water are far beyond concentration of V. Cholerae in water, i.e., $B >> K$. Under this assumption, the incidence rate in the model $\lambda(B)$ become

$$\lambda(B) = \frac{B}{K+B} \approx 1$$

That is, the possibility of infection is about hundred percent to those exposed to pathogens.

The model (1) in the particular conditions where β constant and in absence

of the mechanisms of control is given by :

$$\begin{cases} \frac{dN}{dt} = & \Pi - \mu N - dI, \\ \frac{dS}{dt} = & \Pi - (\mu + \beta)S + r_1 R, \\ \frac{dI}{dt} = & \beta S - (r + \mu + d)I, \\ \frac{dR}{dt} = & rI - (r_1 + \mu)R, \\ \frac{dB}{dt} = & eI - \gamma B. \end{cases} \tag{3}$$

we will reconsider the model (3) later.

3 Basic properties of the model

3.1 Positivity of the solutions

Like all variables of state of the mathematical model (1) presented higher (Closed population, Susceptible, Infected, Recovered and population of the vibrio choleraic in water) are densities, it matters that they are positive. Thus, we need to show positivity of the solutions of (1).

Let us suppose that the initial conditions of the model is given by

$$N(\xi) = \phi_1(\xi), \quad S(\xi) = \phi_2(\xi), \quad I(\xi) = \phi_3(\xi), \quad B(\xi) = \phi_4(\xi), \quad R(\xi) = \phi_5(\xi),$$

with $\xi \in [-\infty, 0]$, where $(\phi_1, \phi_2, \phi_3, \phi_4, \phi_5) \in C([-\infty, 0], \mathbb{R}^5)$ and $\phi_i(t) \geq 0$ $(i = 1, 2, 3, 4, 5)$, where $C([-\infty, 0], \mathbb{R}^5)$ is banach space of continuous functions of $[-\infty, 0]$ towards $\mathbb{R}^5$.

From a biological point of view, we admit that $\phi_i(0) > 0$, $(i = 1, 2, 3, 4, 5)$.

Theorem 3.1. *If there are the initial conditions*

$$N(\xi) = \phi_1(\xi) \geq 0, \quad S(\xi) = \phi_2(\xi) \geq 0, \quad I(\xi) = \phi_3(\xi) \geq 0,$$
$$B(\xi) = \phi_4(\xi) \geq 0, \quad R(\xi) = \phi_5(\xi) \geq 0$$

for all $\xi \in [-\infty, 0]$, *with* $\phi_i(0) > 0$ $(i = 1, 2, 3, 4, 5)$, *then the solutions* $N(t)$, $S(t)$, $I(t)$, $B(t)$ *and* $R(t)$ *of (1) are positive for all* $t \geq 0$.

Proof It is established for $\theta_i(t)$ $(i = 1, 2, 3, 4, 5)$ constant. The case $\theta_i(t)$, $(i = 1, 2, 3, 4, 5)$ variable spreads very easily.

Let us consider

$$T = \sup\{t > 0 : N(t) > 0, S(t) > 0, I(t) > 0, B(t) > 0, R(t) > 0 \ for\, 0 < t < T\}$$

clearly, $T > 0$. However, if $T = \infty$, then $N(t)$, $S(t)$, $I(t)$, $B(t)$ et $R(t)$ are coarsely positive for $t > 0$.

Let us suppose $T < \infty$, then at least one of $N(T)$, $S(T)$, $I(T)$, $B(T)$ or $R(T)$ is equal to zero. In the contrary case, that would contradict the definition of T.

Let us suppose $B(T) = 0$. The equation out of B given by the system (1) is

$$\frac{dB}{dt} = (e - \theta_2(t))I - (\gamma + \theta_3(t))B$$

By solving the associated homogeneous equation and by using the method variation of the constant, one arrives has

$$B(t) = B(0)e^{-(\gamma+\theta_3)t} + [\int_0^t (e - \theta_2)I(u)e^{(\gamma+\theta_3)u}du]e^{-(\gamma+\theta_3)t} > 0$$

which is a contradiction. Therefore, $B(t) > 0$, for all $t > 0$.

Let us suppose $S(T) = 0$. Then according to the equation in S of the system (1) one can write :

$$\begin{aligned} \frac{d}{dt}(Se^{\int_0^t (\beta-\theta_1)\frac{B}{K+B}(u)du+(\mu+\theta_4)t}) &= \Pi e^{\int_0^t (\beta-\theta_1)\frac{B}{K+B}(u)du+(\mu+\theta_4)t} \\ &+ r_1 Re^{\int_0^t (\beta-\theta_1)\frac{B}{K+B}(u)du+(\mu+\theta_4)t} \end{aligned}$$

While integrating this relation of 0 with T, one obtains

$$\begin{aligned} S(T)e^{\int_0^T (\beta-\theta_1)\frac{B}{K+B}(u)du+(\mu+\theta_4)T} - S(0) &= \int_0^T [\Pi e^{\int_0^t (\beta-\theta_1)\frac{B}{K+B}(v)dv+(\mu+\theta_4)u} \\ &+ r_1 Re^{\int_0^t (\beta-\theta_1)\frac{B}{K+B}(v)dv+(\mu+\theta_4)u}]du \end{aligned}$$

what leads to

$$\begin{aligned} S(T) &= S(0)e^{-\int_0^T (\beta-\theta_1)\frac{B}{K+B}(u)du+(\mu+\theta_4)T} \\ &+ e^{-\int_0^T (\beta-\theta_1)\frac{B}{K+B}(u)du+(\mu+\theta_4)T} \int_0^T [\Pi e^{\int_0^t (\beta-\theta_1)\frac{B}{K+B}(v)dv+(\mu+\theta_4)u} \\ &+ r_1 Re^{\int_0^t (\beta-\theta_1)\frac{B}{K+B}(v)dv+(\mu+\theta_4)u}]du > 0 \end{aligned}$$

which is a contradiction. From the last proof arises that $S(t) > 0$ for $t > 0$.

In the same way, according to the equation out of I of the system (1) one has

$$\frac{d}{dt}(Ie^{(r+\mu+d)t}) = e^{(r+\mu+d)t}(\beta - \theta_1)\frac{B}{K+B}S.$$

While integrating of 0 with T one obtains

$$I(T)e^{(r+\mu+d)T} - I(0) = \int_0^T e^{(r+\mu+d)u}(\beta - \theta_1)\frac{B}{K+B}(u)S(u)du$$

which leads to

$$I(T) = I(0)e^{-(r+\mu+d)T} + e^{(r+\mu+d)T}\int_0^T e^{(r+\mu+d)u}(\beta - \theta_1)\frac{B}{K+B}(u)S(u)du > 0.$$

From the last proof arises that $I(t) > 0$ for any value from $t > 0$.

In a similar way, equation in R of the system (1) one can write

$$\frac{d}{dt}(Re^{(r_1+\mu)t}) = (rI + \theta_4 S)e^{(r_1+\mu)t}$$

What enables us to have while integrating 0 into T

$$R(T) = R(0)e^{-(r_1+\mu)T} + e^{-(r_1+\mu)t}\int_0^T (rI(u) + \theta_4 S(u))e^{(r_1+\mu)u}du > 0,$$

which shows that $R(t) > 0$ for all $t > 0$.

Let us suppose $N(T) = 0$, the equation out of N given by the system (1) is

$$\frac{dN}{dt} = \Pi - \mu N - dI.$$

By solving the associated homogeneous equation and by using the method variation of the constant, one arrives has

$$N(t) = N(0)e^{-\mu t} + [\int_0^t (\Pi - dI(u))e^{\mu u}du]e^{-\mu t} > 0$$

which is contradiction. Therefore $N(T) > 0$ for all $t > 0$.

One concludes as well as the solution $N(t)$, $S(t)$, $I(t)$, $B(t)$, $R(t)$ of (1) is positive for any value of $t \geq 0$. □

3.2 Positive invariance of the nonnegative orthant

We have the following result :

Proposition 3.2. *The nonnegative orthant $\mathbb{R}^5_+$ is positively invariant for the system (1).*

Proof The positive invariance of the nonnegative orthant $\mathbb{R}^5_+$ of (1) is immediate with the assumption and positivity of the solutions on the model. □

4 Equilibria

Lemma 4.1. *The disease - free equilibrium of system (1) is given by*

$$E^0 = (\frac{\Pi}{\mu}, \frac{\Pi}{\mu}, 0, \frac{\theta_4(t)\Pi}{\mu(r_1+\mu+\theta_4(t))}, 0)$$

and the endemic equilibrium by

$$E^1 = (N^*, S^*, I^*, R^*, B^*),$$

where

$$\begin{aligned}
N^* &= \frac{1}{\mu}(\Pi - \frac{da_1a_2a_4}{(\beta(t)-\theta_1(t))a_3 - a_1a_2}),\\
S^* &= \frac{\frac{\Pi}{\mu}a_1[(\beta(t)-\theta_1(t))a_3 - a_1a_2] - a_1a_2a_4a_8}{a_1[(\beta(t)-\theta_1(t))a_3 - a_1a_2]},\\
I^* &= \frac{a_1a_2a_4}{(\beta(t)-\theta_1(t))a_3 - a_1a_2},\\
R^* &= \frac{a_7 + a_1a_2a_4a_5}{a_1[(\beta(t)-\theta_1(t))a_3 - a_1a_2]},\\
B^* &= \frac{a_1a_2a_4a_6}{(\beta(t)-\theta_1(t))a_3 - a_1a_2}.
\end{aligned}$$

with

$$\begin{aligned}
&a_1 = \mu(r_1+\mu+\theta_4(t)), \quad a_2 = r+\mu+d, \quad a_3 = (r_1+\mu)(\Pi-d-\mu) - \mu r,\\
&a_4 = \frac{K(\gamma+\theta_3(t))}{e-\theta_2(t)}, \quad a_5 = \mu r - \theta_4(t)(d+\mu), \quad a_6 = \frac{e-\theta_2(t)}{\gamma+\theta_3(t)},\\
&a_7 = \theta_4(t)\Pi((\beta(t)-\theta_1(t))a_3 - a_1a_2), \quad a_8 = (d+\mu)(r_1+\mu) + \mu r + \theta_4(t)\Pi.
\end{aligned}$$

Proof $[N^*, S^*, I^*, R^*, B^*]$ equilibrium of system (1) if and only if :

$$\frac{dI^*}{dt} = 0; \quad \frac{dR^*}{dt} = 0; \quad \frac{dB^*}{dt} = 0; \quad \frac{dN^*}{dt} = 0; \quad \text{and} \quad S^* = N^* - I^* - R^*,$$

which is equivalent to :

$$\begin{cases} (\beta(t) - \theta_1(t))\frac{B^*S^*}{K+B^*} - (r + \mu + d)I^* = 0 \\ rI^* + \theta_4(t)S^* - (r_1 + \mu)R^* = 0 \\ (e - \theta_2(t))I^* - (\gamma + \theta_3(t))B^* = 0 \\ N^* = \frac{1}{\mu}(\Pi - dI^*) \\ S^* = N^* - I^* - R^* \end{cases} \tag{4}$$

The third equation of (4) leads to :

$$B^* = \frac{(e - \theta_2(t))I^*}{\gamma + \theta_3(t)} \tag{5}$$

The fifth equation of (4) makes it possible to write:

$$S^* = \frac{1}{\mu}\Pi - (\frac{d}{\mu} + 1)I^* - R^* \tag{6}$$

The second equation of (4) allows to draw

$$R^* = \frac{\theta_4(t)\Pi + (\mu r - \theta_4(t)(d + \mu))I^*}{\mu(r_1 + \mu + \theta_4(t))}, \tag{7}$$

Thus, (7) in (6) allows to have

$$S^* = \frac{1}{\mu}\Pi - \frac{(d + \mu)(r_1 + \mu) + \mu r + \theta_4(t)\Pi}{\mu(r_1 + \mu + \theta_4(t))}I^*. \tag{8}$$

(5), (8) in the first equation of (4) leads to

$$\frac{(\beta(t) - \theta_1(t))(e - \theta_2(t)[(r_1 + \mu)(\Pi - d - \mu) - \mu r]}{\mu(r_1 + \mu + \theta_4(t))[K(\gamma + \theta_3(t)) + (e - \theta_2(t))I^*]}I^2 - (r + \mu + d)I^* = 0,$$

that is to say

$$\begin{aligned} \{\, (\beta(t) - \theta_1(t))(e - \theta_2(t))[(r_1 + \mu)(\Pi - d - \mu) - \mu r] \\ - \mu(r + \mu + d)(r_1 + \mu + \theta_4(t))(e - \theta_2(t))\,\}I^2 \\ - K\mu(r + \mu + d)(r_1 + \mu + \theta_4(t))(\gamma + \theta_3(t))I^* = 0 \end{aligned}$$

What makes it possible to find:

$$I^* = 0$$

or

$$\begin{aligned} I^* &= \\ &= \frac{K\mu(r_1+\mu+\theta_4(t))(r+\mu+d)(\gamma+\theta_3(t))}{(e-\theta_2(t))[(\beta(t)-\theta_1(t))[(r_1+\mu)(\Pi-d-\mu)-\mu r]-\mu(r+\mu+d)(r_1+\mu+\theta_4(t))]} \end{aligned} \tag{9}$$

Let us suppose:

$$\begin{aligned} &a_1 = \mu(r_1+\mu+\theta_4(t)), \quad a_2 = r+\mu+d, \\ &a_3 = (r_1+\mu)(\Pi-d-\mu)-\mu r, \quad a_4 = \frac{K(\gamma+\theta_3(t))}{e-\theta_2(t)} \end{aligned}$$

Then, according to (9) we have :

$$I^* = \frac{a_1 a_2 a_4}{(\beta(t)-\theta_1(t))a_3 - a_1 a_2} \tag{10}$$

- For $I^* = 0$ one obtains according to (5), (7) and (8) :

$$B^* = 0, \tag{11}$$

$$R^* = \frac{\theta_4(t)\Pi}{\mu(r_1+\mu+\theta_4(t))} \tag{12}$$

and

$$S^* = \frac{\Pi}{\mu} \tag{13}$$

Thanks to the fourth equation of (4), one obtains :

$$N^* = \frac{\Pi}{\mu}, \tag{14}$$

fromwhere disease - free equilibrium is taking into account (11), (12), (13) and (14)

$$E^0 = (\frac{\Pi}{\mu}, \frac{\Pi}{\mu}, 0, \frac{\theta_4(t)\Pi}{\mu(r_1+\mu+\theta_4(t))}, 0) \tag{15}$$

- For

$$I^* = \frac{a_1 a_2 a_4}{(\beta(t)-\theta_1(t))a_3 - a_1 a_2} \tag{16}$$

Let us suppose:

$$a_5 = \mu r - \theta_4(t)(d+\mu), \quad a_6 = \frac{e-\theta_2(t)}{\gamma+\theta_3(t)},$$
$$a_7 = \theta_4(t)\Pi((\beta(t)-\theta_1(t))a_3 - a_1a_2), \quad a_8 = (d+\mu)(r_1+\mu)+\mu r+\theta_4(t)\Pi.$$

One has then taking into account (5), (7), (8), and of the fourth equation of (4) :

$$B^* = \frac{a_1a_2a_4a_6}{(\beta(t)-\theta_1(t))a_3 - a_1a_2}, \tag{17}$$
$$R^* = \frac{a_7 + a_1a_2a_4a_5}{a_1[(\beta(t)-\theta_1(t))a_3 - a_1a_2]}, \tag{18}$$
$$S^* = \frac{\frac{\Pi}{\mu}a_1[(\beta(t)-\theta_1(t))a_3 - a_1a_2] - a_1a_2a_4a_8}{a_1[(\beta(t)-\theta_1(t))a_3 - a_1a_2]}. \tag{19}$$

and,

$$N^* = \frac{1}{\mu}(\Pi - \frac{da_1a_2a_4}{(\beta(t)-\theta_1(t))a_3 - a_1a_2}), \tag{20}$$

fromwhere endemic equilibrium is :

$$E^1 = (N^*, S^*, I^*, R^*, B^*) \tag{21}$$

with N^*, S^*, I^*, R^* and B^* defines respectively by (20), (19), (16), (18) and (17). □

Remark 4.2. *The model (3) does not have disease - free equilibrium for obvious reason and its endemic equilibrium is* $E^1 = (N^*, S^*, I^*, R^*, B^*$ *with*

$$\begin{aligned} I^* &= \frac{\beta\Pi(r_1+\mu)}{(r+\mu+d)(r_1+\mu)(\beta+\mu) - \beta r_1 r} \\ R^* &= \frac{r}{r_1+\mu}I^* \\ B^* &= \frac{eI^*}{\gamma} \\ S^* &= \frac{1}{\beta+\mu}(\Pi + \frac{r_1 r}{r_1+\mu})I^* \\ N^* &= S^* + I^* + R^* \end{aligned}$$

5 Analysis of stability

In this part, we study stability in the case β constant and in absence of the mechanisms of control.

5.1 Basic reproduction number analysis and stability of the disease - free equilibrium

We have in the case considered and taking into account the lemma 4.1 $E^0 = (\frac{\Pi}{\mu}, \frac{\Pi}{\mu}, 0, 0, 0)$.

We will study stability of the disease - free equilibrium by using the linearization method presented in [20]. The jacobian matrix of the system (1) in a point $(N,\ S,\ I,\ R,\ B)$ are given by:

$$J = \begin{pmatrix} -\mu & 0 & -d & 0 & 0 \\ 0 & -\mu - \beta\frac{B}{K+B} & 0 & r_1 & -\beta\frac{KS}{(K+B)^2} \\ 0 & \beta\frac{B}{K+B} & -r-\mu-d & 0 & \beta\frac{KS}{(K+B)^2} \\ 0 & 0 & r & -r_1-\mu & 0 \\ 0 & 0 & e & 0 & -\gamma \end{pmatrix} \tag{22}$$

At the point $E^0 = (\frac{\Pi}{\mu}, \frac{\Pi}{\mu}, 0, 0, 0)$, this matrix is worth

$$J_{E_0} = \begin{pmatrix} -\mu & 0 & -d & 0 & 0 \\ 0 & -\mu & 0 & r_1 & -\beta\frac{\Pi}{\mu K} \\ 0 & 0 & -r-\mu-d & 0 & \beta\frac{\Pi}{\mu K} \\ 0 & 0 & r & -r_1-\mu & 0 \\ 0 & 0 & e & 0 & -\gamma \end{pmatrix} \tag{23}$$

The characteristic polynomial of (23) is given by

$$P(\lambda) = P_1(\lambda)P_2(\lambda), \tag{24}$$

with

$$P_1(\lambda) = (-\mu-\lambda)^2(-r_1-\mu-\lambda),$$

and

$$P_2(\lambda) = \lambda^2 + (r+\mu+d+\gamma)\lambda + \gamma(r+\mu+d) - \beta\frac{\Pi e}{\mu K}$$

Thus,

$$P_\lambda = 0 \Leftrightarrow P_1(\lambda) = 0 \quad or \quad P_2(\lambda) = 0$$

however,

$$P_1(\lambda) = 0 \Leftrightarrow \lambda_1 = \lambda_2 = -\mu < 0, \qquad \text{and} \qquad \lambda_3 = -r_1 - \mu < 0$$

In the same way,

$$P_2(\lambda) = 0 \Leftrightarrow \Delta = (r + \mu + d - \gamma)^2 + 4\beta e \frac{\Pi}{\mu K} > 0$$

what makes it possible to have

$$\lambda_4 = \frac{-r - \mu - d - \gamma - \sqrt{\Delta}}{2} < 0 \qquad \text{and} \qquad \lambda_5 = \frac{-r - \mu - d - \gamma + \sqrt{\Delta}}{2} \quad (25)$$

As regards the sign λ_5, let us notice that one has:

$$\Delta - (r + \mu + d + \gamma)^2 = 4\gamma(r + \mu + d)[\frac{\beta \Pi e}{\mu K \gamma (r + \mu + d)} - 1] \qquad (26)$$

We define the basic reproduction number, R_0, of this model by

$$R_0 = \frac{\beta \Pi e}{\mu K \gamma (r + \mu + d)}, \qquad (27)$$

one has the following Lemma:

Lemma 5.1. *If $R_0 < 1$ then the disease - free equilibrium $E^0 = (\frac{\Pi}{\mu}, \frac{\Pi}{\mu}, 0, 0, 0)$ is globally asymptotically stable in $\mathbb{R}^5_+$. If $R_0 > 1$, it is unstable.*

Proof $E^0 = (\frac{\Pi}{\mu}, \frac{\Pi}{\mu}, 0, 0, 0)$ is asymptotically stable if only if $\lambda_5 < 0$. However according to (25), (26) and (27), that is checked if $R_0 < 1$. For the global attractivity, let us consider the Lyapunov function defines by :

$$L = eI + (r + \mu + d)B$$

Clearly, $L \geq 0$ and we have :

$$\begin{aligned} \dot{L} &= e\dot{I} + (r + \mu + d)\dot{B} \\ &= e\beta \frac{B}{K + B} S - \gamma(r + \mu + d)B \\ &= \frac{e\beta\Pi}{K\mu}(\frac{K}{K + B}.\frac{S\mu}{\Pi} - \frac{1}{R_0})B \leq \frac{e\beta\Pi}{K\mu}(\frac{K}{K + B} - \frac{1}{R_0})B \leq 0, \end{aligned}$$

because $\frac{K}{K+B} < 1$ and $R_0 < 1$. We also remark that $\dot{L} = 0$ if and only if $B = 0$.
Largest under - together compact invariant in $\{(N, S, I, R, B) \in \mathbb{R}^5_+ / \dot{L} = 0\}$ is the singleton $\{E^0\}$. Thus according to the asymptotic stability theorem of Lyapunov - LaSalle (see [19]), E^0 is overall globally asymptotically stable in $\mathbb{R}^5_+$. □

5.2 Stability of endemic equilibrium

5.2.1 Condition of existence of endemic equilibrium

Theorem 5.2. *Endemic equilibrium* $E^1 = (N^*, S^*, I^*, R^*, B^*)$ *exists if and only if* $R_0 > 1$.

Proof $E^1 = (N^*, S^*, I^*, R^*, B^*)$ exists if and only if $I^* > 0$, what is not possible while posing $A = \beta e[(r_1 + \mu)(d + \mu) + \mu r]$ and taking into account (9) that if and only if

$$\beta \Pi e(r_1 + \mu) > A + e\mu(r + \mu + d)(r_1 + \mu)$$

That is to say :

$$\frac{\beta \Pi e(r_1 + \mu)}{\mu K \gamma (r + \mu + d)(r_1 + \mu)} > e(\frac{A}{e(r_1 + \mu)(r + \mu + d)} + 1)$$

it is - with - to say

$$R_0 > 1$$

□

Lemma 5.3. *If* $R_0 > 1$, *endemic equilibrium* $E^1 = (N^*, S^*, I^*, R^*, B^*)$ *of system (1) is globally asymptotically stable in* $\mathbb{R}^5_+$.

Proof The jacobian matrix of system (1) at the point $E^1 = (S^*, I^*, R^*, B^*)$ is taking into account (22) given by :

$$J_{E_1} = \begin{pmatrix} -\mu & 0 & -d & 0 & 0 \\ 0 & -\mu - \beta\frac{B^*}{K+B^*} & 0 & r_1 & -\beta\frac{KS^*}{(K+B^*)^2} \\ 0 & \beta\frac{B^*}{K+B^*} & -r-\mu-d & 0 & \beta\frac{KS^*}{(K+B^*)^2} \\ 0 & 0 & r & -r_1 - \mu & 0 \\ 0 & 0 & e & 0 & -\gamma \end{pmatrix} \quad (28)$$

The corresponding characteristic equation reads

$$det|J_{E_1} - \lambda I| = 0, \tag{29}$$

where I is identity matrix.
(29) is equivalent to

$$\lambda^5 + a_1\lambda^4 + a_2\lambda^3 + a_3\lambda^2 + a_4\lambda + a_5 = 0, \tag{30}$$

with

$$\begin{aligned}
a_1 &= r_1 + \mu + r + \mu + d + \gamma + \mu + \beta\frac{B^*}{K+B^*} \\
a_2 &= (r_1+\mu)(r+\mu+d+\gamma) + \gamma(r+\mu+d) + \beta\frac{KS^*e}{(K+B^*)^2} \\
&\quad + (\mu + \beta\frac{B^*}{K+B^*})(r_1+\mu+r+\mu+d+\gamma) \\
&\quad + \mu(r_1+\mu+r+\mu+d+\gamma+\mu+\beta\frac{B^*}{K+B^*}) \\
a_3 &= \gamma(r_1+\mu)(r+\mu+d) - \beta\frac{KS^*e}{(K+B^*)^2}(r_1+\mu) \\
&\quad + (\mu+\beta\frac{B^*}{K+B^*})[(r_1+\mu)(\mu+d+\gamma) + \mu r + \gamma(r+\mu+d) + \beta\frac{KS^*e}{(K+B^*)^2}] \\
&\quad + \mu[(r_1+\mu)(r+\mu+d+\gamma) + \gamma(r+\mu+d) + \beta\frac{KS^*e}{(K+B^*)^2} \\
&\qquad + (\mu+\beta\frac{B^*}{K+B^*})(r_1+\mu+r+\mu+d+\gamma)] + \beta^2\frac{KS^*e}{(K+B^*)^3} \\
a_4 &= \mu[\gamma(r_1+\mu)(r+\mu+d) - \beta\frac{KS^*e}{(K+B^*)^2}(r_1+\mu)] \\
&\quad + \beta\frac{B^*}{K+B}[\gamma\mu(r+\mu+d) + \gamma r_1(\mu+d)] \\
&\quad + \mu[\gamma(r_1+\mu)(r+\mu+d) - \beta\frac{KS^*e}{(K+B^*)^2}(r_1+\mu) \\
&\qquad + \beta\frac{B^*}{K+B^*}[r_1(r+\mu+d+\gamma) + \gamma(r+\mu+d) + 2\beta\frac{KS^*e}{(K+B^*)^2}] \\
&\qquad + \mu[(r_1+\mu)(r+\mu+d+\gamma) + \gamma(r+\mu+d) + \beta\frac{KS^*e}{(K+B^*)^2}]] \\
a_5 &= -\mu\beta\frac{B^*}{K+B^*}[r_1 r + \beta\frac{KS^*e}{(K+B^*)^2}(r_1+\mu)]
\end{aligned}$$

Thus, conditions necessary and sufficient according to the criteria of Routh - Hurwitz [19] are :

$a_1 > 0, \quad a_1a_2 - a_3 > 0, \quad a_1a_2a_3 + a_1(a_5 - a_1a_4) - (a_3)^2 > 0,$
$a_1a_2a_3a_4 - a_1a_2a_5 - a_1(a_4)^2 + a_4a_5 - (a_3)^2a_4 + a_2a_3a_5 + a_1a_4a_5 - (a_5)^2 > 0,$
$a_1a_2a_3a_4a_5 - a_1(a_2a_5)^2 - (a_1a_4)^2a_5 - a_1a_4(a_5)^2 - (a_3)^2a_4a_5 + a_2a_3(a_5)^2 + a_1a_4(a_5)^2 - (a_5)^3 > 0.$
Clearly, $a_1 > 0$ and $a_2 > 0$.
In addition,

$$\gamma(r_1+\mu)(r+\mu+d) - \beta\frac{KS^*e}{(K+B^*)^2}(r_1+\mu)$$
$$= \gamma(r_1+\mu)(r+\mu+d)[1 - R_0\frac{\mu K^2 S^*}{\Pi(K+B^*)^2}] > 0$$

because $R_0 > 1$. What makes it possible to see that $a_3 > 0$ and $a_4 > 0$ and of to check by calculating the other conditions. Thus the endemic equilibrium E^1 is asymptotically stable. For the global attractivity, we establish it thanks to the method developed in [15]. Let us reconsider for this fact the Lyapunov function

$$L \;=\; eI + (r+\mu+d)B \geq 0.$$

We have :

$$\begin{aligned}
\dot{L} &= e\dot{I} + (r+\mu+d)\dot{B} \\
&= e\beta\frac{B}{K+B}S - \gamma(r+\mu+d)B \\
&= \frac{e\beta\Pi}{K\mu}(\frac{K}{K+B}\frac{S\mu}{\Pi} - \frac{1}{R_0})B \;\leq\; \frac{e\beta\Pi}{K\mu}(\frac{K}{K+B} - \frac{1}{R_0})B.
\end{aligned}$$

When $R_0 > 1$, for any point (N, S, I, R, B) taken into $\mathbb{R}^{*5}_+$ and sufficiently near to E^0, we have $\dot{L} > 0$, therefore it cannot approach E^0 and consequently, E^0 cannot be the limit of an orbit resulting from $\mathbb{R}^{*5}_+$. Thus, only interior equilibrium is E^1. As E^1 is asymptotically stable and that (1) checks the poincarré - Bendixon theorem [7], one concludes that E^1 is globally asymptotically stable. □

Remark 5.4. *The endemic equilibrium of model (3) is also globally asymptotically stable in* $\mathbb{R}^5_+$.

5.2.2 Numerical simulations

To illustrate the theoretical results obtained in this case, we simulated the model (1) thanks to the software matlab. The data and values of the parameters used are those of Cameroon and are summarized in the following table:

Table 2: values of the parameters when β constant

Parameters	Values	Source
Π	200.200	NIS(National Institute of Statistics of Cameroon)
μ	0.0101	NIS
β	$-$	-
K	10^6	Assumed
r_1	0.0025	Assumed
r	0.14	Assumed
d	0.037	National service of Epidemiology of Cameroon
γ	0.33	Assumed
e	10	Assumed

The Figure 2 describe the dynamics of R_0 according to β. It is noted there clearly that $R_0 < 1$ if $\beta < 0,04348$ and $R_0 > 1$ if $\beta > 0,04348$.

The Figure 3 shows the trajectories of model (1) for the values of the parameter given to Table 2 and $\beta = 0.0001;\ 0.01;\ 0.02;\ 0.03;$ and 0.04.

The Figure 4, shows the trajectories of model (1) for values of the parameter given to Table 2 and $\beta = 0.045;\ 0.06;\ 0.07;\ 0.5;$ and 0.8.

6 Conclusion

In this paper, we presented a model of the cholera being able to allow to better include/understand the dynamics of this disease within a nonconstant population. We in addition have proceed with the analysis of the stability of the disease free and endemic equilibria. It was established that the knowledge of the rate of basic reproduction R_0 is enough to conclude on this stability.

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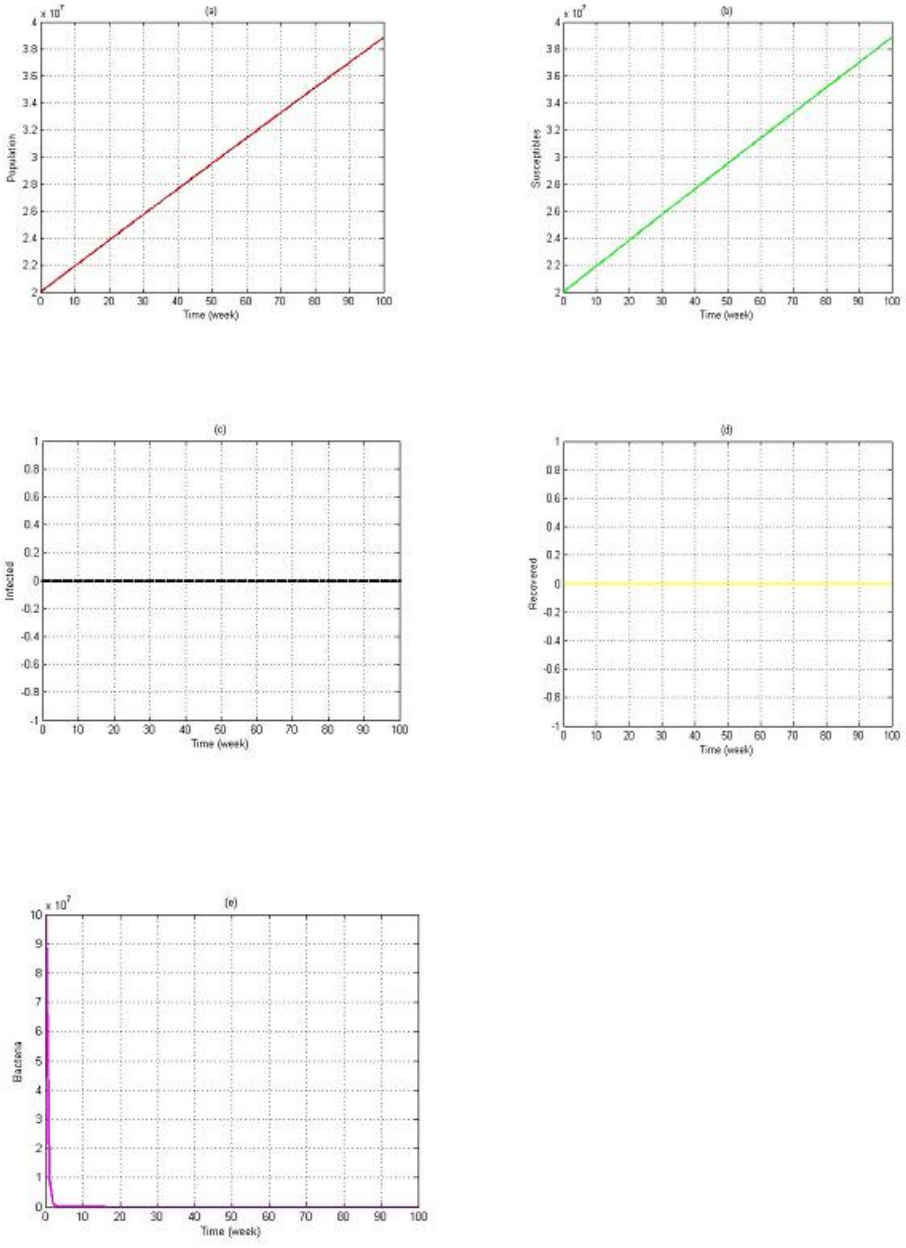

Figure 1: Trajectories of the model (2)

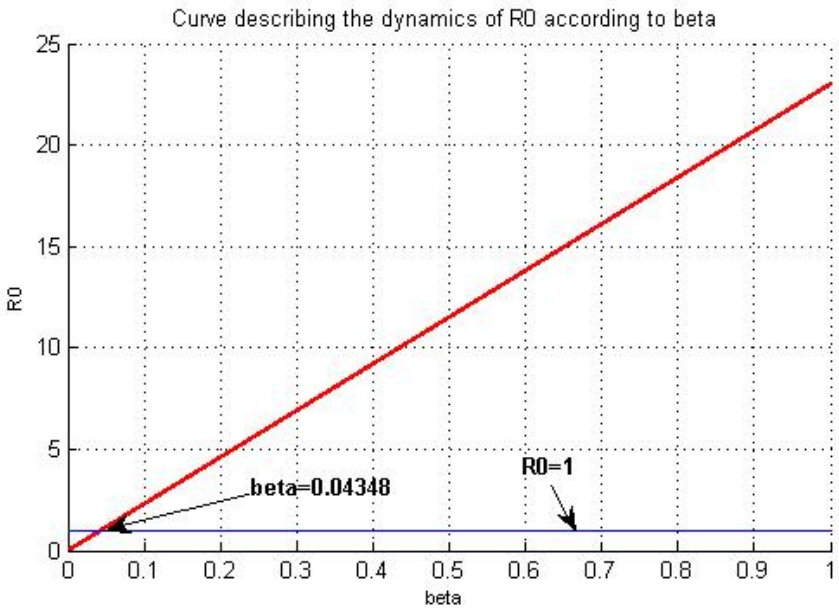

Figure 2: Curve describing the dynamics of R0 according to beta

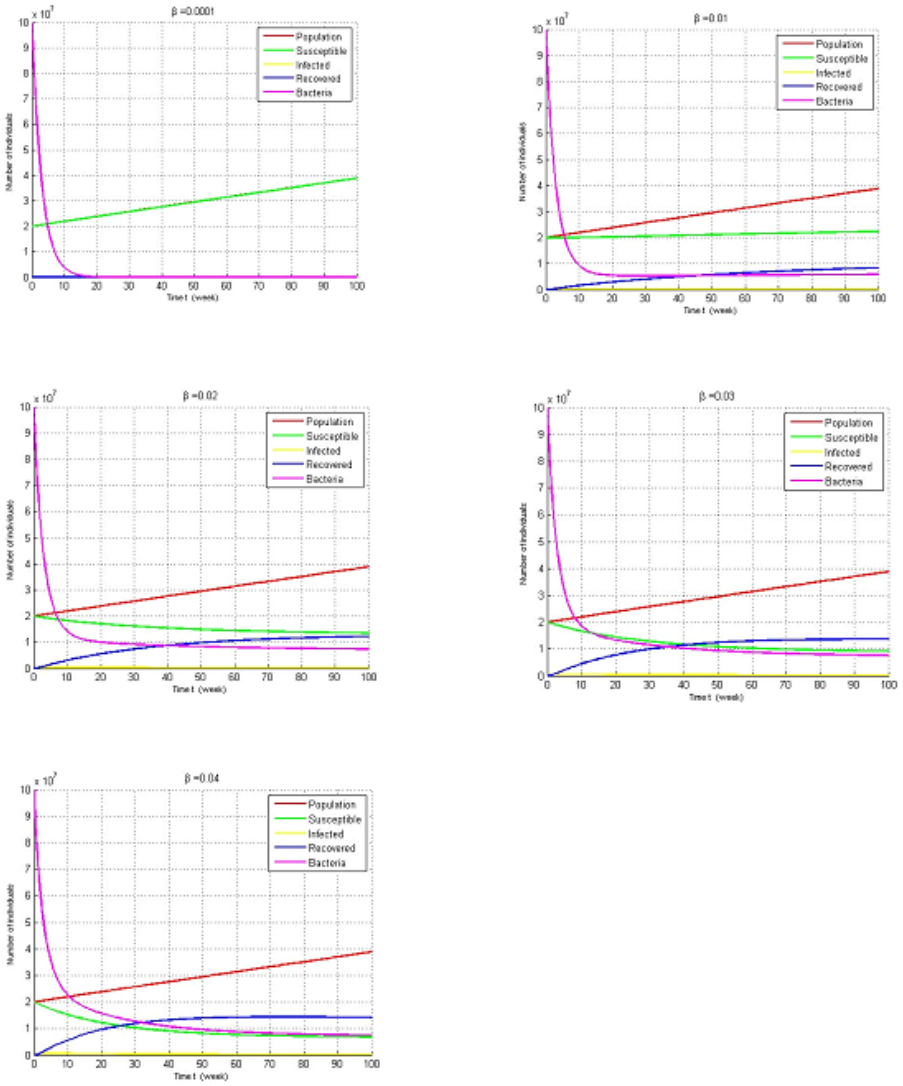

Figure 3: trajectories of model (1) when $R_0 < 1$

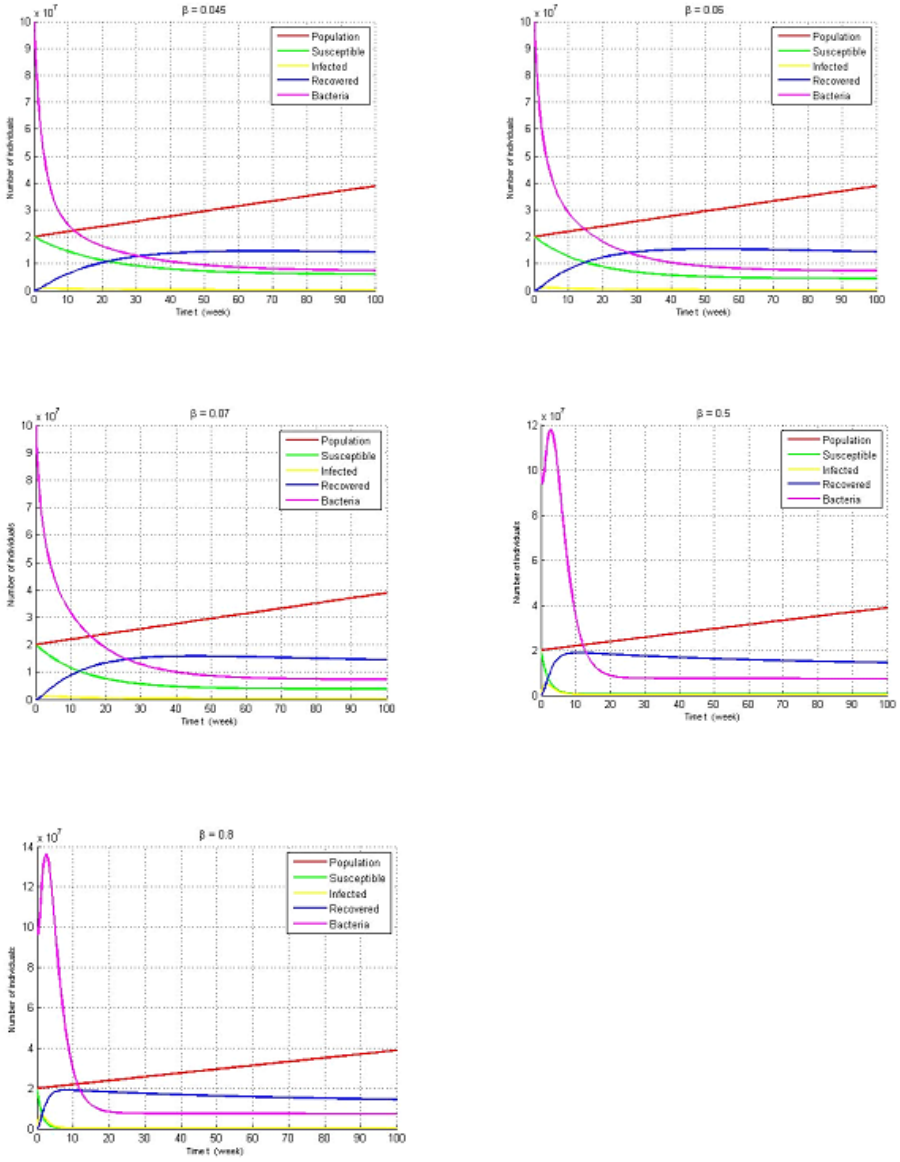

Figure 4: trajectories of model (1) when $R_0 > 1$