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Global stability for cholera epidemic models

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ABSTRACT

Cholera is a water and food borne infectious disease caused by the gram-negative bacterium, *Vibrio cholerae*. Its dynamics are highly complex owing to the coupling among multiple transmission pathways and different factors in pathogen ecology. Although various mathematical models and clinical studies published in recent years have made important contribution to cholera epidemiology, our knowledge of the disease mechanism remains incomplete at present, largely due to the limited understanding of the dynamics of cholera. In this paper, we conduct global stability analysis for several deterministic cholera epidemic models. These models, incorporating both human population and pathogen *V. cholerae* concentration, constitute four-dimensional non-linear autonomous systems where the classical Poincaré-Bendixson theory is not applicable. We employ three different techniques, including the monotone dynamical systems, the geometric approach, and Lyapunov functions, to investigate the endemic global stability for several biologically important cases. The analysis and results presented in this paper make building blocks towards a comprehensive study and deeper understanding of the fundamental mechanism in cholera dynamics.

1. Introduction

Cholera is an ancient disease that continues to cause epidemic and pandemic infection despite ongoing efforts to limit its spread [1,11,16,22,35,38,41,42,53]. Historically, six out of the seven cholera pandemics have swept the globe since 1816 [58–60]. Most recently, the seventh pandemic started from Indonesia in 1961, spread into Europe, South Pacific and Japan in the late 1970s, reached South America in 1990s, and has continued (though much diminished) to the present. The last few years have witnessed many cholera outbreaks in developing countries, including India (2007), Congo (2008), Iraq (2008), Zimbabwe (2008–2009), Vietnam (2009), Nigeria (2010), and Haiti (2010). In the year of 2010 alone, it is estimated that cholera affects 3–5 million people and causes 100,000–130,000 deaths in the world [60]. Particularly, cholera represents a significant public health burden to developing countries and cholera continues receiving worldwide attention.

Cholera is an infection of the small intestine caused by the gram-negative bacterium, *Vibrio cholerae*. Untreated individuals suffer severely from diarrhea and vomiting. It can cause a rapid dehydration and electrolyte imbalance, and can lead to death. As a water/food-borne disease, cholera is typically infected through pathogen ingestion, such as drinking sewage-contaminated water, or eating food prepared by an individual with soiled hands. Meanwhile, different transmission pathways are possible. For example, a cholera outbreak in a Singapore psychiatric hospital indicated that the direct human-to-human transmission was a driving force [13]. In addition, several other aspects must be considered, including the pathogen ecology outside of human hosts [10] and climatological influence [39]. The present work aims to understand the global dynamics of cholera epidemiology in a general mathematical model which has a potential to incorporate these different factors into a unified framework. Such understanding is crucial for effective prevention and intervention strategies against cholera outbreak.

Many mathematical models have already been proposed to investigate the complex epidemic and endemic behavior of cholera. One difficulty in studying cholera dynamics is the coupling between its multiple transmission pathways which involve both direct human-to-human and indirect environment-to-human modes and which lead to combined human-environment epidemiological models. The earliest mathematical model was proposed by Capasso and Paveri-Fontana [4] to study the 1973 cholera epidemic in the Mediterranean region. The model consists of two components, the concentration of the pathogen in water, x_1, and the population of the infected people, x_2. In their original notations, the model is given by

$$\frac{dx_1}{dt} = -a_{11}x_1 + a_{12}x_2, \tag{1.1}$$

$$\frac{dx_2}{dt} = g(x_1) - a_{22}x_2, \tag{1.2}$$

where a_{ij}'s are positive constants. The function $g(x_1)$ is a continuous piecewise-linear function which determines the incidence, i.e., the

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rate of new infection. Particularly, $g(x_1)$ obeys a "saturation" requirement: when the pathogen concentration (x_1) is high, g approaches a constant representing a saturated state of the incidence.

Codeço [6] in 2001 extended the work in [4] and explicitly accounted for the role of the aquatic reservoir in cholera dynamics. She also included the susceptible population into her model to consider the long-term dynamics. The model thus has three components as follows

$$\frac{dS}{dt} = n(H - S) - a\frac{B}{K+B}S, \tag{1.3}$$

$$\frac{dI}{dt} = a\frac{B}{K+B}S - rI, \tag{1.4}$$

$$\frac{dB}{dt} = eI - (mb - nb)B, \tag{1.5}$$

where S and I stand for the susceptible and infected individuals respectively, and B is the concentration of the vibrios in water resource. H stands for the total human population under consideration, n denotes the natural birth/death rate, r is the recovery rate, e is the contribution of each infected person to the concentration of *V. cholerae*, and $mb - nb > 0$ represents the net death rate of the vibrios. The incidence is a non-linear function in B, given by $f(B) = a\frac{B}{K+B}$ with a being the contact rate with contaminated water and K the pathogen concentration that yields 50% chance of catching cholera. This incidence represents a logistic response to the increase in B: when $B \ll K$, f grows linearly with B; when $B \gg K$, f approaches a steady (or, constant) state, a, showing the effect of saturation. Similar to the work of Capasso and Paveri-Fontana [4], this model assumes the ingestion of contaminated water is the only transmission route.

Using similar non-linear incidence in Codeço's model, Hartley et al. [14] in 2006 incorporated a hyper-infective stage of *V. cholerae* (i.e., freshly shed vibrios) into their model:

$$\frac{dS}{dt} = bN - \beta_L S\frac{B_L}{\kappa_L + B_L} - \beta_H S\frac{B_H}{\kappa_H + B_H} - bS, \tag{1.6}$$

$$\frac{dI}{dt} = \beta_L S\frac{B_L}{\kappa_L + B_L} + \beta_H S\frac{B_H}{\kappa_H + B_H} - (\gamma + b)I, \tag{1.7}$$

$$\frac{dR}{dt} = \gamma I - bR, \tag{1.8}$$

$$\frac{B_H}{dt} = \xi I - \chi B_H, \tag{1.9}$$

$$\frac{B_L}{dt} = \chi B_H - \delta_L B_L. \tag{1.10}$$

Here R stands for recovered human population, B_L and B_H denote the lower and hyper infective stages respectively; *V. cholerae* with hyper-infectivity decays into a state of lower infectivity at the rate χ. This model emphasizes the stage of "explosive" infectivity of *V. cholerae,* based on the laboratory measurements that freshly shed *V. cholerae* from human intestines outcompeted other *V. cholerae* by as much as 700-fold for the first few hours in the environment [1,35]. Consequently, this model tries to implicitly highlight the importance of human-to-human interaction in cholera epidemics.

The work in [14] provides deeper insight into cholera epidemics. However, as pointed out in [40], the role of the hyper-infective stage of *V. cholerae* may be better represented by an explicit description of the direct human-to-human interaction. Recently, Mukandavire et al. [36] proposed a model to estimate the reproduction number for the 2008–2009 cholera outbreak in Zimbabwe. Their model includes both environment-to-human and human-to-human transmission pathways:

$$\frac{dS}{dt} = \mu N - \beta_1 S\frac{B}{K+B} - \beta_2 SI - \mu S, \tag{1.11}$$

$$\frac{dI}{dt} = \beta_1 S\frac{B}{K+B} + \beta_2 SI - (\gamma + \mu)I, \tag{1.12}$$

$$\frac{dR}{dt} = \gamma I - \mu R, \tag{1.13}$$

$$\frac{dB}{dt} = \xi I - \delta B. \tag{1.14}$$

In this model, μ denotes the natural human birth/death rate, ξ the rate of human contribution to *V. cholerae,* and δ the net death rate of vibrios. The parameter K is the same as that defined in Codeço's model (1.3)–(1.5). The parameters β_1 and β_2 are rates of ingesting vibrios from contaminated water and through human-to-human interaction, respectively. Thus, the incidence consists of two parts: one is due to the environment-to-human transmission which is again represented by a logistic response curve in B; the other is $\beta_2 SI$ which represents the human-to-human interaction, and this factor is modeled as linear in I.

In addition, Tien and Earn [52] in 2010 published a water-borne disease model which also included the dual transmission pathways, with bilinear incidence rates employed for both the environment-to-human and human-to-human infection routes. No saturation effect was considered in this work.

No doubt the afore-mentioned works have made important contribution in the study of cholera dynamics. However, the interaction between *V. cholerae* and susceptible human could be more complicated than being linear or logistic. Also, the bacterial growth outside of human hosts does not have to follow linear dynamics. For example, Jensen et al. [20] proposed a mathematical model to study how lytic bacteriophage specific for *V. cholerae* affects cholera outbreaks. Their model considers the vibrios (V), the phage (P), the infection (I_-) solely caused by *V. cholerae,* and the infection (I_+) caused by both *V. cholerae* and phage. The model is given

$$\frac{dS}{dt} = -\pi\left(\frac{V}{C(a)k + V}\right)^a S - \delta S + \delta N, \tag{1.15}$$

$$\frac{I_-}{dt} = \pi\left(\frac{l}{l+P}\right)\left(\frac{V}{C(a)k+V}\right)^a S - (\mu_- + \delta)I_-, \tag{1.16}$$

$$\frac{I_+}{dt} = \pi\left(\frac{P}{l+P}\right)\left(\frac{V}{C(a)k+V}\right)^a S - (\mu_+ + \delta)I_+, \tag{1.17}$$

$$\frac{dR}{dt} = \mu_- I_- + \mu_+ I_+ - \delta R, \tag{1.18}$$

$$\frac{dV}{dt} = \left[m\left(1 - \frac{V}{K_v}\right) - \gamma P\right]V + c(I_- + I_+), \tag{1.19}$$

$$\frac{dP}{dt} = (\beta\gamma V - \omega)P + \alpha c I_+, \tag{1.20}$$

where $a = 7$ is a threshold parameter. If we are only interested in cholera epidemics, we can lump I_- and I_+ as one variable. The interaction between human and *V. cholerae* is highly non-linear. The growth of *V. cholerae* is also non-linear.

As mentioned above, two major differences among these cholera models are how the incidence is determined and how the environmental vibrio concentration is formulated. The cholera dynamics is a complex epidemic and endemic process. The challenge in this study is not only due to the strong coupling

among its multiple transmission pathways, but also stems from the intricate *V. cholera* ecology outside of human hosts and climatological influence. In order to include these different factors involved in cholera dynamics, we recently proposed a generalized cholera model [56]. The model unifies previous mathematical models by introducing a general incidence function $f(I,B)$ which can include multiple transmission pathways, and a general pathogen growth rate $h(I,B)$ which can represent varying environmental factors such as cholera ecology in water and climatological influence. The model consists of the following differential equations:

$$\frac{dS}{dt} = bN - Sf(I,B) - bS, \tag{1.21}$$

$$\frac{dI}{dt} = Sf(I,B) - (\gamma + b)I, \tag{1.22}$$

$$\frac{dR}{dt} = \gamma I - bR, \tag{1.23}$$

$$\frac{dB}{dt} = h(I,B). \tag{1.24}$$

Based on biological feasibility, the following conditions for $f(I,B)$ and $h(I,B)$ are assumed for $I \geqslant 0$, $B \geqslant 0$:

(**a**) $f(0,0) = 0$, $h(0,0) = 0$
(**b**) $f(I,B) \geqslant 0$
(**c**) $\frac{\partial f}{\partial I}(I,B) \geqslant 0$, $\frac{\partial f}{\partial B}(I,B) \geqslant 0$, $\frac{\partial h}{\partial I}(I,B) \geqslant 0$, $\frac{\partial h}{\partial B}(I,B) \leqslant 0$
(**d**) $f(I,B)$ and $h(I,B)$ are concave; i.e., the matrices D^2f and D^2h are negative semi-definite.
(**e**) The equation $h(I,B) = 0$ implicitly defines a function $B = g(I)$, which satisfies $g'(I) \geqslant 0$ and $g''(I) \leqslant 0$.

The article [56] conducted some analysis on this model. Based on the next-generation matrix approach [54], the basic reproduction number R_0 was found by

$$R_0 = \frac{N}{\gamma + b}\left[\frac{\partial f}{\partial I}(0,0) - \frac{\partial f}{\partial B}(0,0)\left(\frac{\partial h}{\partial B}(0,0)\right)^{-1}\frac{\partial h}{\partial I}(0,0)\right]. \tag{1.25}$$

Or, using the assumption (e), one obtains

$$R_0 = \frac{N}{\gamma + b}\frac{\partial f}{\partial I}(0,0) + \frac{N}{\gamma + b}\frac{\partial f}{\partial B}(0,0)g'(0) \triangleq R_0^{hh} + R_0^{eh} \tag{1.26}$$

Eq. (1.26) clearly shows that R_0 depends on two factors: one is due to human-to-human transmission (R_0^{hh}) and the other is due to environment-to-human transmission $\left(R_0^{eh}\right)$. If $\frac{\partial f}{\partial I}(0,0) = 0$, then $R_0 = R_0^{eh}$; if $\frac{\partial f}{\partial B}(0,0) = 0$, then $R_0 = R_0^{hh}$. In general, both R_0^{hh} and R_0^{eh} contribute to the basic reproduction rate. Biologically speaking, R_0 measures the average number of secondary infections that occur when one infective is introduced into a completely susceptible host population [18,54,55]. In Eq. (1.26), the term $\frac{1}{\gamma+b}$ represents the expected time of the infection, $\frac{\partial f}{\partial I}(0,0)$ represents the unit human-to-human transmission rate, and $\frac{N}{\gamma+b}\frac{\partial f}{\partial I}(0,0)$ measures the total number of secondary infections caused by the human-to-human transmission. Similarly, the product $\frac{\partial f}{\partial B}(0,0)g'(0)$ represents the unit environment-to-human transmission rate, and $\frac{N}{\gamma+b}\frac{\partial f}{\partial B}(0,0)g'(0)$ measures the total number of secondary infections caused by the environment-to-human transmission.

It is also shown that there exists a forward transcritical bifurcation at $R_0 = 1$ for this model. Specifically, the following theorem summarizes the dynamics known for the system (1.21)–(1.24).

Theorem 1.1 [56]. *When $R_0 < 1$, there is a unique disease-free equilibrium (DFE) which is both locally and globally asymptotically stable; when $R_0 > 1$, the DFE becomes unstable, and there is a unique positive endemic equilibrium which is locally asymptotically stable.*

The global stability of the endemic equilibrium, however, remains unresolved for the system (1.21)–(1.24). In fact, to our knowledge, none of the previous works on cholera modeling have addressed the global dynamics. Thus, the crucial questions of whether the long-term disease dynamics approaches an equilibrium and how this depends on the initial size of the infection, remain to be answered. The study of the endemic global stability is not only mathematically important, but also essential in predicting the evolution of the disease in the long run so that prevention and intervention strategies can be effectively designed, and public health administrative efforts can be properly scaled. The challenge, however, in the global analysis of cholera models is that due to the incorporation of the environmental component B, the models usually constitute four-dimensional non-linear autonomous systems for which the classical Poincaré–Bendixson theory [15] is no longer valid. Hence, other analytical tools must be employed, and possibly new methods need to be created, to overcome this challenge.

As a step towards completely answering this difficult question, we apply three methods, i.e., those based on the monotone dynamical systems [26,28,49–51], the geometric approach [9,29,31], and Lyapunov functions [23,21], to conduct global stability analysis for several cholera models in this paper. The theories of monotone dynamical systems and geometric approach are relatively new compared to the Poincaré-Bendixson framework. These new methods are much involved both conceptually and computationally. Meanwhile, although the method of Lyapunov functions has been widely applied to various dynamical systems, the essential part of our analysis is based on the less well known results of Volterra–Lyapunov stable matrices [45–47]. The models investigated in this paper represent several important, and non-trivial, choices of the incidence $f(I,B)$ and the environment function $h(I,B)$ in the general model (1.21)–(1.24). These include the cases when f is bilinear in I and B due to the standard mass action law, when f is only depending on B in a non-linear manner so that human-to-human transmission is not present, and when f has a linear dependence on I and a non-linear dependence on B. We have found that it is convenient and illustrative (and, in some case, necessary) to employ different approaches to deal with these different situations. The analysis and results presented in this paper can be viewed as building blocks towards a comprehensive study for the global dynamics of the general model (1.21)–(1.24).

We organize the remainder of this paper as follows. In Section 2, we apply the theory of monotone dynamical systems to analyze models with non-linear environment-dependent-only incidence, where the disease transmission is characterized solely by the environment-to-human pathway. A typical example is given by Codeço's model [6], or the system (1.3)–(1.5). In Section 3, we apply the geometric approach to investigate models with incidence depending linearly on human and non-linearly on environment, which in general do not satisfy the requirement of monotone systems. A representative example is the model of Mukandavire et al. [36], or the system (1.11)–(1.14). In Section 4, we consider models with bilinear incidence but with a general non-linear environment function of the pathogen growth rate. A special case of this type of models was discussed in [52]. Such models are neither monotone nor can be easily analyzed by the geometric approach. Fortunately, the method of Lyapunov functions combined with the Volterra–Lyapunov matrix properties lead to the proof of the endemic global stability. Finally, we close the paper by conclusions and discussion.

2. Incidence with environment-to-human transmission only

We first consider the following model

$$\frac{dS}{dt} = bN - Sf(B) - bS, \tag{2.1}$$

$$\frac{dI}{dt} = Sf(B) - (\gamma + b)I, \tag{2.2}$$

$$\frac{dB}{dt} = eI - mB, \tag{2.3}$$

with the incidence function $f(I,B) = f(B)$ depending only on the concentration of cholera vibrios in outside waters, considered as environmental variable, B, and $h(I,B) = eI - mB$ being linear. For convenience of discussion, we have dropped the equation for R, i.e., (1.23), since $S(t) + I(t) + R(t) = N$ and R is not independent. Here the parameter e represents the rate of contribution (e.g., shedding) to *V. cholerae* and m represents the net death rate of vibrios in the environment. From the assumptions (**a**)–(**d**) for the incidence function, we have

$$f(0) = 0, \quad f' \geqslant 0, \quad \text{and} \quad f'' \leqslant 0. \tag{2.4}$$

Note that

$$B' = eI - mB \leqslant eN - mB.$$

It is easy to obtain that $B(t) \leqslant \frac{eN}{m}$. Thus we will study system (2.1)–(2.3) in the feasible region

$$\Delta = \left\{(S,I,B) | S \geqslant 0, I \geqslant 0, 0 \leqslant S + I \leqslant N, 0 \leqslant B \leqslant \frac{eN}{m}\right\}. \tag{2.5}$$

It is easy to verify that Δ is positively invariant. For example, when $S = 0$, one has $S' \geqslant 0$, so S will increase. Similarly, when $I = 0$, $I' \geqslant 0$, so I will increase. It is known $S + I + R = N$, so $S + I \leqslant N$.

The result below directly follows Theorem 1.1.

Proposition 2.1. *The basic reproduction number of the model (2.1)–(2.3) is*

$$R_0 = \frac{N}{\gamma + b} f'(0) \frac{e}{m}. \tag{2.6}$$

If $R_0 < 1$, there is only one non-negative equilibrium point $X_0 = (N, 0, 0)$, which is the disease free equilibrium, and it is globally asymptotically stable. If $R_0 > 1$, there are two non-negative equilibria, X_0 and the endemic equilibrium $X^* = (S^*, I^*, B^*)$, where X_0 is unstable and X^* is locally asymptotically stable.

In order to show the global stability of the endemic equilibrium X^*, we will use a method based on monotone dynamical systems, as developed in [28]. Below we briefly review this method.

Given a C^1 function $x \mapsto F(x) \in \mathbb{R}^n$ for x in a bounded convex open set $D \subset \mathbb{R}^n$. Define the differential equation

$$\frac{dx}{dt} = F(x). \tag{2.7}$$

Denote by $x(t, x_0)$ the solution of (2.7) such that $x(0, x_0) = x_0$. A subset K is said to be *absorbing* in D if $x(t, K_1) \subset K$ for any compact subset $K_1 \subset D$ and sufficiently large t. To study the global stability of an equilibrium solution, $\bar{x}$, we assume

(**H1**) There exists a compact absorbing set $K \subset D$.
(**H2**) The system (2.7) has a unique equilibrium point $\bar{x}$ in D.

The system (2.7) is said to be *uniformly persistent* if there exists a constant $c > 0$ such that each component of any solution $x(t)$ with $x(0) = x_0 \in D$ satisfies

$$\liminf_{t\to\infty} x_1(t) > c, \quad \liminf_{t\to\infty} x_2(t) > c, \ldots, \liminf_{t\to\infty} x_n(t) > c. \tag{2.8}$$

The boundedness of D and uniform persistence imply that the system has a compact absorbing subset of D [3].

The system (2.7) is called *competitive* if there exists a diagonal matrix H with entries ±1 such that each off-diagonal entry of $H\frac{\partial F}{\partial x}H$ is non-positive in D, where $\frac{\partial F}{\partial x}$ is the variational matrix of (2.7). It is known that three-dimensional competitive systems have the Poincaré-Bendixson property:

Theorem 2.2 [49]. *For a competitive system defined in a three-dimensional convex open domain, if a non-empty compact ω-limit set contains no equilibria, then it is a closed orbit.*

We recall here basic definitions related to orbital stability of a periodic orbit [7]. Suppose (2.7) has a periodic solution $x = p(t)$ with the least period $\omega > 0$ and orbit $\gamma = \{p(t) | 0 \leqslant t \leqslant \omega\}$. This orbit is *orbitally stable* if for each $\varepsilon > 0$, there exists a $\delta > 0$ such that any solution $x(t)$, for which the distance of $x(0)$ from γ is less than δ, remains at a distance less than ε from γ for all $t \geqslant 0$. It is *asymptotically orbitally stable* if the distance of $x(t)$ from γ also tends to zero as $t \to \infty$. The orbit γ is asymptotically orbitally stable with *asymptotic phase* if it is asymptotically orbitally stable and there is an $\eta > 0$ such that, any solution $x(t)$, for which the distance of $x(0)$ from γ is less than η, satisfies $|x(t) - p(t - \tau)| \to 0$ as $t \to \infty$ for some τ which may depend on $x(0)$. We now state a criterion given in [37] for the asymptotic orbital stability of a periodic orbit of (2.7).

Theorem 2.3. *A sufficient condition for a periodic orbit $\gamma = \{p(t) | 0 \leqslant t \leqslant \omega\}$ of (2.7) to be asymptotically orbitally stable with asymptotic phase is that the linear system*

$$\frac{dz}{dt} = \left(\frac{\partial F^{[2]}}{\partial x}(p(t))\right) z(t) \tag{2.9}$$

is asymptotically stable, where $\frac{\partial F^{[2]}}{\partial x}$ is the second compound matrix of the Jacobian $\frac{\partial F}{\partial x}$.

Recall for a $n \times n$ matrix A and integer $1 \leqslant k \leqslant n$, the kth *additive compound matrix* of A, denoted by $A^{[k]}$, is defined by

$$A^{[k]} = D_+ (I + hA)^{(k)}|_{h=0}, \tag{2.10}$$

where $(I + hA)^{(k)}$ is the kth exterior power of $(I + hA)$, and D_+ is the corresponding right-hand derivative [37].

Then we state a theorem implicitly given in [28].

Theorem 2.4. *Assume that*

(1) *conditions (**H1**) and (**H2**) hold;*
(2) *$\bar{x}$ is locally asymptotically stable;*
(3) *the system (2.7) satisfies the Poincaré–Bendixson Property;*
(4) *each periodic orbit of (2.7) in D is orbitally asymptotically stable.*

Then the unique equilibrium $\bar{x}$ is globally asymptotically stable in D.

We now examine the system (2.1)–(2.3). We have two propositions which imply that the system is persistent.

Proposition 2.5. *The disease-free equilibrium point E_0 is the only ω-limit point of the system (2.1)–(2.3) on the boundary, $\partial\Delta$, of Δ.*

Proof. The boundary of Δ has 5 faces. In each face, the vector field of the system (2.1)–(2.3) is transversal to it. For example, in the face of $\{(S,I,B) | S + I = N, 0 \leqslant B \leqslant \frac{eN}{m}\}$, the vectors point to inside of Δ. Meanwhile, $\partial\Delta$ has 9 edges. Except for the edge on the S-axis, for other edges the vector fields are transversal to them. On the S-axis, the system reduces to $\frac{dS}{dt} = bN - bS$, since $f(0) = 0$. We have $S(t) \to N$ as $t \to +\infty$. Thus, X_0 is the only ω-limit point of the system (2.1)–(2.3) on the boundary $\partial\Delta$. □

Proposition 2.6. *When $R_0 > 1$, X_0 cannot be the ω-limit point of any orbit starting in the interior, Δ°, of Δ.*

Proof. We define a function

$$L = eI + (\gamma + b)B \geqslant 0.$$

We consider a small neighborhood of X_0 in Δ° such that $B > 0$ is sufficiently small and $S > 0$ is sufficiently close to N. In this neighborhood the orbital derivative of L is

$$\begin{aligned} L' &= eI' + (\gamma + b)B' = eSf(B) - m(\gamma + b)B = m(\gamma + b)\left[\frac{eSf(B)}{m(\gamma + b)} - B\right] \\ &\geqslant m(\gamma + b)\left[\frac{e}{m}\frac{S}{\gamma + b}f'(0)B - B\right] \\ &= Bm(\gamma + b)\left[\frac{e}{m}f'(0)\frac{N}{\gamma + b}\frac{S}{N} - 1\right] > 0, \end{aligned}$$

where we have used the facts $R_0 = \frac{e}{m}\frac{N}{\gamma+b}f'(0)$ and $f(B) = f(0) + f'(0)B + f''(0)B^2 + \cdots \geqslant f'(0)B$, and $f(0) = 0$, $f' \geqslant 0$, $f'' \leqslant 0$, B is positive but small. Therefore, $X_0 = (N, 0, 0)$ cannot be the ω-limit point of any orbit starting in Δ°. □

The following corollary is immediately obtained based on Propositions 2.5 and 2.6.

Corollary 2.7. *The system (2.1)–(2.3) is uniformly persistent.*

The variational matrix of the system (2.1)–(2.3) is given by

$$J = \begin{pmatrix} -f(B) - b & 0 & -Sf'(B) \\ f(B) & -(\gamma + b) & Sf'(B) \\ 0 & e & -m \end{pmatrix}.$$

If we set $H = diag\{1, -1, 1\}$, then HJH has non-positive off-diagonal entries. Hence, it is a three-dimensional competitive system which possesses the Poincaré–Bendixson property [49]. We have the following theorem.

Theorem 2.8. *Any compact ω-limit set of the system (2.1)–(2.3) in the interior of Δ is either a closed orbit or the endemic equilibrium X^*.*

Proof. Suppose γ is an ω-limit set of the system (2.1)–(2.3) in the interior of Δ. If γ does not contain X^*, then it contains no equilibria since X^* is the only interior equilibrium point. Theorem 2.2 implies that γ is a closed orbit. If, instead, γ contains X^*, then any orbit that gets arbitrarily close to X^* will converge to X^* since X^* is locally asymptotically stable. Thus $\gamma = X^*$. □

A closed orbit corresponds to a periodic solution. If it exists for the system (2.1)–(2.3), it will be stable. Specifically, we have the following result.

Theorem 2.9. *The trajectory of any non-constant periodic solution of the system (2.1)–(2.3), if it exists, is asymptotically orbitally stable with asymptotic phase.*

Proof. The second compound matrix of the system (2.1)–(2.3) is given by

$$J^{[2]} = \begin{pmatrix} -2b - \gamma - f(B) & Sf'(B) & Sf'(B) \\ e & -b - m - f(B) & 0 \\ 0 & f(B) & -b - m - \gamma \end{pmatrix}.$$

Then the second compound system defined along the periodic solution $(S(t), I(t), B(t))$ of the system (2.1)–(2.3) is given by

$$X'(t) = -(2b + \gamma + f(B))X + Sf'(B)(Y + Z) \tag{2.11}$$

$$Y'(t) = eX - (b + m + f(B))Y \tag{2.12}$$

$$Z'(t) = f(B)Y - (b + m + \gamma)Z \tag{2.13}$$

Based on Theorem 2.3, if we can prove the system (2.11)–(2.13) is asymptotically stable, then the periodic solution is asymptotically orbitally stable with asymptotic phase.

We define a Lyapunov function

$$V(X, Y, Z, S, I, B) = \sup\left\{|X|, \frac{I}{B}(|Y| + |Z|)\right\}.$$

Since the system (2.1)–(2.3) is persistent, any periodic solution $(S(t), I(t), B(t))$ is at a positive distance from the boundary $\partial\Delta$. So $\frac{I}{B}$ is well-defined, and there is a constant $c > 0$ such that $\frac{I}{B} > c$. Hence, for some positive constant c_0, we have

$$V(X, Y, Z, S, I, B) \geqslant c_0 \sup\{|X|, |Y|, |Z|\},$$

for any $(X, Y, Z) \in \mathbb{R}^3$ and any periodic solution $(S(t), I(t), B(t))$ of the system (2.1)–(2.3).

Let us estimate the right-derivative of V along a solution $(X(t), Y(t), Z(t))$ of the system (2.11)–(2.13) and $(S(t), I(t), B(t))$ of the system (2.1)–(2.3).

$$\begin{aligned} D_+|X(t)| &\leqslant -(2b + \gamma + f(B))|X| + \tfrac{Sf'(B)B}{I}\tfrac{I}{B}(|Y| + |Z|), \\ D_+|Y(t)| &\leqslant e|X| - (b + m + f(B))|Y|, \\ D_+|Z(t)| &\leqslant f(B)|Y| - (b + m + \gamma)|Z|, \end{aligned}$$

and

$$\begin{aligned} D_+\frac{I}{B}(|Y| + |Z|) &= \left(\frac{I'}{I} - \frac{B'}{B}\right)\frac{I}{B}(|Y| + |Z|) + \frac{I}{B}D_+(|Y| + |Z|) \\ &\leqslant \left(\frac{I'}{I} - \frac{B'}{B}\right)\frac{I}{B}(|Y| + |Z|) + \frac{I}{B}(e|X| - (b + m)(|Y| + |Z|)) \\ &= e\frac{I}{B}|X| + \left(\frac{I'}{I} - \frac{B'}{B} - (b + m)\right)\frac{I}{B}(|Y| + |Z|). \end{aligned}$$

We then need to estimate the following two functions

$$\begin{aligned} g_1(t) &= -2b - \gamma - f(B) + \frac{Sf'(B)B}{I}, \\ g_2(t) &= e\frac{I}{B} + \frac{I'}{I} - \frac{B'}{B} - (b + m). \end{aligned}$$

From the system (2.1)–(2.3), we have $\frac{B'}{B} = e\frac{I}{B} - m$. Then

$$g_2(t) = \frac{I'}{I} - b.$$

Similarly, $\frac{I'}{I} = \frac{Sf(B)}{I} - (\gamma + b)$. Then $\frac{S}{I} = \left(\frac{I'}{I} + (\gamma + b)\right)\frac{1}{f(B)}$. Since $f(0) = 0$, $f'' \leqslant 0$ (which implies f' is decreasing), we obtain $\frac{f(B)}{B} = \frac{f(B) - f(0)}{B - 0} = f'(\eta) > f'(B)$, where $0 < \eta < B$. Thus $f(B) > f'(B)B$, and

$$\begin{aligned} g_1(t) &= -2b - \gamma - f(B) + f'(B)B\left(\frac{I'}{I} + (\gamma + b)\right)\frac{1}{f(B)} \\ &= -2b - \gamma - f(B) + \frac{f'(B)B}{f(B)}\left(\frac{I'}{I} + (\gamma + b)\right) \\ &\leqslant -2b - \gamma - f(B) + \frac{I'}{I} + (\gamma + b) = -b - f(B) + \frac{I'}{I} \leqslant \frac{I'}{I} - b. \end{aligned}$$

Therefore,

$$D_+V(t) \leqslant \max\{g_1(t), g_2(t)\}V(t), \tag{2.14}$$

and

$$\max\{g_1(t), g_2(t)\} \leqslant \frac{I'}{I} - b. \tag{2.15}$$

Denote the period of the periodic solution $(S(t), I(t), B(t))$ by τ. We have

$$\int_0^\tau \max\{g_1(t), g_2(t)\}dt \leqslant \int_0^\tau \left(\frac{I'}{I} - b\right)dt = \ln I(t)|_0^\tau - b\tau = -b\tau < 0. \tag{2.16}$$

Thus, the system (2.11)–(2.13) is asymptotically stable. Then, the periodic solution $(S(t),I(t),B(t))$ is asymptotically orbitally stable with asymptotic phase. □

Summing up these results together, we have

Theorem 2.10. *The endemic equilibrium X^* of the system (2.1)–(2.3) is globally asymptotically stable in Δ.*

The proof follows Theorem 2.4 by combining Theorems 2.1, 2.7 and 2.9.

A typical example with non-linear environment-dependent-only incidence is Codeço's model (1.3)–(1.5). The local stability of the endemic equilibrium for this model was originally analyzed in [6], and can also be obtained from Theorem 1.1 as a special case, whereas the global endemic stability is obtained by Theorem 2.10.

3. Incidence depending linearly on human and non-linearly on environment

Next, we consider models with incidence depending linearly on I and non-linearly on B. A representative example in this category is the model of Mukandavire et al. given in the system (1.11)–(1.14). For convenience of discussion, we rewrite the equations below:

$$\frac{dS}{dt} = \mu N - \beta_1 \frac{SB}{K+B} - \beta_2 SI - \mu S, \tag{3.1}$$

$$\frac{dI}{dt} = \beta_1 \frac{SB}{K+B} + \beta_2 SI - (\gamma+\mu)I, \tag{3.2}$$

$$\frac{dB}{dt} = \xi I - \delta B. \tag{3.3}$$

We have dropped the equation for R, i.e., (1.13). Also note that, similar to the model (2.1)–(2.3), the environmental function $h(I,B) = -\xi I - \delta B$ is linear. Using the same argument as before, it is clear to see the region

$$\Delta = \left\{(S,I,B) | S \geqslant 0, I \geqslant 0, 0 \leqslant S+I \leqslant N, 0 \leqslant B \leqslant \frac{\xi}{\delta} N\right\} \tag{3.4}$$

is a positive invariant domain of the system (3.1)–(3.3).

The result below follows Theorem 1.1 and is similar to Proposition 2.1.

Proposition 3.1. *The basic reproduction number of the model (3.1)–(3.3) is*

$$R_0 = \frac{N}{\gamma+\mu}\left(\beta_1 \frac{\xi}{K\delta} + \beta_2\right). \tag{3.5}$$

If $R_0 < 1$, there is only one non-negative equilibrium point $X_0 = (N,0,0)$, which is the disease free equilibrium, and it is globally asymptotically stable. If $R_0 > 1$, there are two non-negative equilibria, X_0 and the endemic equilibrium $X^* = (S^*,I^*,B^*)$, where X_0 is unstable and X^* is locally asymptotically stable.

Similar to the model (2.1)–(2.3), the system (3.1)–(3.3) is uniformly persistent which can be derived from the following two propositions.

Proposition 3.2. *The disease-free equilibrium point X_0 is the only ω-limit point of the system (3.1)–(3.3) on the boundary $\partial\Delta$ of Δ.*

We skip the proof since it is very similar to that of Proposition 2.5.

Proposition 3.3. *When $R_0 > 1$, X_0 cannot be the ω-limit point of any orbit starting in the interior Δ° of Δ.*

Proof. Take the initial value (S_0,I_0,B_0) close to $X_0 = (N,0,0)$. If $B' > 0$, then $B > 0$ and is increasing, thus moving away from X_0. If, instead, $B' \leqslant 0$, then $B \geqslant \frac{\xi}{\delta} I$. Assuming B is small, we have

$$\begin{aligned}\frac{dI}{dt} &= \beta_1 \frac{SB}{K} \frac{1}{1+B/K} + \beta_2 SI - (\gamma+\mu)I \doteq \frac{\beta_1}{K} SB + \beta_2 SI - (\gamma+\mu)I \\ &\geqslant \frac{\beta_1}{K}\frac{\xi}{\delta} SI + \beta_2 SI - (\gamma+\mu)I = (\gamma+\mu)\left[\frac{N}{\gamma+\mu}\left(\frac{\beta_1\xi}{K\delta} + \beta_2\right)\frac{S}{N} - 1\right] I \\ &= (\gamma+\mu)\left[R_0 \frac{S}{N} - 1\right] I > 0,\end{aligned}$$

as long as S is close to N. Therefore, the trajectory always moves away from X_0. □

Combining these two propositions and Theorem 3.1, we obtain

Corollary 3.4. *The system (3.1)–(3.3) is uniformly persistent, and satisfies the assumptions* (**H1**) *and* (**H2**).

It can be easily verified, however, that the model (3.1)–(3.3) is not monotone or competitive due to the incidence depending on both B and I. Thus the analysis conducted in the previous section cannot be extended to this case. Instead, we employ the geometric approach [9,29,31] to analyze the global stability of this model.

To that end, we first recall a Bendixson criterion in $\mathbb{R}^n$ developed in [27,31]. Consider the system (2.7). A Bendixson criterion is a condition satisfied by F which precludes the existence of non-constant periodic solutions. For any solution $x(t,x_0)$ in D, define the second compound equation

$$\frac{dz}{dt} = \frac{\partial F^{[2]}}{\partial x}(x(t,x_0))z(t). \tag{3.6}$$

If D is simply connected, the uniformly asymptotical stability of solutions of (3.6) and uniformly exponential decay of solutions with respect to initial values in each compact subset of D preclude the existence of any invariant simple closed rectifiable curve of the system (2.7) in D. A very useful criterion is given in [31] to characterize this stability, which is a Bendixson criterion for high dimensional systems. The detail is provided below.

Let $x \mapsto P(x)$ be a $\binom{n}{2} \times \binom{n}{2}$ matrix-valued C^1 function in D. Assume P^{-1} exists and is continuous in a compact subset K of D. Set

$$Q = P_F P^{-1} + P\frac{\partial F^{[2]}}{\partial x} P^{-1}, \tag{3.7}$$

where P_F is the derivative of P (entry-wise) along the direction of F. Let $m(Q)$ be the Lozinskiĭ measure of Q with respect to a matrix norm [7], i.e.,

$$m(Q) = \lim_{h\to 0^+} \frac{|I+hQ|-1}{h}. \tag{3.8}$$

Define a quantity $\bar{q}_2$ as

$$\bar{q}_2 = \limsup_{t\to\infty} \sup_{x_0\in K} \frac{1}{t}\int_0^t m(Q(x(s,x_0)))ds. \tag{3.9}$$

Then the Bendixson criterion is given by

$$\bar{q}_2 < 0. \tag{3.10}$$

Recall that a local ϵ-perturbation of F in a neighborhood U of $x_1 \in D$ is a function $g \in C^1(D \to \mathbb{R}^n)$ such that the support, $\mathrm{Supp}(F-g) \subset U$, and $|F-g|_{C^1} < \epsilon$, where

$$|F-g|_{C^1} = \sup\left\{|F(x)-g(x)| + \left|\frac{\partial F}{\partial x}(x) - \frac{\partial g}{\partial x}(x)\right| : x \in D\right\}. \tag{3.11}$$

A Bendixson criterion is said to be *robust under C^1 local perturbations of F* if for each local ϵ-perturbation g of F at $x_1 \in D$, g also satisfies the

Bendixson criterion. A point $x_0 \in D$ is *wandering* for (2.7) if there exists a neighborhood U of x_0 and $T > 0$ such that $U \cap x(t,U)$ is empty for all $t > T$. For example, all equilibria and limit points are non-wandering.

Now we state the closing lemma of Pugh [19,43,44].

Lemma 3.5. *Let $F \in C^1(D \to \mathbb{R}^n)$. Suppose that x_0 is a non-wandering point of (2.7) and that $F(x_0) \neq 0$. Also assume that the positive semi-orbit of x_0 has compact closure. Then, for each neighborhood U of x_0 and $\epsilon > 0$, there exists a C^1 local ϵ-perturbation g of F at x_0 such that*

(1) $\mathrm{Supp}(F-g) \subset U$; *and*
(2) *the perturbed system $\frac{dx}{dt} = g(x)$ has a non-constant periodic solution whose trajectory passes through x_0.*

Using the closing lemma, the following two theorems were established in [29].

Theorem 3.6. *Suppose that assumptions (**H1**) and (**H2**) hold, and assume that (2.7) satisfies a Bendixson criterion which is robust under C^1 local perturbations of F at all non-equilibrium non-wandering points for (2.7). Then the unique equilibrium $\bar{x}$ is globally stable in D provided it is locally asymptotically stable.*

Theorem 3.7. *Assume that D is simply connected and the assumptions (**H1**) and (**H2**) hold. Then the unique equilibrium $\bar{x}$ of (2.7) is globally stable in D if $\bar{q}_2 < 0$.*

We now apply these theorems to our model (3.1)–(3.3). Based on Corollary 3.4, we only need to check the Bendixson criterion $\bar{q}_2 < 0$.

The Jacobian matrix of the system (3.1)–(3.3) is

$$J = \begin{pmatrix} -\frac{\beta_1 B}{K+B} - \beta_2 I - \mu & -\beta_2 S & -\frac{\beta_1 KS}{(K+B)^2} \\ \frac{\beta_1 B}{K+B} + \beta_2 I & \beta_2 S - (\gamma+\mu) & \frac{\beta_1 KS}{(K+B)^2} \\ 0 & \xi & -\delta \end{pmatrix}.$$

The second compound matrix of the system (3.1)–(3.3) is

$$J^{[2]} = \begin{pmatrix} -\frac{\beta_1 B}{K+B} - \beta_2 I + \beta_2 S - \gamma - 2\mu & \frac{\beta_1 KS}{(K+B)^2} & \frac{\beta_1 KS}{(K+B)^2} \\ \xi & -\frac{\beta_1 B}{K+B} - \beta_2 I - \mu - \delta & -\beta_2 S \\ 0 & \frac{\beta_1 B}{K+B} + \beta_2 I & \beta_2 S - \gamma - \mu - \delta \end{pmatrix}.$$

We set the matrix function P by

$$P(S,I,B) = \mathrm{diag}\left\{1, \frac{I}{B}, \frac{I}{B}\right\}.$$

Then

$$P_F P^{-1} = \mathrm{diag}\left\{0, \frac{I'}{I} - \frac{B'}{B}, \frac{I'}{I} - \frac{B'}{B}\right\},$$

and

$$PJ^{[2]}P^{-1} = \begin{pmatrix} -\frac{\beta_1 B}{K+B} - \beta_2 I + \beta_2 S - \gamma - 2\mu & \frac{\beta_1 KS}{(K+B)^2}\frac{B}{I} & \frac{\beta_1 KS}{(K+B)^2}\frac{B}{I} \\ \xi\frac{I}{B} & -\frac{\beta_1 B}{K+B} - \beta_2 I - \mu - \delta & -\beta_2 S \\ 0 & \frac{\beta_1 B}{K+B} + \beta_2 I & \beta_2 S - \gamma - \mu - \delta \end{pmatrix}.$$

The matrix $P_F P^{-1} + PJ^{[2]}P^{-1}$ defined in (3.7) can then be written in a block form:

$$Q = \begin{bmatrix} Q_{11} & Q_{12} \\ Q_{21} & Q_{22} \end{bmatrix},$$

with

$$Q_{11} = -\frac{\beta_1 B}{K+B} - \beta_2 I + \beta_2 S - \gamma - 2\mu, \quad Q_{12} = \left[\frac{\beta_1 KS}{(K+B)^2}\frac{B}{I}, \frac{\beta_1 KS}{(K+B)^2}\frac{B}{I}\right],$$

$$Q_{21} = \begin{bmatrix} \xi\frac{I}{B} \\ 0 \end{bmatrix},$$

$$Q_{22} = \begin{bmatrix} -\frac{\beta_1 B}{K+B} - \beta_2 I - \mu - \delta + \frac{I'}{I} - \frac{B'}{B} & -\beta_2 S \\ \frac{\beta_1 B}{K+B} + \beta_2 I & \beta_2 S - \gamma - \mu - \delta + \frac{I'}{I} - \frac{B'}{B} \end{bmatrix}.$$

Now we define a norm in $\mathbb{R}^3$ as

$$|(u,v,w)| = \max\{|u|, |v| + |w|\}$$

for any vector $(u,v,w) \in \mathbb{R}^3$. Let m denote the Lozinskiĭ measure with respect to this norm. We can then obtain

$$m(Q) \leqslant \sup\{g_1, g_2\}, \tag{3.12}$$

with

$$g_1 = m_1(Q_{11}) + |Q_{12}|,$$
$$g_2 = |Q_{21}| + m_1(Q_{22}),$$

where $|Q_{12}|$ and $|Q_{21}|$ are matrix norms induced by the L_1 vector norm, and m_1 denotes the Lozinskiĭ measure with respect to the L_1 norm. Specifically,

$$m_1(Q_{22}) = \frac{I'}{I} - \frac{B'}{B} - \mu - \delta + \sup\{2\beta_2 S - \gamma, 0\},$$

and

$$\begin{aligned} g_2 &= \frac{I'}{I} - \frac{B'}{B} - \mu - \delta + \sup\{2\beta_2 S - \gamma, 0\} + \xi\frac{I}{B} \\ &= \frac{I'}{I} - \mu + \sup\{2\beta_2 S - \gamma, 0\} \leqslant \frac{I'}{I} - \mu, \end{aligned}$$

provided that

$$N \leqslant \frac{\gamma}{2\beta_2}.$$

Meanwhile,

$$\begin{aligned} g_1 &= -\frac{\beta_1 B}{K+B} - \beta_2 I + \beta_2 S - \gamma - 2\mu + \frac{\beta_1 KS}{(K+B)^2}\frac{B}{I} \\ &= -\frac{\beta_1 B}{K+B} - \beta_2 I + \beta_2 S - \gamma - 2\mu + \frac{K}{K+B}\left(\frac{I'}{I} - \beta_2 S + \gamma + \mu\right) \\ &\leqslant -\frac{\beta_1 B}{K+B} - \beta_2 I + \beta_2 S - \gamma - 2\mu + \frac{I'}{I} - \beta_2 S + \gamma + \mu \\ &= \frac{I'}{I} - \mu - \frac{\beta_1 B}{K+B} - \beta_2 I \leqslant \frac{I'}{I} - \mu. \end{aligned}$$

Therefore,

$$m(Q) \leqslant \frac{I'}{I} - \mu. \tag{3.13}$$

Since $0 \leqslant I(t) \leqslant N$, there exists $T > 0$ such that when $t > T$, $\frac{\ln I(t) - \ln I(0)}{t} < \frac{\mu}{2}$. As a result,

$$\frac{1}{t}\int_0^t m(Q)dt \leqslant \frac{1}{t}\int_0^t \left(\frac{I'}{I} - \mu\right)dt = \frac{\ln I(t) - \ln I(0)}{t} - \mu < -\frac{\mu}{2}, \tag{3.14}$$

which imples $\bar{q}_2 \leqslant -\frac{\mu}{2} < 0$. Hence, we have established the following theorem:

Theorem 3.8. *The endemic equilibrium X^* of the system (3.1)–(3.3) is globally asymptotically stable in Δ.*

4. Bilinear incidence and non-linear environmental function

Now we consider models of the following type:

$$\frac{dS}{dt} = bN - Sf(I,B) - bS, \tag{4.1}$$

$$\frac{dI}{dt} = Sf(I,B) - (\gamma + b)I, \tag{4.2}$$

$$\frac{dB}{dt} = g(I) - \delta B, \tag{4.3}$$

where, again, we have dropped the equation for R, i.e., (1.23). Now the function f is bilinear in I and B,

$$f(I,B) = \beta_1 B + \beta_2 I, \tag{4.4}$$

with $\beta_1 \geqslant 0$, $\beta_2 \geqslant 0$, which represents the classical mass action incidence. Such an incidence function is also used in a recent work of Tien and Earn [52] in their water-borne disease model. However, the difference between our model (4.1)–(4.3) and the model in [52] is that we consider more general, non-linear pathogen function $g(I)$. The function $g(I)$ describes the growth rate of the vibrios in the environment due to the contribution from the infected people (such as shedding *V. cholerae),* which generally does not have to follow linear dynamics. Based on the assumption (**e**), we recast the conditions for the non-linear function $g(I)$ as follows:

(**A1**) $g(0) = 0$; $g(I) > 0$ if $I > 0$.
(**A2**) $g'(I) > 0$; $g''(I) < 0$.

The assumption (**A1**) is natural; it also ensures the existence of a unique disease-free equilibrium $X_0 = (N,0,0)$. The assumption (**A2**) regulates $g(I)$ as biologically realistic based on a consequence of saturation effects: increased infection leads to higher pathogen growth; however, when the number of the infective is high, the growth of the pathogen concentration will respond more slowly than linearly to the increase in I.

Based on the assumption (**A2**), we can easily obtain the following results:

Lemma 4.1. *The function $\frac{g(I)}{I}$ is strictly decreasing on $(0,\infty)$.*

Proof. For any $I > 0$, we have

$$\frac{g(I)}{I} = \frac{g(I) - g(0)}{I - 0} = g'(\beta)$$

for some β between 0 and I due to the mean value theorem. Since $g'' < 0$ on $(0,\infty)$, we obtain $g'(I) < g'(\beta)$. Thus $g'(I) < g(I)/I$, or $Ig'(I) - g(I) < 0$. Hence,

$$\left(\frac{g(I)}{I}\right)' = \frac{Ig'(I) - g(I)}{I^2} < 0,$$

which establishes this lemma. □

Lemma 4.2. *Let I^* be a point in $(0,\infty)$. Then*

$$\frac{g(I) - g(I^*)}{I - I^*} < \frac{g(I^*)}{I^*} \tag{4.5}$$

for all $I > 0$ and $I \neq I^*$.

Proof. When $I < I^*$, we have $\frac{g(I)}{I} > \frac{g(I^*)}{I^*}$ due to Lemma 4.1. Thus $I^*g(I) > Ig(I^*)$, or

$$I^*g(I) - I^*g(I^*) > Ig(I^*) - I^*g(I^*)$$

Using the fact $I - I^* < 0$, we obtain (4.5). Similarly, when $I > I^*$, we obtain

$$I^*g(I) - I^*g(I^*) < Ig(I^*) - I^*g(I^*)$$

which yields (4.5) as well. □

Below we summarize the dynamics already known for the system (4.1)–(4.3), which follows Theorem 1.1.

Proposition 4.3. *The basic reproduction number of the model (4.1)–(4.3) is*

$$R_0 = \frac{N}{\gamma + b}\left[\beta_2 + \frac{\beta_1}{\delta}g'(0)\right]. \tag{4.6}$$

When $R_0 < 1$, there is a unique DFE, $X_0 = (N,0,0)$, which is globally asymptotically stable; when $R_0 > 1$, the DFE becomes unstable, and there is a unique positive endemic equilibrium, $X^* = (S^*,I^*,B^*)$, which is locally asymptotically stable.

At the endemic equilibrium, we have

$$bN - S^*f(I^*,B^*) - bS^* = 0, \tag{4.7}$$

$$S^*f(I^*,B^*) - (\gamma + b)I^* = 0, \tag{4.8}$$

$$g(I^*) - \delta B^* = 0. \tag{4.9}$$

Our goal here is to show that the endemic equilibrium is globally asymptotically stable. With the incidence f depending on both I and B, such models are not monotone or competitive dynamical systems. Meanwhile, since the environmental function $g(I)$ can be arbitrary, the geometric approach may not be easily applied. It is, however, interesting to note that the classical method of Lyapunov functions combined with the Volterra–Lyapunov matrix properties [45,46] can lead to the proof of the endemic global stability. The details are provided below.

We will study the system (4.1)–(4.3) in the biologically feasible domain

$$\Delta = \{(S,I,B) | S \geqslant 0, I \geqslant 0, S + I \leqslant N, B \geqslant 0\} \tag{4.10}$$

which is clearly a positively invariant set in $\mathbb{R}^3$.

We construct a Lyapunov function in the form of

$$V(S,I,B) = w_1(S - S^*)^2 + w_2(I - I^*)^2 + w_3(B - B^*)^2, \tag{4.11}$$

where w_1, w_2 and w_3 are positive constants, the specific values of which are usually difficult to determine and are not of our interest here.

We have

$$\frac{dV}{dt} = \nabla V \cdot \frac{dX}{dt} = 2w_1(S - S^*)[bN - Sf(I,B) - bS] + 2w_2(I - I^*)[Sf(I,B) - (\gamma + b)I] + 2w_3(B - B^*)[g(I) - \delta B]. \tag{4.12}$$

Obviously, when $X = X^*$, $\frac{dV}{dt} = 0$; when X is on the S-axis (i.e., $I = B = 0$), the sign of $\frac{dV}{dt}$ is indefinite. We aim to show that when $X \neq X^*$ and $(I,B) \neq (0,0)$, $\frac{dV}{dt} < 0$ holds everywhere.

Substituting Eqs. (4.7)–(4.9) into Eq. (4.12), we obtain

$$\begin{aligned}\frac{dV}{dt} &= 2w_1(S - S^*)\{-b(S - S^*) - f(I,B)(S - S^*) - S^*[f(I,B) - f(I^*,B^*)]\} + 2w_2(I - I^*)[Sf(I,B) - S^*f(I^*,B^*) - (\gamma + b)(I - I^*)] \\ &\quad + 2w_3(B - B^*)[g(I) - \delta B] = -2w_1[b + f(I,B)](S - S^*)^2 \\ &\quad - 2w_1S^*(S - S^*)[f(I,B) - f(I^*,B^*)] - 2w_2(\gamma + b)(I - I^*)^2 \\ &\quad + 2w_2f(I,B)(I - I^*)(S - S^*) + 2w_2S^*(I - I^*)[f(I,B) - f(I^*,B^*)] \\ &\quad + 2w_3(B - B^*)[g(I) - \delta B - (g(I^*) - \delta B^*)].\end{aligned} \tag{4.13}$$

Now expanding $f(I,B)$ and using the bilinear assumption (4.4), we obtain

$$f(I,B) = f(I^*,B^*) + \beta_2(I - I^*) + \beta_1(B - B^*). \tag{4.14}$$

Meanwhile, applying the mean value theorem to $g(I)$, we obtain

$$g(I) - g(I^*) = g'(\bar{I})(I - I^*) \tag{4.15}$$

for some $\bar{I}$ between I and I^*. Substitution of Eqs. (4.14) and (4.15) into Eq. (4.13) yields

$$\frac{dV}{dt} = (X - X^*)(WA + A^T W^T)(X - X^*)^T, \tag{4.16}$$

where the matrices W and A are given by

$$W = \begin{bmatrix} w_1 & 0 & 0 \\ 0 & w_2 & 0 \\ 0 & 0 & w_3 \end{bmatrix}, \quad A = \begin{bmatrix} -[b + f(I,B)] & -\beta_2 S^* & -\beta_1 S^* \\ f(I,B) & -[\gamma + b - \beta_2 S^*] & \beta_1 S^* \\ 0 & g'(\bar{I}) & -\delta \end{bmatrix}.$$

Assume $X \neq X^*$ and X is not on the S axis. Below we show that there exist $w_1 > 0$, $w_2 > 0$ and $w_3 > 0$ such that the matrix $WA + A^T W^T$ is negative definite.

Notation 4.4. For convenience, we write a matrix $B > 0 (< 0)$ if B is positive (negative) definite.

Definition 4.5. We say a non-singular $n \times n$ matrix B is Volterra–Lyapunov stable if there exists a positive diagonal $n \times n$ matrix M such that $MB + B^T M^T < 0$.

Notation 4.6. For any $n \times n$ matrix B, we let $\widetilde{B}$ denote the $(n-1) \times (n-1)$ matrix obtained from B by deleting its last row and last column. This notation will be frequently used in what follows.

Lemma 4.7 ([8,47]). *Let $D = \begin{bmatrix} d_{11} & d_{12} \\ d_{21} & d_{22} \end{bmatrix}$ be a 2×2 matrix. Then D is a Volterra–Lyapunov stable matrix if and only if $d_{11} < 0$, $d_{22} < 0$, and $\det(D) = d_{11}d_{22} - d_{12}d_{21} > 0$.*

Lemma 4.8 ([45,46]). *Let $D = [d_{ij}]$ be a non-singular $n \times n$ matrix $(n \geqslant 2)$ and $M = \mathrm{diag}(m_1, \ldots, m_n)$ be a positive diagonal $n \times n$ matrix. Let $E = D^{-1}$. Then, if $d_{nn} > 0$, $\widetilde{M}\widetilde{D} + (\widetilde{M}\widetilde{D})^T > 0$, and $\widetilde{M}\widetilde{E} + (\widetilde{M}\widetilde{E})^T > 0$, it is possible to choose $m_n > 0$ such that $MD + D^T M^T > 0$.*

Lemma 4.9. *For the matrix A defined in* Eq. (4.16), *$\widetilde{A}$ is Volterra–Lyapunov stable.*

Proof

$$\widetilde{A} = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix} = \begin{bmatrix} -[b + f(I,B)] & -\beta_2 S^* \\ f(I,B) & -[\gamma + b - \beta_2 S^*] \end{bmatrix}.$$

Clearly $a_{11} < 0$. Next we show $a_{22} < 0$, i.e.,

$$\gamma + b - \beta_2 S^* > 0. \tag{4.17}$$

Setting $I = 0$, $B = B^*$ in Eq. (4.14), we obtain

$$0 < f(0, B^*) = f(I^*, B^*) - \beta_2 I^*.$$

Thus $f(I^*, B^*) > \beta_2 I^*$. Meanwhile, at the endemic equilibrium we have $S^* f(I^*, B^*) = (\gamma + b) I^*$. Hence,

$$\gamma + b = \frac{S^* f(I^*, B^*)}{I^*} > \beta_2 S^*.$$

Finally, it is clear to see $\det(\widetilde{A}) = a_{11}a_{22} - a_{12}a_{21} > 0$ since $a_{12} < 0$, $a_{21} > 0$. Therefore, $\widetilde{A}$ is Volterra–Lyapunov stable based on Lemma 4.7. □

Lemma 4.10. *When $(I,B) \neq (0,0)$, the determinant of $-A$ is positive, where the matrix A is defined in* Eq. (4.16).

Proof. Expanding the matrix $-A$ by the first column, we obtain

$$\det(-A) = [b + f(I,B)][\delta(b + \gamma) - \delta\beta_2 S^* - \beta_1 g'(\bar{I}) S^*] + f(I,B)[\delta\beta_2 S^* + \beta_1 g'(\bar{I}) S^*].$$

The second part of $\det(-A)$ is clearly positive. Next we show

$$\delta(b + \gamma) - \delta\beta_2 S^* - \beta_1 g'(\bar{I}) S^* > 0. \tag{4.18}$$

Based on Lemma 4.2 and Eq. (4.15), we have, for all $I > 0$ and $I \neq I^*$,

$$g'(\bar{I}) = \frac{g(I) - g(I^*)}{I - I^*} < \frac{g(I^*)}{I^*} = \frac{\delta B^*}{I^*}. \tag{4.19}$$

Thus $I^* g'(\bar{I}) - \delta B^* < 0$, which yields

$$B_1 \triangleq B^* - \frac{g'(\bar{I})}{\delta} I^* > 0. \tag{4.20}$$

Now, substitute the point $(I,B) = (0, B_1)$ into Eq. (4.14) to obtain

$$0 < f(0, B_1) = f(I^*, B^*) - \beta_2 I^* + \beta_1 \frac{g'(\bar{I})}{\delta} I^*. \tag{4.21}$$

Combining the results in (4.21) and (4.8), we obtain (4.18). Hence, $\det(-A) > 0$. □

Using the transpose of the matrix of cofactors, we write the inverse of $-A$ by

$$(-A)^{-1} = \frac{1}{\det(-A)} \begin{bmatrix} c_{11}(+) & c_{21}(-) & c_{31}(-) \\ c_{12}(+) & c_{22}(+) & c_{32}(+) \\ c_{13}(+) & c_{23}(+) & c_{33}(+) \end{bmatrix}, \tag{4.22}$$

where c_{ij} denotes the cofactor of the (i,j) entry of the matrix $-A$, and the + or − in the parenthesis indicates the sign of c_{ij}. Note that $\det(-A) > 0$ based on Lemma 4.10. Specifically, we have

$$\begin{aligned}
c_{11} &= \delta(b + \gamma) - \delta\beta_2 S^* - \beta_1 g'(\bar{I}) S^* > 0, \\
c_{21} &= -(\delta\beta_2 S^* + g'(\bar{I})\beta_1 S^*) < 0, \\
c_{31} &= -\beta_1\beta_2 (S^*)^2 - \beta_1 S^* [\gamma + b - \beta_2 S^*] < 0, \\
c_{12} &= \delta f(I,B) > 0, \\
c_{22} &= \delta(b + f(I,B)) > 0, \\
c_{32} &= b\beta_1 S^* > 0, \\
c_{13} &= f(I,B) g'(\bar{I}) > 0, \\
c_{23} &= g'(\bar{I})(b + f(I,B)) > 0, \\
c_{33} &= (b + f(I,B))[\gamma + b - \beta_2 S^*] + S^* \beta_2 f(I,B) > 0,
\end{aligned}$$

where we have applied (4.18) to obtain $c_{11} > 0$, and (4.17) to show $c_{31} < 0$ and $c_{33} > 0$.

Lemma 4.11. *Let $D = -A$ and $E = (-A)^{-1}$, where A is defined in* Eq. (4.16). *Then there exists a positive 2×2 diagonal matrix $\widetilde{W} = \begin{bmatrix} w_1 & 0 \\ 0 & w_2 \end{bmatrix}$ such that $\widetilde{W}\widetilde{D} + (\widetilde{W}\widetilde{D})^T > 0$ and $\widetilde{W}\widetilde{E} + \left(\widetilde{W}\widetilde{E}\right)^T > 0$.*

Proof. Note that $A^{-1} = -E$. Using Eq. (4.22), we obtain

$$\widetilde{A^{-1}} = \frac{1}{\det(-A)} \begin{bmatrix} -c_{11} & -c_{21} \\ -c_{12} & -c_{22} \end{bmatrix}.$$

Based on Lemma 4.7, it is straightforward to verify that $\widetilde{A^{-1}}$ is Volterra–Lyapunov stable. Hence, there exists a positive 2×2 diagonal matrix $\widetilde{W}$ such that $\widetilde{W}\widetilde{A^{-1}} + (\widetilde{W}\widetilde{A^{-1}})^T < 0$. Since $E = (-A)^{-1}$, we obtain $\widetilde{W}\widetilde{E} + (\widetilde{W}\widetilde{E})^T > 0$, i.e.,

$$\frac{1}{\det(-A)}\begin{bmatrix} 2w_1c_{11} & w_1c_{21}+w_2c_{12} \\ w_1c_{21}+w_2c_{12} & 2w_2c_{22} \end{bmatrix} > 0.$$

Hence, the determinant of the above matrix must be positive, i.e.,

$$4w_1w_2c_{11}c_{22} - (w_1c_{21}+w_2c_{12})^2 > 0.$$

Substituting the expressions for c_{ij} $(i,j = 1,2)$ and manipulating the algebra, we obtain

$$\begin{aligned} 0 &< 4w_1w_2c_{11}c_{22} - (w_1c_{21}+w_2c_{12})^2 \\ &= J - 2w_1w_2(2b + f(I,B))g'(\bar{I})\beta_1 S^* - (w_1S^*)^2\beta_1 g'(\bar{I})[2\beta_2 + \beta_1 g'(\bar{I})], \end{aligned}$$

where

$$J = 4w_1w_2(b+f(I,B))[\gamma + b - \beta_2 S^*] - [w_2 f(I,B) - w_1\beta_2 S^*]^2.$$

Clearly we must have $J > 0$. Now,

$$\widetilde{W}\widetilde{D} + \left(\widetilde{W}\widetilde{D}\right)^T = \begin{bmatrix} 2w_1[b+f(I,B)] & w_1\beta_2 S^* - w_2 f(I,B) \\ w_1\beta_2 S^* - w_2 f(I,B) & 2w_2[\gamma + b - \beta_2 S^*] \end{bmatrix}.$$

Note that the (1,1) and (2,2) entries of this 2×2 matrix are positive, and that its determinant is exactly J. Hence, it is clear to see $\widetilde{W}\widetilde{D} + \left(\widetilde{W}\widetilde{D}\right)^T > 0$. The proof is then complete. □

Theorem 4.12. *The matrix A defined in* Eq. (4.16) *is Volterra-Lyapunov stable.*

Proof. Based on Lemmas 4.8 and 4.11, there exists a positive 3×3 diagonal matrix W such that $W(-A) + (-A)^T W^T > 0$. Thus $WA + A^T W^T < 0$. □

Therefore, we obtain $\frac{dV}{dt} < 0$ when $X \neq X^*$ and X is not on the S-axis (a set of measure zero). Thus we have established the following theorem:

Theorem 4.13. *The endemic equilibrium of the model system* (4.1)–(4.3) *is globally asymptotically stable.*

5. Conclusions and discussion

With the environmental component incorporated and multiple transmission pathways coupled, the cholera models distinguish themselves from regular SIR and SEIR epidemiological models which have been extensively studied and whose global dynamics have been relatively well established (see [5,25,17,18,26,28,30,32,34,48,57], among others). Using the methods of monotone dynamical systems, geometric approach, and Lyapunov functions, we have investigated in this paper the global asymptotic stability of the endemic equilibria for several deterministic cholera models and obtained new global stability results. These models represent biologically important, and mathematically non-trivial, cases in the study of cholera dynamics. The analysis and results presented in this paper build a solid base for future work on the global dynamics of the most general cholera model and for deeper understanding of the fundamental disease mechanism. However, it should be noticed that all models we analyzed in the article do not include seasonal fluctuations. These models also do not consider the natural cycle of growth and dispersal of vibrios in the environment. Further research on building more realistic models for dynamics of cholera is highly demanded.

In this paper, the three techniques we employed all have strength and weakness. The method of monotone dynamical systems [12,28,49], when applicable, is easier to implement than the geometric approach, since it essentially treats a three-dimensional autonomous system as a two-dimensional one. Unfortunately, most high-dimensional infectious disease models do not possess the nice properties of monotone systems, which limits the application of this approach. The geometric approach, originally proposed by Li and Muldowney [9,29,31], has gained some popularity in recent years (see, e.g., [2,24]) as it has less constraints on the model systems. Among the three, this method seems to have the best potential to deal with more general model systems. The disadvantage, however, is that the implementation of the geometric approach is not straightforward and involves extra non-trivial technical details, particularly the estimate of the Lozinskiĭ measure. In addition, the method of Lyapunov functions has been known for many decades. The challenge in the application of this method is that there is no systematic way to construct Lyapunov functions (particularly, the determination of the appropriate coefficients is often a matter of luck), so that its success largely depends on trial and error as well as on specific problems. In this paper, by combining this classical approach with the Volterra–Lyapunov matrix analysis [45–47], we have leveraged the difficulty of determining specific coefficient values and, as such, wider application of Lyapunov functions to dynamical systems could be promoted. As can been seen from our analysis in Section 4, the extension of this approach to even higher dimensional systems is possible but becomes much harder, since the proof of Volterra–Lyapunov stable matrices involves considerably more work in higher dimensions.

The work presented in this paper is not limited to cholera models. Indeed, a number of known infectious diseases [33,52], such as Typhoid fever, Amebiasis, Dracunculiasis, Giardia, Cryptosporidium, and Campylobacter, involve environmental components (typically water-borne pathogen) and can be modeled in a similar manner as those for cholera. The analysis and results from this work can thus contribute to a wide range of problems in epidemiological studies.

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