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Dynamics of cholera outbreak with bacteriophage and periodic rate of contact

Prabir Panja[1] · **Shyamal Kumar Mondal**[1] · **Joydev Chattopadhyay**[2]

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Abstract In this paper, a cholera epidemic model with periodic transmission rate has been considered and discussed. It is shown that the disease free equilibrium point is globally asymptotically stable and also seen that the cholera disease is disappeared if the basic reproduction number is less than one. When the basic reproduction number is grater than one, then the endemic equilibrium is globally asymptotically stable. Finally, numerical simulations have been given for the existence of the analytical results.

Keywords Cholera disease · Epidemic model · Local stability · Global stability · Bacteriophage

1 Introduction

The cholera, a waterborne gastroenteric infection, remains a significant threat to public health in the developing countries. It is caused by the bacterium *Vibrio cholerae*. It is typically transmitted through water and food that have been contaminated with fecal matter from a person who is infected with the disease. Now-a-days, several number of mathematical models have been developed for understanding the dynamics of cholera disease. A mathematical model for cholera epidemic occurred in the European Mediterranean region had been developed and discussed by Capasso [1] in 1973. In this model, Capasso used two differential equations to describe the dynamics of infected people in the infected region and the dynamics of the bacterium *V. cholerae*. Codeco [2] extended the model of Capasso by introducing one additional equation of susceptible human population and described the dynamics of the persistence of the disease cholera. After that Codeco's model was extended by Hartley [3] including hyperinfectious vibrio bacterium. Again, Hartley's mathematical model was analysed by Liao and Wang [4].

Cholera disease is typically seasonal due to climatic factors, physical and many biological factors. It is observed that in Bangladesh the seasonality of cholera exhibits two peaks per year and differs from that of other diarrheal diseases [5]. Cholera disease typically increases from November to January and April to May. In the same time, the seasonal cholera disease is occurred in the peak form in April, May and June [6] in every year. There are many research papers on the cholera disease such as [7–13] etc.

It is known that the bacteriophage might control the natural population of pathogens. Moreover, the recent studies in marine microbiology also have revealed the elegant balance between bacteriophage and their mycobacterial prey. In 2009, Nelson et al. [14] explored that in a closed experimental system, the transmission of *V. cholerae* may be minimized when these two factors such as bacteriophage and bacterium are combined in the aquatic environments. Therefore, the dynamical interaction between bacteriophage and bacterium in pond water suggests that a model of cholera transmission should incorporate a measure for the rapid decay of bacterial culturability and predation by bacteriophage.

✉ Prabir Panja
prabirpanja@gmail.com

✉ Shyamal Kumar Mondal
shyamal_260180@yahoo.com

Joydev Chattopadhyay
joydev@isical.ac.in

[1] Department of Applied Mathematics with Oceanology and Computer Programming, Vidyasagar University, Midnapore 721 102, W.B., India

[2] Agricultural and Ecological Research Unit, ISI, 203 B.T.Road, Kolkata, India

There are two hundreds species that infect V. cholerae known as vibriophage. In 2006 a mathematical model was described by Jensen et al. [15] in the role of bacteriophage in the control of cholera outbreak. They suggests that either bacteria in the environmental reservoir are hyperinfectious or most victims ingest bacteria amplified in food or drinking water contaminated by environmental water carrying few viable V. cholerae. The consequent reduction of bacteria numbers in the effluent might fully account for the decline in disease incidence and density of phage preying on these bacteria. In this interpretation, the outbreak drives the changes in phage populations, rather than the reverse. They showed that the large numbers of phage to the reservoir at the time of the bacterial bloom decreases the size of the epidemic. If there are few number of phage such 10^5 virion per liter or less then there is virtually no effect on the epidemic. There are many research papers on baceriophage dynamics such as [16–19] etc. A cholera epidemic model of an optimal cost effectiveness study on Zimbabwe cholera seasonal data from 2008 to 2011 was developed by Sardar et al. [20] in 2013. We have modified this model by introducing the bacteriophage and discussed the dynamical behavior of the proposed cholera epidemic model.

In this paper, the dynamical behavior of the interaction between cholera pathogen *V. cholerae* and bacteriophage has been discussed. Then, the extinction and uniform persistence of the disease have been explored here. Also, the existence and stability of positive ω-periodic solution have been discussed precisely. Finally, a numerical simulations have been presented to support the analytic results of the proposed model.

2 Model formulation

In this paper, it is considered that an area is effected with *V. cholerae*. So, the population $N(t)$ at time t, consists of three kinds of populations such as (i) susceptible human $S(t)$, (ii) infected human $I(t)$ and (iii) recovered human $R(t)$ i.e., $N(t) = S(t) + I(t) + R(t)$. Here, the bacterial population at time t is also considered of two types such as: (i) hyper-infectious bacteria $B_H(t)$ and (ii) low-infectious bacteria $B_L(t)$. Also here, the population of bacterio-phage $P(t)$ has been introduced.

Now, the susceptible population is increased (i) by a constant recruitment of newborn at a rate Λ_H and (ii) by those recovered persons who loses their temporary immunity to cholera at a rate w. It is reduced by getting infected on contact with hyper-infectious and low-infectious bacterium at a rates $\beta_H(t)\frac{B_H}{K_H+B_H}$ and $\beta_L(t)\frac{B_L}{K_L+B_L}$ respectively and also decreased by natural death at a rate μ_d, where $\beta_H(t)$ and $\beta_L(t)$ have been defined in this paper as follows:

$$\beta_H(t) = \beta_{H0}\left(1 + \delta cos\left(\frac{2\pi t}{365}\right)\right)$$
$$\beta_L(t) = \beta_{L0}\left(1 + \delta cos\left(\frac{2\pi t}{365}\right)\right)$$

and δ is the amplitude of seasonality.

Here, infected human is increased by those susceptible humans who get infected in contact with hyper-infectious and low-infectious vibrios and decreased by (i) those who are recovered from cholera at a rate γ, (ii) those who die due to cholera infection at a rate μ_c and (iii) those who die naturally at a rate μ_d.

Again, recovered human population is increased by those infected people who get recovery from the disease at a rate γ. It is observed that the recovered population is reduced due to the loss of natural immunity to cholera at a rate w and due to the natural dies at a rate μ_d.

Hyper-infectious bacterium is enriched from the amount of hyper-infectious V. cholerae bacterium in the contaminated aquatic environment due to infected human feces, vomiting etc. at a rate ξ.

It is assumed that hyper-infectivity bacterium losse their hyper-infectivity at a rate χ. Here, it is also assumed that the both bacterium populations decrease by the consumption of phage (bacterio phage). The number of phage produced per infected bacterium (burst size) is denoted by β_1. The death rate of phage in the reservoir is w_1 per day. Therefore, under the above considerations a mathematical model of *V. cholerae* has been suggested as follows:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \Lambda_H + wR - \beta_H(t)\frac{B_H S}{K_H+B_H} - \beta_L(t)\frac{B_L S}{K_L+B_L} - \mu_d S\\
\frac{dI}{dt} &= \beta_H(t)\frac{B_H S}{K_H+B_H} + \beta_L(t)\frac{B_L S}{K_L+B_L} - (\mu_d+\mu_c+\gamma)I\\
\frac{dR}{dt} &= \gamma I - (w+\mu_d)R\\
\frac{dB_H}{dt} &= \xi I - \chi B_H - \gamma_1 B_H P\\
\frac{dB_L}{dt} &= \chi B_H - \delta_L B_L - \gamma_1 B_L P\\
\frac{dP}{dt} &= \beta_1\gamma_1(B_H + B_L)P - w_1 P
\end{aligned}\right\} \quad (1)$$

The initial conditions are taken as $S(0) \geq 0, I(0) \geq 0, R(0) \geq 0, B_H(0) \geq 0, B_L(0) \geq 0, P(0) \geq 0$.

Theorem 1 *The solution of the proposed model (1)* $(S(t), I(t), R(t), B_H(t), B_L(t), P(t))$ *is uniformly and ultimately bounded i.e., there exists a positive real number M such that* $(S(t), I(t), R(t), B_H(t), B_L(t), P(t)) \leq (M, M, M, M, M, M)$ *for* $t \geq T$ *where* T *is a fixed time.*

Proof From the first three equations of proposed model (1), it is obtained that

$$\begin{aligned}
\frac{d(S+I+R)}{dt} &= \Lambda_H - \mu_d(S+I+R) - \mu_c I\\
&\leq \Lambda_H - \mu_d(S+I+R) \qquad (2)
\end{aligned}$$

Solving Eq. (2) by using standard comparison theorem [21], there exists $t_1 > 0$ such that $S + I + R \leq \frac{\Lambda_H}{\mu_d}$ for all $t \geq t_1$. Then, we have

$$S \leq \frac{\Lambda_H}{\mu_d}, I \leq \frac{\Lambda_H}{\mu_d} \text{ and } R \leq \frac{\Lambda_H}{\mu_d}, \quad \text{for all} \quad t \geq t_1. \tag{3}$$

Again, from the fourth equation of the proposed model (1), it is obtained that

$$\begin{aligned} \frac{dB_H}{dt} &\leq \xi \frac{\Lambda_H}{\mu_d} - \chi B_H - \gamma_1 B_H P \\ &\leq \xi \frac{\Lambda_H}{\mu_d} - \chi B_H \end{aligned} \tag{4}$$

Hence, again solving Eq. (4) by using standard comparison theorem, there exists $t_2 \geq t_1$ such that

$$B_H(t) \leq \frac{\Lambda_H}{\chi \mu_d}, \quad \text{for all} \quad t \geq t_2. \tag{5}$$

From the fifth equation of the proposed model (1), it is obtained that

$$\begin{aligned} \frac{dB_L}{dt} &\leq \frac{\xi \Lambda_H}{\chi \mu_d} - \delta_L B_L - \gamma_1 B_L P \\ &\leq \frac{\xi \Lambda_H}{\chi \mu_d} - \delta_L B_L \end{aligned} \tag{6}$$

Again, also solving Eq. (6) by using standard comparison theorem, there exists $t_3 \geq t_2 \geq t_1$ such that

$$B_L(t) \leq \frac{\xi \Lambda_H}{\mu_d \delta_L}, \text{ for all } \quad t \geq t_3. \tag{7}$$

Again, from the sixth equation of the proposed model (1), it is obtained that

$$\frac{dP}{dt} \leq \beta_1 \gamma_1 \left(\frac{\xi \Lambda_H}{\chi \mu_d} + \frac{\xi \Lambda_H}{\mu_d \delta_L} \right) P - w_1 P \tag{8}$$

Hence, solving Eq. (8) by using standard comparison theorem, there exists $T \geq t_1, t_2, t_3$ such that

$$P(t) \leq e^{\left(\frac{\beta_1 \gamma_1 \xi \Lambda_H}{\mu_d} \left(\frac{1}{\chi} + \frac{1}{\delta_L} \right) \right)}. \tag{9}$$

From Eqs. (3), (5), (7) and (9), let us define $M = max \{ \frac{\Lambda_H}{\mu_d}, \frac{\xi \Lambda_H}{\chi \mu_d}, \frac{\xi \Lambda_H}{\delta_L \mu_d}, e^{(\frac{\beta_1 \gamma_1 \xi \Lambda_H}{\mu_d} (\frac{1}{\chi} + \frac{1}{\delta_L}))} \}$.

Thus it follows that, $S(t) \leq M$, $I(t) \leq M$, $R(t) \leq M$, $B_H(t) \leq M$, $B_L(t) \leq M$ and $P(t) \leq M$ for all $t \geq T$. Therefore, the solution of the system are uniformly and ultimately bounded.

3 Local stability of disease free periodic equilibrium point

Let (R^n, R^n_+) be the standard ordered n-dimensional Euclidean space with a norm $||.||$. For $u, v \in R^n$, we denote $u \geq v$ if $u - v \in R^n_+; u > v$, if $u - v \in R^n; u \gg v$, if $u - v \in Int(R^n_+)$.

Let $A(t)$ be a continuous, cooperative, irreducible and ω periodic $n \times n$ matrix function. Then $\phi_A(t)$ be a fundamental solution matrix of

$$\frac{dx}{dt} = A(t)x \tag{10}$$

Let $\rho(\phi_A(\omega))$ be the spectral radius of $\phi_A(\omega)$. According to Perron–Frobenius theorem, $\rho(\phi_A(\omega))$ is the simple principal eigenvalue of $\phi_A(\omega)$ and it admits an eigenvector v^* which is grater than equal to zero vector.

Lemma 1 *(Zhang and Zhao [22]) Let* $s = \frac{1}{\omega} ln \rho(\phi_A(\omega))$, *then there exists a positive* ω *periodic function* $v(t)$ *such that* $e^{st} v(t)$ *is a solution of (10).*

In the following, we calculate the basic reproduction number of proposed system (1). It is easy to see that the proposed system (1) has exactly one disease free equilibrium point $E_0(S_0, 0, 0, 0, 0, 0)$ where $S_0 = \frac{\Lambda_H}{\mu_d}$.

Now, $F(t) = \begin{bmatrix} 0 & \frac{\beta_H(t)\Lambda_H}{K_H \mu_d} & \frac{\beta_L(t)\Lambda_H}{K_L \mu_d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$,

$V(t) = \begin{bmatrix} (\gamma + \mu_c + \mu_d) & 0 & 0 \\ -\xi & \chi & 0 \\ 0 & -\chi & \delta_L \end{bmatrix}$

Let $Y(t, s)$ is an 3×3 matrix solution of the system

$$\frac{dY(t,s)}{dt} = -V(t)Y(t,s) \tag{11}$$

for any $t \leq s$, $Y(s, s) = I$ where I is an 3×3 identity matrix.

Let C_ω be the ordered banach space of all ω periodic functions from R to R^3 which is equipped with maximum norm $||.||_\infty$ and the positive cone $C^+_\omega = \{\phi \in C_\omega : \phi(t) \geq 0, \text{ for all t in } R\}$. Now, using Eq. (11) we consider the linear operator $L : C_\omega \longrightarrow C_\omega$ by

$$(L\phi)(t) = \int_0^{+\infty} Y(t, t-a) F(t-a) \phi(t-a) da \tag{12}$$

for any $t \in R$ and $\phi \in C_\omega$.

Finally, from the Eq. (12) we define the basic reproduction number R_0 for the system (1) as the spectral radius of L i.e., $R_0 = \rho(L)$ which has been motivated by the concept of next generation method introduced in the article of [23–25]. From the above discussion, the following theorem for the local asymptotically stability of disease free equilibrium $E_0(S_0, 0, 0, 0, 0, 0)$ has been obtained.

Theorem 2 *(Wang and Zhao [23]) The following statements are valid*

1. $R_0 = 1$ *if and only if* $\rho(\phi_{F-V}(\omega)) = 1$
2. $R_0 > 1$ *if and only if* $\rho(\phi_{F-V}(\omega)) > 1$
3. $R_0 < 1$ *if and only if* $\rho(\phi_{F-V}(\omega)) < 1$

Thus, we can say that the disease free equilibrium $E_0(S_0, 0, 0, 0, 0, 0)$ *is locally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

4 Global stability of disease free periodic equilibrium point

Theorem 3 *If* $R_0 < 1$, *then the disease free periodic state is globally asymptotically stable.*

Proof From second, fourth and fifth equations of the system (1) we have

$$\begin{aligned}\frac{dI}{dt} &= \beta_H(t)\frac{B_H S}{K_H + B_H} + \beta_L(t)\frac{B_L S}{K_L + B_L} \\ &\quad -(\gamma + \mu_d + mu_c)I \\ &\le \beta_H(t)\frac{B_H}{K_H + B_H}\frac{\Lambda_H}{\mu_d} + \beta_L(t)\frac{B_L}{K_L + B_L}\frac{\Lambda_H}{\mu_d} \\ &\quad -(\gamma + \mu_d + mu_c)I \\ &\le \beta_H(t)\frac{\Lambda_H B_H}{K_H \mu_d} + \beta_L(t)\frac{\Lambda_H B_L}{\mu_d K_L}\frac{\Lambda_H}{\mu_d} \\ &\quad -(\gamma + \mu_d + mu_c)I \qquad (13)\end{aligned}$$

$$\frac{dB_H}{dt} \le \xi(t)I - \chi B_H \qquad (14)$$

$$\frac{dB_L}{dt} \le \chi B_H - \delta_L B_L \qquad (15)$$

Then, for all $t \ge 0$, hence $0 \le S(t) \le \frac{\Lambda_H}{\mu_d}$, $B_H(t) \ge 0$, $B_L(t) \ge 0$ and $P(t) \ge 0$. Now, from the Eqs. (13), (14) and (15) we consider the following auxiliary system:

$$\begin{aligned}\frac{dI}{dt} &= \beta_H(t)\frac{\Lambda_H B_H}{K_H \mu_d} + \beta_L(t)\frac{\Lambda_H B_L}{\mu_d K_L}\frac{\Lambda_H}{\mu_d} \\ &\quad -(\gamma + \mu_d + mu_c)I \\ \frac{dB_H}{dt} &= \xi I - \chi B_H \\ \frac{dB_L}{dt} &= \chi B_H - \delta_L B_L\end{aligned}$$

which can be written as

$$\frac{dX}{dt} = (F(t) - V(t))X \qquad (16)$$

where $X = (I(t), B_H(t), B_L(t))^T$.

Then using above Lemma 1, there exists a positive ω-periodic function $\bar{X}(t)$ such that $X(t) = e^{st}\bar{X}(t)$ is a solution of the above Eq. (16) where $s = \frac{1}{\omega} ln\rho(\phi_{F-V}(\omega))$. Again, from Theorem 2, we know that for $R_0 < 1$, $\rho(\phi_{F-V}(\omega)) < 1$, so s must be a negative constant. Therefore, when $t \to \infty$, we have $X(t) \to 0$.

$$i.e., \lim_{t\to\infty} I(t) = 0, \lim_{t\to\infty} B_H(t) = 0 \text{ and } \lim_{t\to\infty} B_L(t) = 0.$$

$$i.e., \lim_{t\to\infty} R(t) = 0, \lim_{t\to\infty} P(t) = 0 \text{ and } \lim_{t\to\infty} S(t) = \frac{\Lambda_H}{\mu_d}$$

Hence, the above implies that the disease free equilibrium point E_0 is globally asymptotically stable.

5 Uniform persistence of the disease

Theorem 4 *If* $R_0 > 1$, *there exists a positive constant* ϵ *such that for all initial value* $(S(0), I(0), R(0), B_H(0), B_L(0), P(0)) \in \{(S, I, R, B_H, B_L, P) \in R^6_+ : I > 0, B_H > 0, B_L > 0\}$, *the solution of system (1) satisfies the following*

$$\lim_{t\to\infty} inf\, I(t) \ge \epsilon, \lim_{t\to\infty} inf\, B_H(t) \ge \epsilon \text{ and } \lim_{t\to\infty} inf\, B_L(t) \ge \epsilon.$$

i.e., for $R_0 > 1$, *the disease in system (1) is uniformly persistent.*

Proof Let us consider the sets $X = R^6_+, X_0 = \{(S, I, R, B_H, B_L, P) \in R^6_+ : I > 0, B_H > 0, B_L > 0\}$ and $\partial X_0 = X \backslash X_0$. Next, we define a poincare map $P : R^6_+ \longrightarrow R^6_+$ satisfying $P(x^0) = u(\omega, x^0), \forall x^0 \in R^6_+$ where $u(t, x^0)$ be the unique solution of system (1) satisfying $u(0, x^0) = x^0$.

At first, we show that P is uniformly persistent with respect to $(X_0, \partial X_0)$. It is easy to see from the system (1) that X and X_0 are positively invariant. Moreover, ∂X_0 is relatively closed set in X. Now from Theorem 1, it follows that the solutions of the system (1) are uniformly and ultimately bounded. Thus, the semiflow P is point dissipative on R^6_+ and $P : R^6_+ \to R^6_+$ is compact by Theorem 3.4.8 in [26]. Then, it follows that P admits a global attractor which attracks every bounded set in R^6_+. Now, we define another set M_∂ as

$$\begin{aligned}M\partial = \{&(S(0), I(0), R(0), B_H(0), B_L(0), P(0)) \in \partial X_0 : \\ &P^m(S_0, I_0, R_0, B_{H0}, B_{L0}, P_0) \in \partial X_0, \forall m \in N \cup 0\}.\end{aligned}$$

Next, it is claimed that

$$M\partial = \{(S, 0, R, 0, 0, P) : S \ge 0, R \ge 0, P \ge 0\}.$$

In fact, it is obvious that

$$\{(S, 0, R, 0, 0, P) : S \ge 0, R \ge 0, P \ge 0\} \subseteq M\partial$$

For any $(S(0), I(0), R(0), B_H(0), B_L(0), P(0)) \in \partial X_0/\{(S, 0, R, 0, 0, P) : S \geq 0, R \geq 0, P \geq 0\}$, if $I(0) = 0, B_H(0) = 0, B_L(0) > 0$ it is clear that $S > 0$ and $B_L > 0$ for all $t > 0$. Now from the second equation of (1) we have $\dot{I}(0) = \beta_L(t)\frac{S(0)B_L(0)}{K_L+B_L(0)} > 0 \Rightarrow I(0) > 0$. Thus from the fourth equation of (1) we have $\dot{B_H}(0) = \xi I(0) > 0$ else if $I(0) = 0, B_L(0) = 0$ and $B_H > 0$. Then similarly we can show that $\dot{I}(0) > 0$ and $B_H(0) > 0$ and similarly for other cases also. Therefore, if $(S(0), I(0), R(0), B_H(0), B_L(0), P(0)) \notin \{(S, 0, R, 0, 0, P) : S \geq 0, R \geq 0, P \geq 0\}$ then $(S(t), I(t), R(t), B_H(t), B_L(t), P(t)) \notin \partial X_0$ for simultaneously small $t > 0$. This implies that $M_\partial \subseteq \{(S, 0, R, 0, 0, P) : S \geq 0, R \geq 0, P \geq 0\}$. Therefore, we have $M_\partial = \{(S, 0, R, 0, 0, P) : S \geq 0, R \geq 0, P \geq 0\}$. Clearly, E_0 is one fixed point of P in M_∂. If $(S(t), I(t), R(t), B_H(t), B_L(t), P(t))$ is a solution of system (1) initiating from M_∂, it then follows from (1) that $S(t) \to S_0, I(t) \to 0, R(t) \to 0, B_H(t) \to 0, B_L(t) \to 0, P(t) \to 0$ as $t \to \infty$. So any solution of (1) initiating in M_∂ will remain into M_∂.

We will now show that $\{E_0\}$ is an acyclic covering of E_0. It is enough to show that $\{E_0\}$ isolated invariant subset of M_∂ i.e., $W^s(E_0) \cap X_0 = \emptyset$, where $W^s(E_0)$ is the stable set of E_0.

Let $x^0 = (S(0), I(0), R(0), B_H(0), B_L(0), P(0)) \in X_0$, then by the continuity of solution with respect to initial values $\forall x \in (0, \frac{\Lambda_H}{\mu_d})$, then there exists $\xi > 0$ such that $\forall x^0 \in X_0$ with $||x^0 - E_0|| \leq \xi$, it follows that $||u(t, x^0) - u(t, E_0)|| \leq \epsilon \forall t \in [0, w]$. To show $x^0 \in X_0 \Rightarrow x^0 \notin W^s(E_0)$, it is enough to show that $\lim_{m\to\infty} d(P^m(x^0), E_0) \geq \xi$ for some $m > 0$. If not let $\exists x^0 \in X_0$ such that $\lim_{m\to\infty} d(P^m(x^0), E_0) < \eta$ for all $m > 0$. This implies that $||u(t, P^m(x^0)) - u(t, E_0)|| \leq \epsilon$, $\forall t \in [0, w]$.

To show, $x^0 \in X_0 \Rightarrow x^0 \notin W^s(E_0)$, it is enough to show that $\lim_{m\to\infty} sup\ \mathrm{d}\,(P^m(x^0), E_0) \geq \xi$ for some $m > 0$. If not let $\exists x^0 \in X_0$ such that $\lim_{m\to\infty} sup\ \mathrm{d}\,(P^m(x^0), E_0) \geq \eta$ for all $m > 0$. This implies that $||u(t, P^m(x^0)) - u(t, E_0)|| < \epsilon$, $\forall t \in [0, w]$. For any $t \geq 0$, let $t = mw + t_1$ where $t_1 \in [0, w]$ and $m = [\frac{t}{w}]$ which is the greatest integer less than or equal to $\frac{t}{w}$. Then, we have $||u(t, P^m(x^0)) - u(t, E_0)|| = ||u(t_1, P^m(x^0)) - u(t, E_0)|| \leq \epsilon, \forall t \in [0, w]$.

By selecting $(S(t), I(t), R(t), B_H(t), B_L(t), P(t)) = u(t, x^0)$, it follows that

$$\frac{\Lambda_H}{\mu_d} - \epsilon \leq S(t) \leq \frac{\Lambda_H}{\mu_d} + \epsilon, 0 \leq I \leq \epsilon, 0 \leq R \leq \epsilon, 0 \leq B_H \leq \epsilon, 0 \leq B_L \leq \epsilon, 0 \leq P \leq \epsilon$$

for all $t \geq 0$. Then, we have $\frac{S(t)}{K_H+B_H} \geq (\frac{\Lambda_H}{\mu_d K_H} - \frac{\epsilon}{K_H+\epsilon})$ and $\frac{S(t)}{K_L+B_L} \geq (\frac{\Lambda_H}{\mu_d K_L} - \frac{\epsilon}{K_L+\epsilon})$. Therefore, from system (1) we have

Table 1 The parameters used in the simulations

Parameters	Values	Unit	References
Λ_H	15	day^{-1}	Assumed
μ_d	5.48×10^{-5}	day^{-1}	[3]
μ_c	0.015	day^{-1}	[3]
γ	0.004	day^{-1}	[3]
ξ	100	Cells/L day^{-1}	[2]
χ	33.6	Cells/L day^{-1}	[20]
γ_1	1.4×10^{-9}	L/virion/day	[16]
δ_L	0.2333	day^{-1}	[2]
β_1	100	Virion/cell	[17]
w	0.025	day^{-1}	Assumed
w_1	0.5–7.9	Virion/day	[15]

$$\frac{dI}{dt} \geq \beta_H(t)\left(\frac{\Lambda_H}{\mu_d K_H} - \frac{\epsilon}{K_H+\epsilon}\right)B_H + \beta_L(t)\left(\frac{\Lambda_H}{\mu_d K_L} - \frac{\epsilon}{K_L+\epsilon}\right)B_L \tag{17}$$

$$\frac{dB_H}{dt} = \xi I - \chi B_H \tag{18}$$

$$\frac{dB_L}{dt} = \chi B_H - \delta_L B_L \tag{19}$$

Then, from Eqs. (17),(18) and (19) a matrix $M_\epsilon(t)$ can be obtained as follows:

$$M_\epsilon(t) = \begin{bmatrix} 0 & \beta_H(t)\frac{\epsilon}{K_H+\epsilon} & \beta_L(t)\frac{\epsilon}{K_L+\epsilon} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

Already, from Theorem 2, it is known that as $R_0 > 1$ so $\rho(\phi_{F-V}(\omega)) > 1$, choosing ϵ is very very small such that $\rho(\phi_{F-V-M_\epsilon}(\omega)) > 1$. Again, by Lemma 1 and the standard comparison principle, there exists a positive ω periodic function $f_2(t)$ such that $J(t) \geq f_2(t)e^{s_2(t)}$ where $J(t) = (I(t), B_H(t), B_L(t))^T$ and $s_2 = \frac{1}{\omega} ln\rho(\phi_{F-V}(\omega)) > 0$. This implies that

$$\lim_{t\to\infty} I(t) = \infty, \lim_{t\to\infty} B_H(t) = \infty \text{ and } \lim_{t\to\infty} B_L(t) = \infty$$

which is a contradiction in M_∂. Hence, $W^s(E_0) \cap X_0 = \emptyset$. Then, by Theorem 1.3.1 [26] we obtain that P is uniformly persistent with respect to $(X_0, \partial X_0)$. Thus, by Theorem 1.3.1 [26] it follows that the solution of (1) is uniformly persistent.

6 Periodic solution

In this section, the existence and stability of a positive periodic solution of the system (1) have been investigated in Theorem 5 as follows:

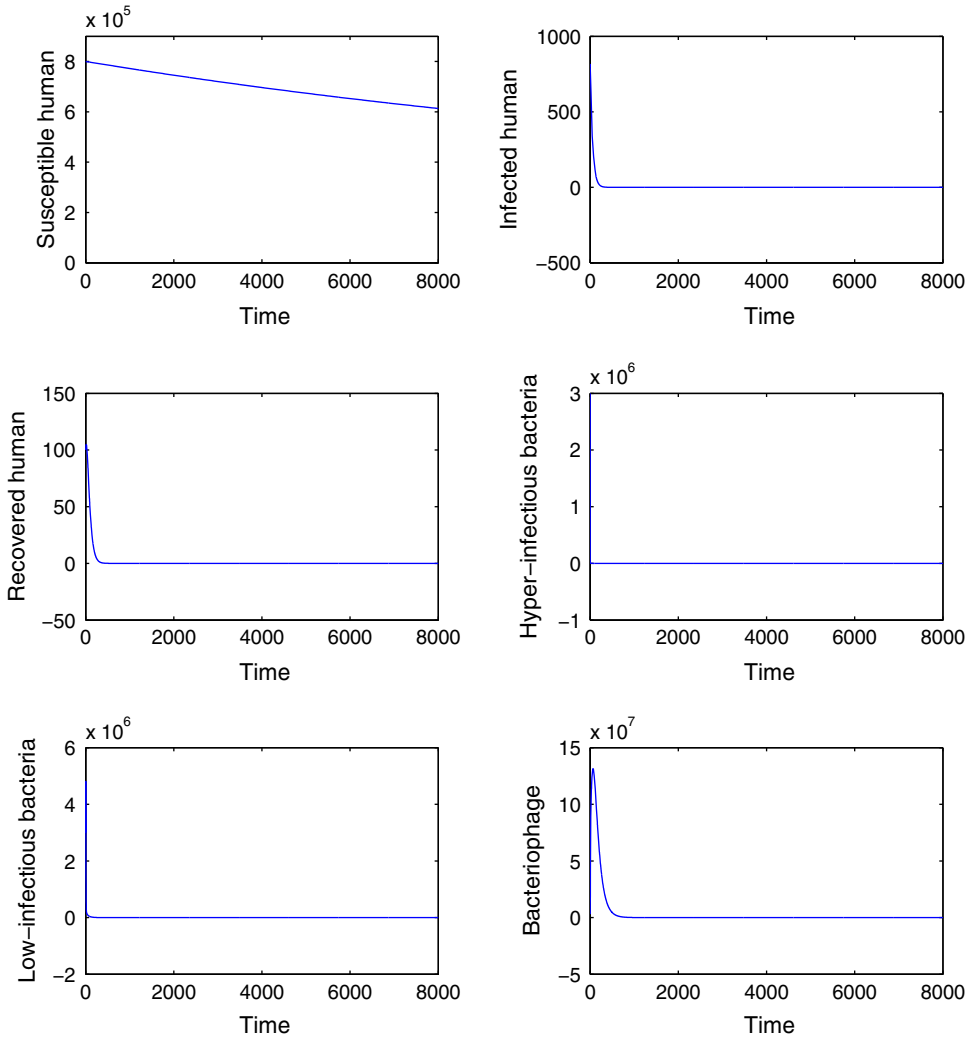

Fig. 1 The graphical structure of solution of the proposed system (1) near the disease free equilibrium point when $R_0 < 1$

Theorem 5 *If* $R_0 > 1$, *then the system* (1) admits a positive ω-periodic solution which is globally asymptotically stable.

Proof We have already proved in Theorem 3 that the poincare map, $P : R_+^6 \longrightarrow R_+^6$ of the system (1) is point dissipative and compact as well as P is uniformly persistent with respect to $(X_0, \partial X_0)$. Then, it follows from Theorem 1.3.6 [26] that the poincare map P has a fixed point $(\tilde{S}, \tilde{I}, \tilde{R}, \tilde{B_H}, \tilde{B_L}, \tilde{P}) \in Int(R_+^6)$. Hence, $u(t, (\tilde{S}, \tilde{I}, \tilde{R}, \tilde{B_H}, \tilde{B_L}, \tilde{P})) \in Int(R_+^6)$ for all $t > 0$. Thus, $(\tilde{S}, \tilde{I}, \tilde{R}, \tilde{B_H}, \tilde{B_L}, \tilde{P})$ is a positive $\omega-$ periodic solution of system (1) due to the definition of the semiflow P. □

Let $\tilde{X} = (\tilde{S}, \tilde{I}, \tilde{R}, \tilde{B_H}, \tilde{B_L}, \tilde{P})$ be positive ω-periodic solution of system (1) and $X(t) = (S(t), I(t), R(t), B_H(t), B_L(t), P)$ be any solution of system (1) initiating from nonnegative initial values. Then, a Lyapunov function is defined as follows:

$$L(S, I, R, B_H, B_L, P) = |S(t) - \tilde{S}(t)| + |I(t) - \tilde{I}(t)| + |R(t) - \tilde{R}(t)| + \frac{\mu_d}{\xi}|B_H(t) - \tilde{B_H}(t)| + \frac{\mu_d}{\xi}|B_L(t) - \tilde{B_L}(t)| + |P(t) - \tilde{P}(t)| \quad (20)$$

Now, the right upper derivative $D^+L(t)$ of Eq. (20) of the system (1) is obtained as follows:

$$D^+L(S, I, R, B_H, B_L, P) = sign(S(t) - \tilde{S}(t)) \left\{ \beta_H(t)\frac{\tilde{B_H}\tilde{S}}{K_H + \tilde{B_H}} + \beta_L(t)\frac{\tilde{B_L}\tilde{S}}{K_L + \tilde{B_L}} - \beta_H(t)\frac{B_H S}{K_H + B_H} - \beta_L(t)\frac{B_L S}{K_L + B_L} + w(R - \tilde{R}) - \mu_d(S - \tilde{S}) \right\} + sign(I(t) - \tilde{I}(t)) \left\{ \beta_H(t)\frac{B_H S}{K_H + B_H} + \beta_L(t)\frac{B_L S}{K_L + B_L} - \beta_H(t)\frac{\tilde{B_H}\tilde{S}}{K_H + \tilde{B_H}} - \beta_L(t)\frac{\tilde{B_L}\tilde{S}}{K_L + \tilde{B_L}} - (\gamma + \mu_c + \mu_d)(I(t) - \tilde{I}(t)) \right\}$$

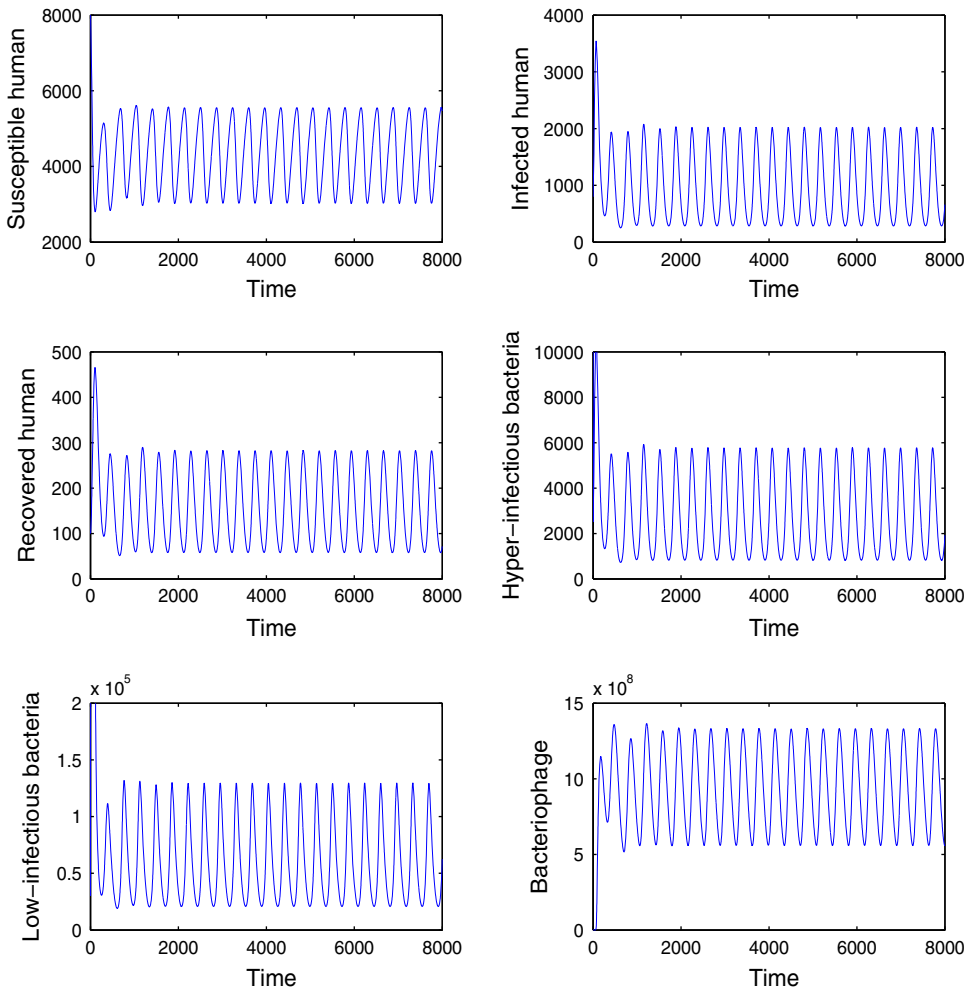

Fig. 2 The representation of solution of the proposed system (1) near the endemic equilibrium point when $R_0 > 1$

$$
\begin{aligned}
&+sign(R(t)-\tilde{R}(t))\left\{\gamma(I(t)-\tilde{I}(t))\right.\\
&\left.-(w+\mu_d)(R(t)-\tilde{R}(t))\right\}+sign(B_H(t)\\
&-\tilde{B_H}(t))\frac{\mu_d}{\xi}\left\{\xi(I(t)-\tilde{I}(t))-\chi(B_H(t)-\tilde{B_H}(t))\right.\\
&\left.-\gamma_1(\tilde{B_H}\tilde{P}-B_HP)\right\}+sign(B_L(t)\\
&-\tilde{B_L}(t))\frac{\mu_d}{\xi}\left\{\chi(B_H(t)-\tilde{B_H}(t))-\delta_L(B_L(t)-\tilde{B_L}(t))\right.\\
&\left.-\gamma_1(\tilde{B_L}(t)\tilde{P}(t)-B_L(t)P(t))\right\}+sign(P(t)-\tilde{P}(t))\\
&\times\left\{\beta_1\gamma_1(B_H(t)P(t)-\tilde{B_H}(t)\tilde{P}(t))\right.\\
&\left.+\beta_1\gamma_1(B_L(t)P(t)-\tilde{B_L}(t)\tilde{P}(t))-w_1(P(t)-\tilde{P}(t))\right\}\\
&\leq-\mu_d|S(t)-\tilde{S}(t)|-\mu_c|I(t)-\tilde{I}(t)|-\mu_d|R-\tilde{R}|\\
&-\frac{\mu_d\delta_L}{\xi}|B_L(t)-\tilde{B_L}(t)|-\frac{w_1}{\beta_1}|P(t)-\tilde{P}(t)|\\
&\leq-K(|S(t)-\tilde{S}(t)|+|I(t)-\tilde{I}(t)|+|R-\tilde{R}|\\
&+|B_L(t)-\tilde{B_L}(t)|+|P(t)-\tilde{P}(t)|) \qquad (21)
\end{aligned}
$$

where $K = min\{\mu_d, \mu_c, \frac{\mu_d\delta_L}{\xi}, \frac{w_1}{\beta_1}\}$.

Now, integrating the above Eq. (21) from $\bar{t}$ to ∞, it is obtained that

$$
\begin{aligned}
&L(t)+K\int_{\bar{t}}^{\infty}(|S(t)-\tilde{S}(t)|+|I(t)-\tilde{I}(t)|+|R-\tilde{R}|\\
&+|B_L(t)-\tilde{B_L}(t)|+|P(t)-\tilde{P}(t)|)ds\\
&\leq L(\bar{t}) \qquad (22)
\end{aligned}
$$

provided that $t > \bar{t}$. Then, from Eq. (22) it follows that

$$
\begin{aligned}
&\sup_{t\to\infty}K\int_{\bar{t}}^{\infty}(|S(t)-\tilde{S}(t)|+|I(t)-\tilde{I}(t)|+|R-\tilde{R}|\\
&+|B_L(t)-\tilde{B_L}(t)|+|P(t)-\tilde{P}(t)|)ds\\
&\leq\frac{L(\bar{t})}{K}<+\infty
\end{aligned}
$$

i.e., $\lim_{t\to\infty}|S(t)-\tilde{S}(t)|=0$, $\lim_{t\to\infty}|I(t)-\tilde{I}(t)|=0$,
$\lim_{t\to\infty}|R(t)-\tilde{R}(t)|=0$,

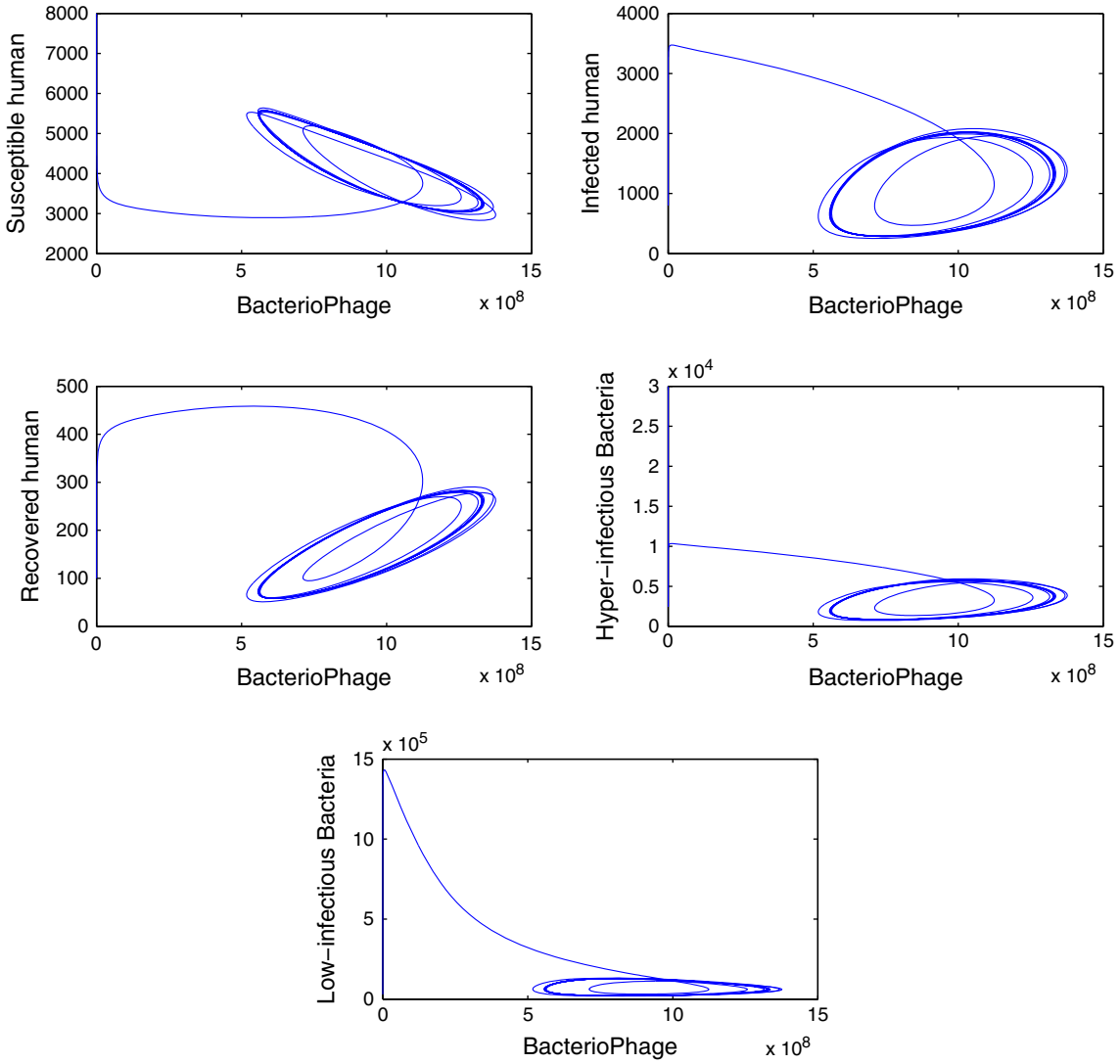

Fig. 3 The limit cycle of the proposed system (1) with respect to the bacteriophage

$$\lim_{t\to\infty} |B_H(t) - \tilde{B_H}(t)| = 0, \lim_{t\to\infty} |B_L(t) - \tilde{B_L}(t)| = 0$$
$$\text{and } \lim_{t\to\infty} |P(t) - \tilde{P}(t)| = 0.$$

Therefore, the solution $(\tilde{S}(t), \tilde{I}(t), \tilde{R}(t), \tilde{B_H}(t), \tilde{B_L}(t), \tilde{P}(t))$ is globally asymptotically stable.

7 Numerical simulations

For numerical simulation to illustrate the proposed mathematical model, the standard software MATLAB 2010a has been used. After finding the value of R_0 numerically using the parametric values in Table 1, it has been shown that when disease persists and disappears from the human population.

Now, using the following initial values of the state variables such as $S(0) = 800{,}000, I(0) = 800, R(0) = 100, B_H(0) = 3{,}000{,}000, B_L(0) = 3{,}000{,}000, P(0) = 300{,}000$ and also taking $K_H = 10^9, K_L = 10^9, \delta = 0.75, B_{H0} = 0.2143, B_{L0} = 0.2$, Fig. 1 has been drawn from which it is observed that when $R_0 = 0.6043 < 1$, then it is confirmed that the disease free equilibrium point of the system (1) is globally asymptotically stable. Therefore, it is concluded that the cholera disease will be disappeared from the human population when the basic reproduction number must be less than one in the presence of bacteriophage.

Again, using the following initial values of the state variables such as $S(0) = 8000, I(0) = 800, R(0) = 100, B_H(0) = 30{,}000, B_L(0) = 30{,}000, P(0) = 3000$ and also $K_H = 10^9, K_L = \frac{10^9}{7}, \delta = 0.75, B_{H0} = 0.2143, B_{L0} = 0.2$, Fig. 2 has been drawn from which it is observed that when $R_0 = 4.2030 > 1$, then it is confirmed that the disease persists in the system (1) and it is globally asymptotically stable. Therefore, it is concluded that the cholera disease will be

positively persisted in the human population when the basic reproduction number is grater than one in the presence of bacteriophage.

Using the same parametric values and initial condition that is used in Fig. 2, Fig. 3 has been drawn and from this figure it is seen that the limit cycle of each population such as susceptible human, infected human, recovered human, hyper-infectious *V. cholerae* bacteria and low-infectious *V. cholerae* bacteria with respect to bacteriophage is stable. Again, it is known that the stable limit cycles are example of attractors. So, they imply self-sustained oscillations i.e., the closed trajectory describes perfect periodic behavior of the system and any small perturbation from this closed trajectory causes the system to return to it, making the system stick to the limit cycle.

8 Conclusion

In this paper, a cholera epidemic model with periodic transmission rate has been discussed. Here, the total human population is divided into three subpopulations such as (i) susceptible human (ii) infected human (iii) recovered human and total bacterial population into three subpopulations such as (i) hyper-infectious *V. cholerae* bacterium (ii) low-infectious bacterium (iii) bacteriophage. A transmission model that accurately predicts the magnitude of an emerging outbreak would provide public health authorities with useful information to appropriately scale their responses. Interventions that target vital steps in transmission might be effective for the prevention of the outbreak. Host immunity, pathogen hyperinfectivity and phages are all factors that can be leveraged for outbreak control. The disease free equilibrium point is globally asymptotically stable and the cholera disease is disappeared if the basic reproduction number is less than one. It is observed that when the basic reproduction number is grater than one, then the endemic equilibrium is globally asymptotically stable and the disease persists in the human population. It is also observed that the system has a stable limit cycle with respect to bacteriophage and this closed trajectory describes perfect periodic behavior of the proposed system. So, Numerical simulations of the mathematical model supports our analytical results.

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