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Analysis of a Chemostat Model for Bacteria and Bacteriophage*

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Abstract. In this paper we consider the dynamical properties of the time delayed chemostat model composed of the resource, a virulent bacteriophage and two bacteria (one is sensitive and the other is immune to predation by the bacteriophage). First, we give a model and summarize several known results on the basic properties of the model such as the existence of the equilibria, boundedness of the solution, the local and global asymptotic stability of the equilibria. We show that a positive equilibrium point (the coexistence state composed of the resource, two bacteria and the bacteriophage) is locally asymptotically stable for small values of the delay, loses the stability under the increasing of the value of the delay and becomes locally asymptotically stable again by further increasing of the value of the delay.

1. Introduction

A chemostat is a continuous culture device in which water containing a nutrient flows steadily into a container. The nutrient is consumed by the organisms in the vessel, which are also swept by the steady overflow. For a review of the chemostat, see [8].

We put in the chemostat one resource $R(t)$, one bacteriophage $P(t)$ and two bacteria $S_1(t)$ and $S_2(t)$, the former is sensitive to predation of the bacteriophage

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and the latter is resistant (see Fig.1). The model is given by

$$\begin{aligned}
\dot{R}(t) &= \mu(C - R(t)) - e_1\alpha_1(R)S_1(t) - e_2\alpha_2(R)S_2(t) \\
\dot{S}_1(t) &= \alpha_1(R)S_1(t) - \mu S_1(t) - \gamma_1 S_1(t)P(t) \\
\dot{S}_2(t) &= \alpha_2(R)S_2(t) - \mu S_2(t) \\
\dot{P}(t) &= \beta\gamma_1 e^{-\mu\tau}S_1(t-\tau)P(t-\tau) - \mu P(t) - \gamma_1 S_1(t)P(t).
\end{aligned} \tag{1}$$

The resistant-bacteria $S_2(t)$ is not attacked by the phage and considered as a mutant of the sensitive bacteria. Further $\mu > 0$ is the flow rate through the chemostat and $C > 0$ is the input concentration of the resource. Two bacteria can grow up by taking the resource at a rate of $\alpha_i(R)S_i$ $(i = 1, 2)$, where $\alpha_i(R)$ is the bacteria's taking up rate of the resource, which is an increasing function of the resource concentration rising from zero at $R = 0$. Since it contains measurable parameters, the Michaelis-Menten formulation is most often used as the resource uptake function, i.e. $\alpha_i(R) = m_iR/(n_i + R)$, where m_i(per hour) is the maximal growth rate, n_i(μg per ml) is the Michaelis-Menten constant with units of concentration (see Smith and Waltman [8]). $e_i > 0$ is the amount of the resource for a new bacteria, that is each production of a new bacteria needs up e_i(μg per new cell) of the resource. Here, we assume $e_1 = e_2$. Bacteriophages attack sensitive bacteria. When a bacteriophage enters into a sensitive bacteria at time t, sensitive bacteria becomes infected bacteria at a rate of $\gamma_1 S_1(t)P(t)$ and the phage multiples until the infected bacteria is destroyed. Here $\gamma_1 > 0$ is the attacking rate of the phage to the sensitive bacteria. After the latent period $\tau \geq 0$ (the time delay between the attack by a phage on the bacteria and the resulting reproduction of new phages), the infected bacteria releases a number β (> 1) of bacteriophage by lysis. Since the flow rate is μ, the number of new phages at time t is given by $\beta\gamma_1 e^{-\mu\tau}S_1(t-\tau)P(t-\tau)$.

In this paper, we consider the function $\alpha_i(R)$ as Michaelis-Menten functional response in the numerical simulation, and the estimates on the other parameters are taken from the papers by Levin, Stewart and Chao [7] and Lenski and Levin [6], i.e.

$$\begin{aligned}
&\mu = 0.2/h, C = 100\mu g/ml, \gamma_1 = 6.24 \times 10^{-8} ml/(h \cdot cell), \\
&n = 4\mu g/ml, m = 0.738/h, e_i = 2.6 \times 10^{-6}\mu g/cell \quad (i = 1, 2).
\end{aligned} \tag{2}$$

We will summarize the basic properties of the model such as the existence of the nonnegative equilibria, the boundedness of the solutions, local (or global) asymptotic stability of nonnegative equilibria in Sec. 2 (see [3]). We show that the equilibrium point composed of only the resource is globally asymptotically stable under high chemostat turnover rate. For the lower turnover rate, the equilibrium point with the resource and sensitive bacteria can be locally asymptotically stable when the equilibria containing the immune bacteria do not exist. Further the equilibrium point with the resource and sensitive bacteria can be globally asymptotically stable for any length of time delay under the relatively small reproduction rate of new bacteriophage. The positive equilibrium point is known to be locally asymptotically stable when the time delay is neglected.

We show in Sec. 3 that the point remains to be locally asymptotically stable for small values of the delay, loses the stability under the increasing of the value of the delay and becomes locally asymptotically stable again by further increasing of the value. The final section contains the summary and proposes some future problems.

2. Basic Properties

It is known that system (1) can be transformed by introducing the dimensionless time $\tilde{t} = \gamma_1 Ct/e_1$ and dimensionless delay time $\tilde{\tau} = \gamma_1 C\tau/e_1$, and by rescaling the variables, into the dimensionless form such as

$$\begin{aligned}
\dot{R}(t) &= \mu(1 - R(t)) - \alpha_1(R)S_1(t) - \alpha_2(R)S_2(t)\\
\dot{S}_1(t) &= \alpha_1(R)S_1(t) - \mu S_1(t) - S_1(t)P(t)\\
\dot{S}_2(t) &= \alpha_2(R)S_2(t) - \mu S_2(t)\\
\dot{P}(t) &= \beta e^{-\mu\tau}S_1(t-\tau)P(t-\tau) - \mu P(t) - S_1(t)P(t).
\end{aligned} \tag{3}$$

Throughout the paper we assume

(H) $\alpha_1(R) > \alpha_2(R)$ for all $R > 0$,

which implies that sensitive-bacteria $S_1(t)$ is superior to resistant-bacteria $S_2(t)$ with respect to taking up of the resource.

The initial conditions for (3) are

$$\begin{aligned}
(R(\theta), S_1(\theta), &S_2(\theta), P(\theta)) = (\phi_1(\theta), \phi_2(\theta), \phi_3(\theta), \phi_4(\theta)),\\
&\phi_i(\theta) \geq 0, \phi_i(0) > 0, i = 1, ..., 4, \theta \in [-\tau, 0]
\end{aligned} \tag{4}$$

where $(\phi_1(\theta), \phi_2(\theta), \phi_3(\theta), \phi_4(\theta)) \in C([-\tau, 0], R^4_{+0})$, the Banach space of continuous functions mapping the interval $[-\tau, 0]$ into R^4_{+0} with suitable norm. Here $R^4_{+0} = \{(R, S_1, S_2, P) \in R^4 | R \geq 0, S_1 \geq 0, S_2 \geq 0, P \geq 0\}$. It is easy to prove that the interior of R^4_{+0} is invariant for (3) with initial condition (4) (see, for example [2] or [4]).

Now τ is the dimensionless latent period. Since the property of bacteriophage essentially depends on the two parameters τ and β, along the paper we will keep fixed the other dimensionless parameters μ, m_i, n_i at the values:

$$\mu = 8.33 \times 10^{-2}, m_1 = 0.30745, m_2 = 0.153725, n_i = 0.04 \quad (i = 1, 2). \tag{5}$$

We will consider the dynamics of the model (3) for the parameters: $(\beta, \tau) \in (1, +\infty) \times R_{+0}$. All the results given in this section can be proved similarly as those given in [3].

2.1. Existence of Equilibrium Points

It is easy to check that the equilibrium $E_0 = (1, 0, 0, 0)$ without organisms always exists. Each sensitive (or resistant) bacteria can remain with the resource at

$E_1 = (\bar{R}_1, \bar{S}_1, 0, 0)$ (or $E_2 = (\bar{R}_2, 0, \bar{S}_2, 0)$), where $(\bar{R}_i, \bar{S}_i) > 0$ and satisfy that $\mu = \alpha_i(\bar{R}_i)$ and $\bar{R}_i + \alpha_i(\bar{R}_i)\bar{S}_i/\mu = 1$ for $i = 1, 2$. It is clear that each E_i $(i = 1, 2)$ exists if and only if $\mu = \alpha_i(\bar{R}_i) < \alpha_i(1)$, respectively. Further, E_i $(i = 1, 2)$ satisfy $1 > \bar{R}_i$. But both bacteria S_1 and S_2 cannot remain simultaneously only with the resource at equilibrium point like $E = (*, *, *, 0)$ by (H). Let us denote $E_3 = (\hat{R}, \hat{S}_1, 0, \hat{P})$ and $E_4 = (R^*, S_1^*, S_2^*, P^*)$.

Fig. 1. System of a chemostat

Theorem 2.1. *When $\mu > \alpha_1(1)$, only $E_0 = (1, 0, 0, 0)$ exists. When $\mu < \alpha_2(1)$,*

(i) *E_0, E_1 and E_2 exist for all $\tau \geq 0$ and $\beta > 1$.*
(ii) *E_3 exists if and only if*

$$\tau < \tau^*(\bar{R}_1) = \frac{1}{\mu} \ln \frac{\beta}{\beta^*(\bar{R}_1)}, \quad \textit{where} \quad \beta^*(\bar{R}_1) = 1 + \frac{\alpha_1(\bar{R}_1)}{1 - \bar{R}_1} \tag{6}$$

is satisfied.
(iii) *When E_3 exists and*

$$\mu < \alpha_2(\hat{R}) \tag{7}$$

is satisfied, E_4 exists and

$$\tau < \tau^*(R^*) = \frac{1}{\mu} \ln \frac{\beta}{\beta^*(R^*)}, \quad \textit{where} \quad \beta^*(R^*) = 1 + \frac{\alpha_1(R^*)}{1 - R^*} \tag{8}$$

holds true. When $\alpha_2(1) < \mu < \alpha_1(1)$, there exists no E_2 in the above.

For the first case in Theorem 2.1, in the sense of equilibrium points, where the flow rate of the chemostat is very high, only the resource can remain in the chemostat and all the biotic species will be washed out.

Note that for the existence of the coexistence state E_4, we need both relatively small latent period τ and relatively large reproductive rate of new phage β (see Fig. 2).

Fig. 2. Existence of equilibrium points ($\mu < \alpha_2(1)$).
E_0, E_1, E_2 exists in all regions; E_3 exists in the regions B and C; E_4 exists in C
All parameters except β and τ are fixed as those given by (5).

2.2. Boundedness

Now we introduce a new variable $m_1(t)$ (the density of a phage-infected sensitive bacteria: see Fig. 1) into (3) and (4):

$$\begin{aligned}
\dot{R}(t) &= \mu(1 - R(t)) - \alpha_1(R)S_1(t) - \alpha_2(R)S_2(t) \\
\dot{S}_1(t) &= \alpha_1(R)S_1(t) - \mu S_1(t) - S_1(t)P(t) \\
\dot{S}_2(t) &= \alpha_2(R)S_2(t) - \mu S_2(t) \\
\dot{m}_1(t) &= S_1(t)P(t) - \mu m_1(t) - e^{-\mu\tau}S_1(t-\tau)P(t-\tau) \\
\dot{P}(t) &= \beta e^{-\mu\tau}S_1(t-\tau)P(t-\tau) - \mu P(t) - S_1(t)P(t),
\end{aligned} \tag{9}$$

and define

$$m_1(0) = \int_{-\tau}^{0} e^{\mu\theta} S_1(\theta)P(\theta)d\theta > 0$$

as its initial value. It is easy to check that the solution of (3) satisfying (4) is identical with the corresponding solution of (9), since the former is independent of $m_1(t)$. Hence the solution of (3) is bounded if and only if so is the corresponding solution of (9).

Theorem 2.2.
(i) *Any solution of* (9) *is bounded. That is, for sufficiently large* $t > 0$ *and any* $\epsilon > 0$*, the solution* $(R(t), S_1(t), S_2(t), m_1(t), P(t))$ *satisfies*

$$0 \le R(t) + S_1(t) + S_2(t) + m_1(t) + \frac{P(t)}{\beta} \le 1 + \epsilon.$$

(ii) *If* $\mu > \beta - 1$, *then* $m_1(t) \to 0$ *and* $P(t) \to 0$ *as* $t \to \infty$.

2.3. Local Stability

Now we will discuss the local asymptotic stability of the equilibria. Denote a nonnegative equilibrium point of (3) as $E = (\tilde{R}, \tilde{S}_1, \tilde{S}_2, \tilde{P})$. Let us define $x(t) = (R(t) - \tilde{R}, S_1(t) - \tilde{S}_1, S_2(t) - \tilde{S}_2, P(t) - \tilde{P})$. Then the linearized equation of (3) at E is described by $\dot{x}(t) = Ax(t) + Bx(t - \tau)$, where A and B are 4×4 matrices given by

$$A = \begin{pmatrix} -\mu - \alpha_1'(\tilde{R})\tilde{S}_1 - \alpha_2'(\tilde{R})\tilde{S}_2 & -\alpha_1(\tilde{R}) & -\alpha_2(\tilde{R}) & 0 \\ \alpha_1'(\tilde{R})\tilde{S}_1 & \alpha_1(\tilde{R}) - \mu - \tilde{P} & 0 & -\tilde{S}_1 \\ \alpha_2'(\tilde{R})\tilde{S}_2 & 0 & \alpha_2(\tilde{R}) - \mu & 0 \\ 0 & -\tilde{P} & 0 & -\mu - \tilde{S}_1 \end{pmatrix},$$

$$B = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & \beta e^{-\mu\tau}\tilde{P} & 0 & \beta e^{-\mu\tau}\tilde{S}_1 \end{pmatrix}.$$

Note that the matrix B also depends on delay τ, which is different from usual delay models. Here all α_i and their derivatives α_i' $(i = 1, 2)$ are evaluated at $R = \tilde{R}$. The characteristic equation of (3) at E is given by

$$\det[A + Be^{-\Lambda\tau} - \Lambda I] = 0, \tag{10}$$

where I is the identity matrix and Λ denotes the characteristic roots. It is easy to check that (10) always has one root $-\mu < 0$.

Theorem 2.3.

(i) E_0 *is locally asymptotically stable if* $\mu > \alpha_1(1)$.

(ii) *When* $\mu < \alpha_1(1)$, E_1 *is locally asymptotically stable if* $\tau > \tau^*(\bar{R}_1)$, *is unstable if* $\tau < \tau^*(\bar{R}_1)$ *and is linearly neutrally stable if* $\tau = \tau^*(\bar{R}_1)$.

(iii) E_2 *is always unstable.*

(iv) E_3 *is unstable if* $\mu < \alpha_2(\hat{R})$. *Further* E_3 *is locally asymptotically stable if* $\alpha_2(\hat{R}) < \mu < \alpha_1(\hat{R})$ *and* $\tau = 0$.

(v) E_4 *is locally asymptotically stable when* $\tau = 0$.

Let us assume that all parameters except β and τ are fixed as those given by (5) and consider the case $\mu < \alpha_1(1)$ (see Fig. 2). From Theorem 2.3, E_0 and E_2 are unstable in all regions; E_1 is locally asymptotically stable in region A, is unstable in regions B and C and linear neutrally stable when $\tau = \tau^*(\bar{R}_1)$; E_3 is locally asymptotically stable if $\alpha_2(\hat{R}) < \mu < \alpha_1(\hat{R})$ and $\tau = 0$; E_4 is locally asymptotically stable when $\tau = 0$.

2.4. Global Stability

We will discuss the global asymptotic stability of the equilibria.

Theorem 2.4.

- (i) *Suppose that the functions* $(1/R-1)\alpha_i(R)$ $(i=1,2)$ *are bounded for* $0 \leq R \leq 1+\epsilon$. *Then* E_0 *is globally asymptotically stable for any* $\tau > 0$ *if* $\mu > \alpha_1(1)$.
- (ii) *Suppose that the functions* $\alpha_i(R)$ $(i=1,2)$ *are given by* $\alpha_i(R) = m_i R$ *or* $\alpha_i(R) = m_i R/(n_i+R)$, $(m_i > 0, n_i > 0)$. *Further, assume that* $\beta < (\mu+\bar{S}_1)/(\bar{S}_1)$ *and* $\alpha_1(1) > \mu > \alpha_2(1)$. *Then* E_1 *is globally asymptotically stable for any* $\tau > 0$.
- (iii) *Suppose that the functions* $\alpha_i(R)$ $(i=1,2)$ *are given as those in* (ii). *Then* E_4 *with* $\tau = 0$ *is globally asymptotically stable if it exists.*

The global asymptotic stability of E_4 seems not to hold for all $\tau < \tau^*(R^*)$. In fact, we will show some examples that E_4 exists but it is unstable (see Sec. 3). It is known for a chemostat delay model with one bacteria and its virulent phage that a positive equilibrium is not always locally stable and the stability switch occurs [4]. But Theorem 2.4 (iii) shows that E_4 is globally asymptotically stable if time delay is neglected.

3. Simulation

We have proved that E_3 is unstable if $\mu < \alpha_2(\hat{R})$ and E_4 is local asymptotically stable when $\tau = 0$. Since the coefficients of characteristic equation (10) depend on the time delay, its local stability analysis is very complicated. According to the geometric stability switch criterion established by Beretta and Kuang [2], the stability of a steady state is simply determined by locating the zeros of some functions of delay τ which can be expressed explicitly and thus can be easily depicted by Mathematica.

Here we review the geometric stability switch theory. Let us denote the characteristic equation (10) as $P(\Lambda) + Q(\Lambda)e^{-\Lambda\tau} = 0$, where $P(\Lambda)$ and $Q(\Lambda)$ are polynomials in Λ. If we assume that $P(0) + Q(0) \neq 0$, then $\Lambda = 0$ cannot be a root of the characteristic equation, and a stability switch necessarily occurs with $\Lambda = i\omega$ since (3) is a retarded functional differential equation. Without loss of generality assume $\omega > 0$. Now we replace that $P(i\omega) = P_R(i\omega) + iP_I(i\omega)$ and $Q(i\omega) = Q_R(i\omega) + iQ_I(i\omega)$. Then the characteristic equation for $\Lambda = i\omega$ gives equations $P_R + Q_R \cos\omega\tau + Q_I \sin\omega\tau = 0$, $P_I + Q_I \cos\omega\tau - Q_R \sin\omega\tau = 0$, which gives

$$\cos\omega\tau = -\frac{P_R Q_R + P_I Q_I}{|Q(i\omega)|^2}, \quad \sin\omega\tau = -\frac{P_R Q_I - P_I Q_R}{|Q(i\omega)|^2}. \tag{11}$$

If ω satisfies the above, then ω must satisfy that $|P(i\omega)|^2 = |Q(i\omega)|^2$. Now we define $F(\omega)$ as follows:

$$F(\omega) \equiv |P(i\omega)|^2 - |Q(i\omega)|^2 = 0. \tag{12}$$

Further define the angle $\theta \in [0, 2\pi]$, as the solution of (11)

$$\cos\theta(\tau) = -\frac{P_R Q_R + P_I Q_I}{|Q(i\omega)|^2}, \quad \sin\theta(\tau) = -\frac{P_R Q_I - P_I Q_R}{|Q(i\omega)|^2}, \tag{13}$$

and the relation between the arguments θ in (13) and $\omega\tau$ in (11) for $\tau > 0$ must be $\omega\tau = \theta + 2n\pi, n \in N_0 := \{0, 1, 2, \cdots\}$. Hence we can obtain as follows, and a stability switch may occur at τ_n:

$$\tau_n = \frac{\theta + 2n\pi}{\omega},\ \tau_n > 0,\ n \in N_0.$$

The following theorem shows that we can know the direction of the stability switch to check the sign of the derivative of $s_n(\tau)$ with respect to τ at $\tau = \tau_n$. That is, as we increase time delay τ, the eigenvalue will move to the right half plane of the complex space if the derivative of $s_n(\tau)$ is positive. If the derivative is negative, then the eigenvalue moves into the left half plane.

Fig. 3. E_0, E_1, E_2 exists for all $\tau \geq 0$. E_3 exists only in B and C. E_4 exists in C.

Stability switch theorem

Assume that ω is a positive real root of (12), and at some $\tau^* > 0$,

$$s_n(\tau^*) = \tau^* - \tau_n = 0 \quad \text{for some} \quad n \in N_0.$$

Then a pair of simple conjugate pure imaginary roots $\Lambda = \pm i\omega(\tau)$ of the characteristic equation exists at $\tau = \tau^*$ which crosses the imaginary axis according to

$$\text{sign}\Big\{\frac{d\,\text{Re}\,\Lambda}{d\tau}|_{\Lambda = i\omega(\tau^*)}\Big\} = \text{sign}\Big\{\frac{ds_n(\tau)}{d\tau}|_{\tau=\tau^*}\Big\}.$$

In the following, we fix $\beta = 8$ and the other parameters except for τ as those given by (5). Then we have $E_1 = (0.0148, 0.9852, 0, 0), \alpha_1(1) = 2\,\alpha_2(1) = 0.2956$, $\tau^*(\bar{R}_1) = 23.99$, $\tau^*(R^*) = 23.0286$. Since $\mu < \alpha_2(1)$, we have Fig. 2 and for $\beta = 8$, the following Fig. 3 is obtained. E_0 and E_2 are always unstable and E_1 is locally asymptotically stable in A and unstable in B and C by Theorem 2.3. Since $\mu < \alpha_2(\hat{R}) = 0.14756$ for $\tau = 0$, E_3 is unstable at $\tau = 0$. By Theorem 2.3 (v), E_4 is locally asymptotically stable for $\tau = 0$.

Let us consider local stability of E_4 in C of Fig. 3. After factoring $\Lambda + \mu$ from the characteristic equation given by (10), we have

$$\Lambda^3 + a(\tau)\Lambda^2 + b(\tau)\Lambda + c(\tau)(d(\tau)\Lambda^2 + e(\tau)\Lambda + f(\tau))e^{-\Lambda\tau} = 0$$

where

$$\begin{aligned}
a(\tau) &= 3\mu + \alpha_1'(R^*)S_1^* + \alpha_2'(R^*)S_2^* + P^* + S_1^* - \alpha_1(R^*) - \alpha_2(R^*)\\
b(\tau) &= 3\mu^2 + 2(P^* + S_1^* - \alpha_1(R^*) - \alpha_2(R^*))\mu - \alpha_1(R^*)S_1^*\\
&\quad - \alpha_2(R^*)[P^* - S_1^* - \alpha_1(R^*)] + \alpha_1'(R^*)S_1^*(2\mu + P^* + S_1^* - \alpha_2(R^*))\\
&\quad + \alpha_2'(R^*)S_2^*(2\mu + P^* + S_1^* - \alpha_1(R^*))
\end{aligned}$$

$$
\begin{aligned}
c(\tau) = {} & \alpha_2'(R^*)S_2^*[S_1^*(\mu - \alpha_1(R^*)) + \mu(\mu + P^* - \alpha_1(R^*))] - (\alpha_2(R^*) - \mu) \\
& \times [\alpha_1'(R^*)S_1^*(\mu + P^* + S_1^*) + S_1^*(\mu - \alpha_1(R^*)) + \mu(\mu + P^* - \alpha_1(R^*))] \\
d(\tau) = {} & -\beta S_1^* e^{-\mu\tau} \\
e(\tau) = {} & -\beta S_1^* e^{-\mu\tau}(2\mu + \alpha_1'(R^*)S_1^* + \alpha_2'(R^*)S_2^* - \alpha_1(R^*) - \alpha_2(R^*)) \\
f(\tau) = {} & -\beta S_1^* e^{-\mu\tau}[\alpha_2'(R^*)S_2^*(\mu - \alpha_1(R^*)) \\
& - (\alpha_2(R^*) - \mu)(\mu + \alpha_1'(R^*)S_1^* - \alpha_1(R^*))].
\end{aligned}
$$

Fig. 4. The distribution of zeros of $s_n^+(\tau), n = 0$,
corresponding to the equilibrium point E_4 of system (3).
Here $\beta = 8, m_1 = 0.30745, n_i = 0.04, m_2 = 0.153725, \mu = 0.0833$.

Fig. 4 shows the distribution of zeros of functions $s_n^+(\tau), n = 0$. In fact, $s_0^+(\tau)$ has two zeros, the first at the value $\tau_0 = 0.3066$, the second at $\tau_1 = 22.8489$, and $s_n^+(\tau) < 0$ on $[0, \tau^*(R^*)]$ for all $n \geq 1$. From Theorem 2.3 (v), we know that E_4 is stable at $\tau = 0$. In the interval $[0, \tau_0)$, no stability switch occurs, hence E_4 remains stable in this interval, and delay τ_0 gives the system instability (see Fig. 5). In the interval (τ_0, τ_1), E_4 is unstable. The delay τ_1 gives the system stability (see Fig. 6), that is, E_4 is stable for $\tau_1 < \tau < \tau^*(R^*) = 23.0286$.

Now consider local stability of $E_3 = (\hat{R}, \hat{S}_1, 0, \hat{P}) = (\hat{R}, \mu/G, 0, \alpha_1(\hat{R}) - \mu)$ in B, C of Fig. 3, where $G = \beta e^{-\mu\tau} - 1$. The characteristic equation at E_3 gives two roots $\Lambda = -\mu$ and $\Lambda = \alpha_2(\hat{R}) - \mu$, and the others are roots of the equation

$$\Lambda^2 + a(\tau)\Lambda + c(\tau) + (b(\tau)\Lambda + d(\tau))e^{-\Lambda\tau} = 0,$$

where

$$
\begin{aligned}
& a(\tau) = \hat{S}_1(G + 1 + \alpha_1'(\hat{R})), c(\tau) = \hat{S}_1[\mu - \alpha_1(\hat{R}) + \alpha_1'(\hat{R})(\alpha_1(\hat{R}) + \hat{S}_1)], \\
& b(\tau) = -\hat{S}_1(G + 1), d(\tau) = -\hat{S}_1(G + 1)[\mu - \alpha_1(\hat{R}) + \alpha_1'(\hat{R})\hat{S}_1].
\end{aligned}
$$

E_3 exists for $0 \leq \tau < \tau^*(\bar{R}_1) = 23.99$. Fig. 7 shows the distribution of zeros of functions $s_n^+(\tau), n = 0$. In fact, $s_0^+(\tau)$ has two zeros, the first at the value $\tau_0 = 0.0073$, the second at $\tau_1 = 21.9958$ on the interval $I = [0, 23.99)$, and $s_n^+(\tau) < 0$ on $[0, \tau^*(\bar{R}_1)]$ for all $n \geq 1$.

Fig. 5. (a): $s_0^+(\tau)$ and the stability switch of equilibrium point E_4 $(\beta = 8)$. At the value $\tau_0 = 0.3066$, the stability switch occurs toward instability and the equilibrium point becomes unstable. (b) or (c): the solution with $\tau = \tau_0$ (or $\tau > \tau_0$).

The stability switch may occur at τ_0 and τ_1. When $\tau = 0$, E_3 is unstable since $\mu < \alpha_2(\hat{R}) = 0.14756$. In the interval $I = [0, \tau_0)$, no stability switch occurs, hence E_3 remains unstable in this interval. Since the eigenvalue passes through the imaginary axis from the left to the right at τ_0 and returns to the left at τ_1, E_3 remains to be unstable for all τ in C of Fig. 3. Next, we consider local stability of E_3 in B. E_3 exists in region B, but E_4 does not exist for $\tau^*(R^*) = 23.0286 < \tau < \tau^*(\bar{R}_1) = 23.99$. Numerical simulations show that the solutions converge to E_3. Thus, E_3 seems to be locally asymptotically stable for $\tau^*(R^*) < \tau < \tau^*(\bar{R}_1)$. Finally, we consider the stability switch for E_1. In Sec. 2, we showed for $\mu < \alpha_1(1)$ that $E_1 = (\bar{R}_1, \bar{S}_1, 0, 0)$ is locally asymptotically stable if $\tau > \tau^*(\bar{R}_1)$, is unstable if $\tau < \tau^*(\bar{R}_1)$ and is linearly neutrally stable if $\tau = \tau^*(\bar{R}_1)$. Here, we make sure that E_1 is unstable when $\tau < \tau^*(\bar{R}_1)$ by using geometric stability switch theory. We have as characteristic roots of (10), $\Lambda = -\mu, \Lambda = \alpha_2(\bar{R}_1) - \mu = \alpha_2(\bar{R}_1) - \alpha_1(\bar{R}_1) < 0$ and the others are roots of the following equation

$$\Lambda^2 + a(\tau)\Lambda + c(\tau) + (b(\tau)\Lambda + d(\tau))e^{-\Lambda\tau} = 0$$

Fig. 6. (a): $s_0^+(\tau)$ and the stability switch of equilibrium point $E_4(\beta = 8)$.
At the value $\tau_1 = 22.8489$ the stability switch occurs toward stability, the equilibrium point becomes locally asymptotically stable.
(b) or (c): the solution with $\tau = \tau_1$ (or $\tau > \tau_1$).

where

$$\begin{aligned}a(\tau) &= (1-\bar{R}_1)(\beta^*(\bar{R}_1) + \alpha_1'(\bar{R}_1)), c(\tau) = (1-\bar{R}_1)^2\alpha_1'(\bar{R}_1)\beta^*(\bar{R}_1)\\ b(\tau) &= -(1-\bar{R}_1)\beta e^{-\mu\tau}, d(\tau) = -(1-\bar{R}_1)^2\alpha_1'(\bar{R}_1)\beta e^{-\mu\tau}.\end{aligned}$$

We have the distribution of zeros of functions $s_n^+(\tau), n = 0, 1, \cdots$. $\tau_0 = \min\{\tilde{\tau} : s_0^+(\tilde{\tau}) = 0\} = 0.6576$, $\tau_1 = \max\{\tilde{\tau} : s_0^+(\tilde{\tau}) = 0\} = 23.6545$ (Fig. 8). When $\tau = 0$, E_1 is unstable with $\rho = 1$ (the number of characteristic roots with positive real parts). On the interval $I = [0, \tau^*(\bar{R}_1))$, there are 10 zeros of all functions $s_n^+(\tau), n = 0, 1, \cdots 4$. As τ increasing from τ_0 to τ_1, we have $\rho > 1$, and $\rho = 1$ for $\tau_1 < \tau < \tau^*(\bar{R}_1)$, hence E_1 is unstable for $0 \le \tau < \tau^*(\bar{R}_1)$.

Similarly to the case $\beta = 8$, we can obtain Fig. 9. Note that under the choice of parameter values given by (5), the stable coexistence of (R, S_1, S_2, P) at E_4 is realized only for rather restricted region.

Fig. 7. The distribution of zeros of $s_n^+(\tau), n = 0$, corresponding to the equilibrium point E_3 of system (3). Here $\beta = 8, m_1 = 0.30745, n_i = 0.04, \mu = 0.0833$.

4. Conclusion

In this paper we studied a chemostat model (3) for bacteria and virulent bacteriophage, in which the steady state is reduced by a factor that depends on the latency delay τ through a factor $e^{-\mu\tau}$, where μ is the flow rate through the chemostat. The resulting characteristic equation also contains this factor.

We have proved the local and global stability of equilibria as follows:

E_0 When $\mu > \alpha_1(1)$, E_0 is globally stable.

E_1 When $\mu < \alpha_1(1)$, E_1 is locally asymptotically stable if $\tau > \tau^*(\bar{R}_1)$, is unstable if $\tau < \tau^*(\bar{R}_1)$ and is linearly neutrally stable if $\tau = \tau^*(\bar{R}_1)$. Further E_1 is globally asymptotically stable for any $\tau > 0$ when the condition given in Theorem 2.4(ii) is satisfied.

E_2 E_2 is always unstable.

E_3 When $\mu < \alpha_2(\hat{R})$, E_3 is unstable. Further E_3 is locally asymptotically stable if $\alpha_2(\hat{R}) < \mu < \alpha_1(\hat{R})$ and $\tau = 0$.

E_4 When $\tau = 0$, E_4 is globally asymptotically stable.

We cannot prove the local stability of E_3 and E_4 for $\tau > 0$ since the coefficients of characteristic equation (10) depend on the time delay τ. So we execute numerical analysis by using the geometric stability switch criterion established by Beretta and Kuang [4].

First, we considered the positive equilibrium point E_4. E_4 exists for $0 < \tau < \tau^*(R^*)$ and is stable at $\tau = 0$. According to our analysis, there are two threshold values τ_0 and τ_1 $(0 < \tau_0 < \tau_1 < \tau^*(R^*))$, such that the positive equilibrium point E_4 is unstable only when $\tau \in [\tau_0, \tau_1]$ (see Fig. 4). That is, there are two critical values τ_0 and τ_1 such that E_4 continuously changes its stability from being stable, to unstable, and then to stable in order as τ increases from zero. Furthermore,

E_4 bifurcates to periodic solutions when τ passes through τ_0 (or τ_1) from the left (or the right), respectively.

Fig. 8. The distribution of zeros of $s_n^+(\tau), n = 0, 1, \cdots$, corresponding to the boundary equilibrium point E_1 of system (3). Here $\beta = 8, m_1 = 0.3075, n_i = 0.04, \mu = 0.0833$.

Fig. 9. The stable and unstable regions of the positive equilibrium point E_4 of system (3). Here parameter values are those given by (5).

Next, we considered the equilibrium point E_3 without resistant bacteria. We showed that E_3 exists for $0 < \tau < \tau^*(\bar{R}_1)$ and is unstable at $\tau = 0$ since $\mu < \alpha_2(\hat{R})$. We described that E_3 is unstable for $0 \leq \tau \leq \tau^*(R^*)$ and is locally asymptotically stable for $\tau^*(R^*) < \tau < \tau^*(\bar{R}_1)$ (see case $\beta = 8$). It is expected that E_3 is locally asymptotically stable when there is no positive equilibrium point E_4.

In general by increasing the value of time delay, the system usually loses its stability. In many delay differential equations, we know that the large time delay usually plays destabilizing role. That is, if a steady state exists and is unstable at τ^*, then it remains unstable for $\tau > \tau^*$. But for system (3), first we lose the stability of a positive equilibrium point but the point becomes stable again by further increasing of the value of time delay. This is because our system has a coefficient that depends on the time delay and the characteristic equation has delay dependent coefficients.

Further the implicit expression of $s_0^+(\tau) = 0$ is very complicated and it is very difficult to get the global asymptotic stability region of E_4. Therefore, the theoretic analysis of the global asymptotic stability of E_4 is still a future problem.

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