ROCKY MOUNTAIN
JOURNAL OF MATHEMATICS
Volume 41, Number 2, 2011

WELL-POSEDNESS AND DISSIPATIVITY FOR A MODEL OF BACTERIOPHAGE AND BACTERIA IN A FLOW REACTOR

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ABSTRACT. The Levin-Stewart model of bacteriophage predation of bacteria in a chemostat is modified for a flow reactor in which bacteria are motile, phage diffuse, and advection brings fresh nutrient and removes medium, cells and phage. A fixed latent period for phage results in a system of delayed reaction-diffusion equations with non-local nonlinearities. We show that the model generates a well-posed dynamical system which has a compact global attractor.

1. Introduction. Levin et al. [**10**] and Lenski and Levin [**9**] model bacteriophage predation on a bacterial host which in turn consumes a limiting nutrient in a chemostat by the system

$$
\begin{aligned}
S'(t) &= D(S^0 - S(t)) - f(S(t))B(t) \\
B'(t) &= (f(S(t)) - D)\, B(t) - kB(t)P(t) \\
I'(t) &= kB(t)P(t) - DI(t) - e^{-D\tau} kB(t-\tau)P(t-\tau) \\
P'(t) &= -DP(t) - kB(t)P(t) + \beta e^{-D\tau} kB(t-\tau)P(t-\tau).
\end{aligned} \tag{1}
$$

S is the resource supporting bacterial growth, B is uninfected bacteria, I is phage-infected bacteria and P is phage, short for bacteriophage. S^0 is input nutrient concentration supplied to bacteria, D is the dilution rate of the chemostat and $f(S)$ is the specific growth rate of bacteria at resource level S. The specific growth rate f is typically taken to be of Monod type:

$$f(S) = \frac{mS}{a+S}$$

where $m, a > 0$. However, we need only assume that $f : \mathbf{R}_+ \to \mathbf{R}_+$ is C^1 and

$$f(0) = 0, \qquad f'(S) > 0, \qquad f(\infty) < \infty. \tag{2}$$

Supported by NSF Grant DMS 0918440.
Received by the editors on May 25, 2010.

DOI:10.1216/RMJ-2011-41-2-597

Phage attach to the cell surface of a bacterium and inject their DNA into it. This causes the bacterium to begin to synthesize viral DNA and viral proteins in order to make new virus. After a time τ, called the latent period, this is complete and the bacterium lyses open releasing the new virus. Latent periods vary by bacterial type but are usually in the half hour to hour range. Denote by β the average number of progeny released when an infected cell lyses. The factor $e^{-D\tau}$ in the equations accounts for the fraction of infected bacteria that survive being washed out of the chemostat during the latent period. More generally, the probability of phage, nutrient, or bacteria avoiding washout in a time period of length t is e^{-Dt}.

Several important assumptions are made in formulating the model: (1) nutrient uptake by infected cells is negligible, (2) infected cells do not grow and divide, (3) phage binding to infected cells can be neglected, and (4) deactivation of phage can be neglected. We have scaled out the yield constant, a positive number multiplying $f(S)$ in the equation for S.

Nonnegative initial data for B and P must be prescribed on $[-\tau, 0]$ but only $S(0)$ need be prescribed.

The interesting dynamics generated by system (1) have been investigated recently in [**2, 16, 18**].

Our interest in the present paper is to study the behavior of the analogous phage-bacteria model in a tubular flow reactor where spatial effects become important. The flow reactor has often figured in ecological modeling [**1, 3, 8, 14, 15**] because it is one of the simplest spatially non-homogeneous environments featuring advection and diffusion. The flow reactor consists of the portion $0 \leq x \leq L$ of a tube with axis of symmetry along the x-axis through which liquid medium flows with constant velocity in the direction of increasing x. The fluid upstream of $x = 0$ brings nutrient at constant concentration into the reactor; unused nutrient and any contents of the reactor are carried out of the reactor at $x = L$ by the flow. We assume that bacteria and virus in the flow reactor undergo random diffusion as well as advecting with the flow. Bacterial chemotaxis is neglected in the current model, although we aim to consider it in the future.

For a flow reactor of length L, with flow velocity v, and diffusion coefficients d_i, $i = 0, 1, 2, 3$ for the constituents, the model equations take the form:

$$
\begin{aligned}
S_t &= d_0 S_{xx} - vS_x - Bf(S) \\
B_t &= d_1 B_{xx} - vB_x + Bf(S) - kBP \\
P_t &= d_3 P_{xx} - vP_x - kBP \\
&\quad + k\beta \int_0^L G(\tau, x, y) B(t-\tau, y) P(t-\tau, y)\, dy
\end{aligned}
\tag{3}
$$

with Danckwerts boundary conditions (see [**1, 8**]):

$$
\begin{aligned}
d_0 S_x(t,0) - vS(t,0) &= -vS^0 \\
d_1 B_x(t,0) - vB(t,0) &= 0 \\
d_3 P_x(t,0) - vP(t,0) &= 0 \\
M_x(t,L) &= 0, \quad M = S, B, P
\end{aligned}
\tag{4}
$$

$G(t,x,y)$ is the probability density that an infected bacterium is at position x at time t given that at time $t = 0$ its position was y. It is the Green's function satisfying, as a function of (t,x),

$$G_t = d_2 G_{xx} - vG_x, \qquad G(0,x,y) = \delta(x-y)$$

with boundary conditions as above for P, but with d_2 in place of d_3, and where $y \in [0,L]$; δ denotes the Dirac "function." See [**4, 7**] for the connection between probability theory and Green's functions. Here, d_2 is the motility coefficient for infected cells, denoted by I, which may differ from un-infected cells denoted by B.

The integral term in the P equation:

$$k \int_0^L G(\tau, x, y) B(t-\tau, y) P(t-\tau, y)\, dy$$

gives the amount of infected cells which were infected at time $t - \tau$ at various positions $y \in [0,L]$ but at time t are at x where they lyse.

Initial data must be prescribed:

$$
\begin{aligned}
S(0,x) &= S^*(x) \\
B(\theta,x) &= B^*(\theta,x), \quad (\theta,x) \in [-\tau,0] \times [0,L] \\
P(\theta,x) &= P^*(\theta,x)
\end{aligned}
\tag{5}
$$

Infected cell density is given by

$$I(t,x) = \int_0^\tau \int_0^L G(a,x,y)kB(t-a,y)P(t-a,y)\,dy\,da \tag{6}$$

where it is understood that equations (5) extend functions B and P for negative values of their argument. The integral captures all cells infected after time $t-\tau$ but before time t which are still in the reactor at time t. I satisfies

$$\begin{aligned} I_t &= d_2 I_{xx} - vI_x + kBP \\ &\quad - k\int_0^L G(\tau,x,y)B(t-\tau,y)P(t-\tau,y)\,dy \\ 0 &= d_2 I_x(t,0) - vI(t,0) = I_x(t,L). \end{aligned} \tag{7}$$

Equations like (3) containing non-local terms were introduced by Marcati and Posio [**11**] in a vector-disease model and by Gourley and Britton [**5**] and Thieme and Zhao [**19**] for predator-prey models.

We show that the system (3)–(5) can be formulated as a delay differential equation in the Banach space $C([0,L],\mathbf{R}_+)\times C([0,L],\mathbf{R}_+)\times C([0,L],\mathbf{R}_+)$:

$$\begin{aligned} \frac{dR}{dt} &= A_0R(t) + f(S^0 - R(t))B(t) \\ \frac{dB}{dt} &= A_1B(t) + f(S^0 - R(t))B(t) - kB(t)P(t) \\ \frac{dP}{dt} &= A_3P(t) - kB(t)P(t) + \beta g(kB(t-\tau)P(t-\tau)) \end{aligned} \tag{8}$$

where $R = S^0 - S$ takes values in $[0, S^0]$ and satisfies homogeneous boundary conditions. The A_i denote appropriate differential operators with domain incorporating homogeneous boundary conditions from (4), and where $g : C([0,L],\mathbf{R}_+) \to C([0,L],\mathbf{R}_+)$ is the compact, positive operator given by integration against Green's function G. Technically, the formulation (8) requires the restriction of initial data S^* to take values not exceeding S^0, which is reasonable since this set is positively invariant and attracting by standard parabolic comparison arguments. The abstract formulation (8) leads to well-posedness results and implies that the system generates a nonlinear semiflow on a suitable space. In addition, we show that solutions are uniformly ultimately bounded and that the dynamical system has a compact global attractor of bounded sets. These results will lay the foundation for future work focusing on persistence of bacteria and bacteriophage and on the existence of coexistence equilibria.

2. Preliminaries. Given $d > 0$, the eigenvalue problem

$$\begin{aligned} \lambda\phi &= d\phi'' - v\phi' \\ 0 &= d\phi'(0) - v\phi(0) = \phi'(L) \end{aligned} \tag{9}$$

is of critical importance here. The self-adjoint form of the differential equation

$$(de^{-(v/d)x}\phi')' = \lambda e^{-(v/d)x}\phi$$

reveals the weight function $e^{-(v/d)x}$ in the orthogonality relations. Eigenvalues of (9), $\{\lambda_n\}_{n\geq 1}$, ordered from largest to smallest, are negative and $\lambda_n \to -\infty$. When it is important to specify a value of d, we include it in our notation as $\lambda_n(d)$. Corresponding normalized eigenfunctions are denoted by $\{\phi_n(x)\}$:

$$\int_0^L \phi_n^2(x)e^{-(v/d)x}dx = 1, \ n \geq 1$$

Without loss of generality, we can take $\phi_1(x) > 0$, $0 \leq x \leq L$. The corresponding principal eigenvalue can be expressed as

$$\lambda_1 = -\frac{v}{L}\lambda^*(d/Lv) \tag{10}$$

where $\lambda^* : (0,\infty) \to (1,\infty)$ is strictly decreasing with $\lambda^*(0+) = \infty$ and $\lambda^*(\infty) = 1$. See [**1**].

The parabolic initial boundary value problem

$$\begin{aligned} U_t &= dU_{xx} - vU_x, \quad t > 0, \ 0 \leq x \leq L \\ 0 &= dU_x(t,0) - vU(t,0) = U_x(t,L), \quad t > 0 \\ U(0,x) &= U_0(x), \quad 0 \leq x \leq L \end{aligned} \tag{11}$$

has the formal solution

$$U(t,x) = \int_0^L G(t,x,y)U_0(y)\,dy$$

in terms of the Green's function

$$G(t,x,y) = e^{-(v/d)y} \sum_{n\geq 1} e^{\lambda_n t}\phi_n(x)\phi_n(y). \tag{12}$$

The following result is classical (see [**14**]). If $\phi \in C([0,L],\mathbf{R})$, we write $\phi \geq 0$ if $\phi(x) \geq 0$ for all x, $\phi > 0$ if $\phi \geq 0$ and $\phi(x) > 0$ for some x, and $\phi \gg 0$ if $\phi(x) > 0$ for all x. All norms in this paper are supremum norms.

Proposition 2.1. *Define*

$$[T(t)\phi](x) = \int_0^L G(t,x,y)\phi(y)\,dy, \quad x \in [0,1],\ t > 0.$$

Then $\{T(t)\}_{t\geq 0}$, with $T(0) = I$ the identity operator, defines a strongly continuous semigroup of bounded linear operators on $C([0,L],\mathbf{R})$. There exists $M > 0$ such that

$$\|T(t)\phi\| \leq Me^{\lambda_1 t}\|\phi\|, \quad t > 0,\ \phi \in C([0,L],\mathbf{R}) \tag{13}$$

and $T(t)$ is a contraction:

$$\|T(t)U_0\| \leq \|U_0\|, \quad t \geq 0. \tag{14}$$

$T(t)$ is a compact operator for each $t > 0$ and it is strongly positive, that is,

$$\phi > 0, \quad t > 0 \Longrightarrow T(t)\phi \gg 0. \tag{15}$$

Indeed, $G(t,x,y) > 0$ for $t > 0$, $x, y \in [0,L]$. The unique solution of (11) is given by $U(t,x) = [T(t)U_0](x)$.

3. The solution semiflow.

3.1. Existence, continuation, and continuous dependence of solutions on initial data. In this section, we focus on well-posedness issues for the initial value problem (3)–(5).

Let $X = C([-\tau, 0] \times [0, L], \mathbf{R})$ be the Banach space of continuous real-valued functions on $[-\tau, 0] \times [0, L]$ with the supremum norm and $Y = C([0, L], \mathbf{R})$ the Banach space of continuous real-valued functions on $[0, L]$ with supremum norm. We use $\| \bullet \|$ for both norms, the context signaling the appropriate interpretation. X can be identified with $C([-\tau, 0], Y)$. We denote by X_+ and Y_+ the cone of nonnegative functions in X and Y, respectively. Then our state space is $Z_+ \equiv Y_+ \times X_+ \times X_+$, the nonnegative cone in the Banach space $Z = Y \times X^2$, the latter given the norm $\|(S, B, P)\| = \max\{\|S\|, \|B\|, \|P\|\}$. If $\sigma > 0$ and $B : [-\tau, \sigma) \times [0, L] \to \mathbf{R}$ is continuous and $0 \leq t < \sigma$, then we define $B_t \in X$ by

$$B_t(\theta, x) = B(t + \theta, x), \quad \theta \in [-\tau, 0],\ x \in [0, L].$$

We use the same notation for a continuous map $B : [-\tau, \sigma) \to Y$. This notation should not conflict with our earlier use of subscripts for partial derivatives as we will not use the latter in the remainder of this section.

Let A denote the differential operator defined by $A\psi = d\psi'' - v\psi'$ with domain $D = \{\psi \in C^2[0, L] : d\psi'(0) - v\psi(0) = 0 = \psi'(L)\}$ and let A_i denote A with $d = d_i$. Let $T_i(t) : Y \to Y$ be the strongly continuous semigroup generated by the closure of A_i in $C([0, L], \mathbf{R})$ described in Proposition 2.1. Each $T_i(t)$ is compact for $t > 0$ and positive in the sense that $T_i(t)Y_+ \subset Y_+$.

Setting $R = S^0 - S$, which takes values in $[0, S^0]$, we formulate (3)–(4) as the delay differential equation in the Banach space $(Y_+)^3$ given by:

$$\begin{aligned}
\frac{dR}{dt} &= A_0 R(t) + f(S^0 - R(t))B(t)\\
\frac{dB}{dt} &= A_1 B(t) + f(S^0 - R(t))B(t) - kB(t)P(t) \qquad (16)\\
\frac{dP}{dt} &= A_3 P(t) - kB(t)P(t) + \beta g(kB(t - \tau)P(t - \tau))
\end{aligned}$$

where $g : C([0,L],R_+) \to C([0,L],R_+)$ is the compact, positive operator given by integration against Green's function G:

$$[g(U)](x) = \int_0^L G(\tau,x,y)U(y)\,dy = [T_2(\tau)U](x).$$

In addition, initial conditions are given by

$$\begin{aligned} R(0) &= R^* = S^0 - S^* \\ B(\theta) &= B^*(\theta), \quad \theta \in [-\tau,0] \\ P(\theta) &= P^*(\theta) \end{aligned} \tag{17}$$

where $(S^*,B^*,P^*) \in Z_+$ and it is assumed that $0 \le S^* \le S^0$. Thus, we will seek solutions of (16)–(17) which take values in the convex subset

$$C = \{(R,B,P) \in (Y_+)^3 : R \le S^0\}.$$

If we write $u = (R,B,P)$, then (16)–(17) takes the form

$$\frac{du}{dt} = Au + F(u_t), \quad u_0 = u^*$$

where $A = (A_0, A_1, A_3)$ and $F = (F_1, F_2, F_3)$ and $F_i : \mathcal{C} \to Y$ is defined by:

$$\begin{aligned} F_0(R,B,P)(x) &= B(0,x)f(S^0 - R(x)) \\ F_1(R,B,P)(x) &= B(0,x)f(S^0 - R(x)) - kB(0,x)P(0,x) \\ F_3(R,B,P)(x) &= -kB(0,x)P(0,x) \\ &\quad + k\beta g(B(-\tau,\cdot)P(-\tau,\cdot))(x) \end{aligned}$$

where

$$\mathcal{C} = \{(R,B,P) \in Z_+ : R \le S^0\}.$$

It is convenient to use the notation (R,B,P) both for a vector in C and for a vector in $\mathcal{C}$ where, hopefully, the context will provide the appropriate meaning. It is easy to see that $F : \mathcal{C} \to Y^3$ is continuous. Indeed for each $L > 0$ there exists $K(L) > 0$ such that

$$\|F(z) - F(\widetilde{z})\| \le K(L)\|z - \widetilde{z}\|, \quad z, \widetilde{z} \in \mathcal{C}, \ \|z\|, \|\widetilde{z}\| \le L.$$

The mild formulation of (16)–(17) consists of finding continuous functions $R : [0, \sigma) \to Y_+$, with $R(t) \le S^0$, and $B, P : [-\tau, \sigma) \to Y_+$ satisfying the integral equations

$$(18)\qquad \begin{aligned} R(t) &= T_0(t)R^*(0) + \int_0^t T_0(t-s)F_0(R(s), B_s, P_s)\, ds \\ B(t) &= T_1(t)B^*(0) + \int_0^t T_1(t-s)F_1(R(s), B_s, P_s)\, ds, \quad t \ge 0 \\ P(t) &= T_3(t)P^*(0) + \int_0^t T_3(t-s)F_3(R(s), B_s, P_s)\, ds \end{aligned}$$

together with $B_0 = B^*$ and $P_0 = P^*$.

Theorem 3.1. *For each $(R^*, B^*, P^*) \in \mathcal{C}$, there exists a unique noncontinuable solution $(R(t), B(t), P(t)) \in C$ of the initial value problem (18) defined for $0 \le t < \sigma$ for some $\sigma \in (0, \infty)$. If $\sigma < \infty$, then $\|B_t\| + \|P_t\| \to \infty$ as $t \nearrow \sigma$.*

Proof. We use Theorem 2 in [**12**, reproduced as Theorem 1.2 in Chapter 8 of [**20**] and Corollary 4 in [**12**]. In the notation of Corollary 4, $K = C$ and the affine evolution operator $\mathcal{S}(t, s)$ defined by $\mathcal{S}(t, s) = (T_0(t-s), T_1(t-s), T_3(t-s))$ is linear and $\mathcal{S}(t, s) : C \to C$ by Proposition 2.1, see especially (14). It suffices to establish the subtangential condition:

$$(19)\qquad \lim_{h \searrow 0} \frac{1}{h} d(B(0) + hF_1(R, B, P); Y_+) = 0, \quad (R, B, P) \in \mathcal{C}$$

where $B(0) = B(0, \cdot)$ and $d(M; Y_+) = \inf\{\|M - N\| : N \in Y_+\}$, and the analogous subtangential conditions for R and P. We have

$$[B(0) + hF_1(R, B, P)](x) = B(0, x)[1 + h\left(f(S^0 - R(x)) - kP(0, x)\right)].$$

Since $B(0, x) \ge 0$ and $1 + h(f(S^0 - R(x)) - kP(0, x)) > 1/2$ for all $x \in [0, L]$, if $h > 0$ is sufficiently small, we see that $d(B(0) + hF_1(R, B, P); Y_+) = 0$ for sufficiently small $h > 0$. Therefore, (19) holds.

We may express $f(S) = Sg(S)$ where $g : [0, \infty) \to [0, \infty)$ is continuous. We abuse notation by defining $[0, S^0]$ to be the subset of Y taking values in the interval. The subtangential condition for R involves

$$\begin{aligned}[R + hF_0(R, B, P)](x) &= R(x) + hf(S^0 - R(x))B(0, x)\\ &= S^0 - (R(x) - S^0)(1 - hg(S(x)B(0, x)).\end{aligned}$$

Obviously, $[R + hF_0(R, B, P)](x) \geq 0$, and the final expression shows that it is smaller that S^0 for small h. Thus, $d(R+hF_0(R, B, P); [0, S^0]) = 0$ for sufficiently small $h > 0$, which implies the required subtangential condition.

Finally, since $B, P \geq 0$ and T_2 is a positive operator

$$\begin{aligned}[P(0) + hF_3(R, B, P)](x) &= P(0, x) - hkP(0, x)B(0, x)\\ &\quad + hk\beta[T_2(\tau)B(-\tau, \cdot)P(-\tau, \cdot)](x)\\ &\geq P(0, x)[1 - hkB(0, x)],\end{aligned}$$

we have that $d(P(0) + hF_3(S, B, P); Y_+) = 0$ for sufficiently small $h > 0$. Therefore the required subtangential conditions are satisfied. The existence result and blow-up condition now follow from Theorem 2 and Corollary 4 in [**12**]. $\square$

Proposition 3.1. *In Theorem* 3.1, $\sigma = \infty$.

Proof. If $\sigma < \infty$, then $\|B_t\| + \|P_t\| \to \infty$ as $t \nearrow \sigma$ by Theorem 3.1. We will show this cannot happen.

$$B(t) \leq T_1(t)B^*(0) + f(S^0)\int_0^t T_1(t-s)B(s)\,ds.$$

Since the norm on Y is monotone,

$$\begin{aligned}\|B(t)\| &\leq \|T_1(t)B^*(0)\| + f(S^0)\int_0^t \|T_1(t-s)B(s)\|\,ds\\ &\leq \|B^*(0)\| + f(S^0)\int_0^t \|B(s)\|\,ds\end{aligned}$$

where we used that T_1 is a contraction semigroup. Gronwall's inequality implies that $\|B(t)\| \leq \|B^*\|e^{f(S^0)t}$. Now,

$$P(t) \leq T_3(t)P^*(0) + k\beta\int_0^t T_3(t-s)T_2(\tau)B_s(-\tau)P_s(-\tau)\,ds.$$

Arguing as above

$$\begin{aligned}\|P(t)\| &\le \|T_3(t)P^*(0)\| \\ &\qquad + k\beta\int_0^t \|T_3(t-s)T_2(\tau)B_s(-\tau)P_s(-\tau)\|\,ds \\ &\le \|P^*\| + k\beta\int_0^t \|B_s\|\|P_s\|\,ds.\end{aligned}$$

This implies that

$$\|P_t\| \le \|P^*\| + k\beta\int_0^t \|B_s\|\|P_s\|\,ds.$$

Gronwall's inequality implies that

$$\|P_t\| \le \|P^*\|\exp\left(k\beta\int_0^t \|B_s\|\,ds\right). \tag{20}$$

These estimates show that $\|B_t\| + \|P_t\|$ remains bounded on any finite interval. □

Our next result gives continuous dependence of solutions on initial data and describes their smoothness properties.

Proposition 3.2. *Equation* (18) *generates a continuous semiflow* $\Phi : [0,\infty)\times\mathcal{C}\to\mathcal{C}$ *given by*

$$\Phi(t,(S^*,B^*,P^*)) = (S^0 - R(t), B_t, P_t).$$

Moreover, solutions $u(t) \equiv (R(t),B(t),P(t))$ *of* (18) *satisfy* (16) *for* $t>\tau$.

Proof. Define the nonlinear solution semiflow associated with (18) $\Psi : [0,\infty)\times\mathcal{C}\to\mathcal{C}$ by

$$\Psi(t,(R^*,B^*,P^*)) = (R(t),B_t,P_t), \quad t\ge 0.$$

By [**13**] or by [**20**, Theorem 2.6, Chapter 2], Ψ is a continuous semiflow on $\mathcal{C}$. As $S = S^0 - R$, $\Phi : [0,\infty)\times\mathcal{C}\to\mathcal{C}$ defined by $\Phi(t,(S^*,B^*,P^*)) =$

$(S^0 - R(t), B_t, P_t)$ where $S^* = S^0 - R^*$ gives the solution semiflow for (3).

By [**13**] or [**20**, Theorem 2.6, Chapter 2], due to the analyticity of the semigroups T_i and smoothness of $F = (F_0, F_1, F_3)$, solutions $u(t) \equiv (R(t), B(t), P(t))$ of (18) satisfy (16) for $t > 0$ if u^* is suitably restricted (see item (3) of Theorem 2.6), and for $t > \tau$ otherwise. □

3.2. L^1-bounds on solutions. For $i = 0, 1, 2, 3$, let $e_i(x) = e^{-(v/d_i)x}$ and ϕ_{1i} denote the normalized principal eigenvector and λ_{1i} the corresponding principal eigenvalue of (9) with $d = d_i$.

Set

$$\begin{aligned} s(t) &= \int_0^L S(t,x)\phi_{10}(x)e_0(x)\,dx \\ b(t) &= \int_0^L B(t,x)\phi_{11}(x)e_1(x)\,dx \\ i(t) &= \int_0^L I(t,x)\phi_{12}(x)e_2(x)\,dx \\ p(t) &= \int_0^L P(t,x)\phi_{13}(x)e_3(x)\,dx. \end{aligned}$$

Then s is a measure of the total nutrient in the tube while b, i, p give totals for uninfected,infected cells, and virus, respectively. Multiplying (3) and (7) by appropriate $e_i\phi_{1i}$ and integrating gives

$$\begin{aligned} s' &= vS^0\phi_{10}(0) + \lambda_{10}s - \int_0^L Bf(S)\phi_{10}e_0\,dx \\ b' &= \lambda_{11}b + \int_0^L Bf(S)\phi_{11}e_1 dx - k\int_0^L BP\phi_{11}e_1\,dx \\ i' &= \lambda_{12}i + k\int_0^L BP\phi_{12}e_2 dx - k\int_0^L\int_0^L GBPdy\phi_{12}e_2\,dx \\ p' &= \lambda_{13}p - k\int_0^L BP\phi_{13}e_3 dx + k\beta\int_0^L\int_0^L GBPdy\phi_{13}e_3\,dx, \end{aligned} \tag{21}$$

where we have dropped arguments in the last integrals for brevity. Let

$c_i > 0,\ i = 0, 1, 2, 3$ to be determined. Then

$$\begin{aligned}
&(c_0 s + c_1 b + c_2 i + c_3 p)' \\
&\qquad = c_0 v S^0 \phi_0(0) + (\lambda_{10} c_0 s + \lambda_{11} c_1 b + \lambda_{12} c_2 i + \lambda_{13} c_3 p) \\
&\qquad\quad + \int_0^L Bf(S)(c_1 \phi_{11} e_1 - c_0 \phi_{10} e_0)\, dx \\
&\qquad\quad + k \int_0^L BP(c_2 \phi_{12} e_2 - c_1 \phi_{11} e_1 - c_3 \phi_{13} e_3)\, dx \\
&\qquad\quad + k \int_0^L \int_0^L GBP\, dy(\beta c_3 \phi_{13} e_3 - c_2 \phi_{12} e_2)\, dx.
\end{aligned}$$

In reverse order, choose c_3, c_2, c_1, c_0 as follows

$$\begin{gathered}
c_3 = 1, \qquad c_2 \phi_{12} e_2 > c_3 \beta \phi_{13} e_3, \\
c_1 \phi_{11} e_1 + c_3 \phi_{13} e_3 > c_2 \phi_{12} e_2, \qquad c_0 \phi_{10} e_0 > c_1 \phi_{11} e_1.
\end{gathered}$$

Then $w(t) \equiv c_0 s + c_1 b + c_2 i + c_3 p$ is an L^1-measure of the total contents of the bio-reactor and it satisfies

$$w' \le c_0 v S^0 \phi_0(0) - \Lambda w,$$

where

$$-\Lambda = \max_i \lambda_{1i}. \tag{22}$$

Therefore,

$$w(t) \le w(0) e^{-\Lambda t} + \frac{c_0 v S^0}{\Lambda}(1 - e^{-\Lambda t}). \tag{23}$$

The reader may object to the use of (3) and (7) rather than its mild formulation (18) in obtaining (23). In fact, the same result can be obtained using (18). One simply takes the appropriate inner product of both sides with the functions ϕ_{1i} and then makes use of the self-adjointness

$$\langle T_i(t) F_i, \phi_{1i} \rangle = \langle F_i, T_i(t) \phi_{1i} \rangle = e^{\lambda_{1i} t} \langle F_i, \phi_{1i} \rangle,$$

where $\langle f, g \rangle = \int_0^L f g e_i\, dx$.

Because $e_i\phi_{1i} \gg 0$ are continuous, (23) trivially implies the following result.

Proposition 3.3. *There exist constants* $C_1, C_2 > 0$ *such that*

$$V(t) \equiv \int_0^L (S(t,x) + B(t,x) + I(t,x) + P(t,x))\, dx, \quad t \geq 0$$

satisfies

$$V(t) \leq C_1 V(0) e^{-\Lambda t} + C_2(1 - e^{-\Lambda t}), \quad t \geq 0 \tag{24}$$

for every solution of (18)*, where* Λ *is defined by* (22)*.*

3.3. Global attractor. We begin by showing that bounded sets of initial data have bounded forward orbits and that there is a uniform asymptotic bound on solutions.

Proposition 3.4. *There is a continuous function* $K : [0,\infty) \to [0,\infty)$ *and* $U > 0$ *such that for every solution of* (3)

$$\|S(t)\| + \|B_t\| + \|P_t\| \leq K(\|S^*\| + \|B^*\| + \|P^*\|), \quad t \geq 0$$

and

$$\limsup_{t\to\infty}(\|S(t)\| + \|B_t\| + \|P_t\|) \leq U.$$

Proof. We leverage the L^1 bounds obtained in the previous section to obtain L^∞ bounds. We follow closely the arguments given in Proposition 8.9 in [**17**]. Since $S(t) \leq S^0$, we need only focus on B and P. In fact, the argument for B is so similar to those given in Proposition 8.9 for the dependent variables S and u considered there, because we may ignore the term $-kBP$, that we do not repeat them here. Therefore, there exists a constant $\widetilde{B}$ depending only on $\|B^*\|$ such that $B(t,x) \leq \widetilde{B}$ for $t \geq -\tau$, $0 \leq x \leq L$. We show how to obtain an L^∞-bound for P. Let $G^* = \max G(\tau, x, y)$ where the maximum is taken over $(x,y) \in [0,L]^2$. Estimate (23) implies the existence of Q, depending on the L^1 norms of $S^*, B^*(0,\cdot), P^*(0,\cdot)$, such that

$$\int_0^L P(t,y)\, dy \leq Q, \quad t \geq -\tau.$$

We start from the equation for P given in (18). Using that

$$F_3(S(s), B_s, P_s)(x) \le k\beta G^* \widetilde{B} \int_0^L P(s-\tau, y)\, dy$$
$$\le k\beta G^* \widetilde{B} Q, \quad s \ge 0,\ 0 \le x \le L,$$

and taking advantage of the positivity of T_3, we have that

$$P(t) \le T_3(t)P^*(0) + k\beta G^* \widetilde{B} Q \int_0^t T_3(s) 1\, ds,$$

where 1 denotes the constant function equal to one. Thus,

$$\|P(t)\| \le M e^{\lambda_1(d_3)t} \|P^*(0)\| + k\beta G^* \widetilde{B} Q(-M/\lambda_1(d_3)),$$

where we use that $\|T_3(t)\| \le M e^{\lambda_1(d_3)t}$. The right side gives a uniform bound on $\|P(t)\|$ which depends only on $\|P^*(0)\|$, $\widetilde{B}$, Q and various constants.

Since $\lambda_1(d_3) < 0$,

$$\limsup_{t\to\infty} \|P(t)\| \le k\beta G^* \widetilde{B} Q \frac{M}{|\lambda_1(d_3)|}.$$

A similar bound for $\limsup_{t\to\infty} \|B(t)\|$ is given in [**17**, Proposition 8.9]. □

Proposition 3.4 leads directly to the following result.

Theorem 3.2. *Every orbit $\{(S(t), B_t, P_t) : t \ge 0\}$ has compact closure in Z_+. Furthermore, there exists a compact, connected, invariant attractor for Φ which attracts bounded sets in Z_+.*

Proof. This argument is now routine. See Theorem 2.7 in [**3**] and Theorem 2.1 in [**19**]. Proposition 3.4 implies that semiflow Φ is point dissipative and that bounded sets have bounded orbits. The compactness of the semiflow Φ, see [**13**] and Theorem 2.6 of Chapter 2 [**20**], implies that it is asymptotically smooth so the result follows from Theorem 3.4.8 in [**6**]. □

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