

Mathematical models of microbial growth and competition in the chemostat regulated by cell-bound extracellular enzymes

Betty Tang^{1*} and Gail S. K. Wolkowicz^{2**}

¹ Department of Mathematics, Arizona State University, Tempe, AZ 85287, USA

² Department of Mathematics and Statistics, McMaster University, Hamilton, Ontario L8S 4K1, Canada

Received January 4, 1991; received in revised form July 15, 1991

Abstract. A mathematical model of growth and competitive interaction of microorganisms in the chemostat is analyzed. The growth-limiting nutrient is not in a form that can be directly assimilated by the microorganisms, and must first be transformed into an intermediate product by cell-bound extracellular enzymes. General monotone functions, including Michaelis–Menten and sigmoidal response functions, are used to describe nutrient conversion and growth due to consumption of the intermediate product. It is shown that the initial concentration of the species is an important determining factor for survival or washout. When there are two species whose growth is limited by the same nutrient, three different modes of competition are described. Competitive coexistence steady states are shown to be possible in two of them, but they are always unstable. In all of our numerical simulations, the system approaches a steady state corresponding to the washout of one or both of the species from the chemostat.

Key words: Population dynamics – Growth – Competition

1 Introduction

In this paper we present and analyze a mathematical model describing microbial growth and competition in the chemostat where extracellular enzymes produced by the microorganisms play an important role in the nutrient uptake process.

The chemostat is a laboratory apparatus used for the continuous culture of microorganisms. It can be viewed as a laboratory idealization of a natural lake system and is useful for studying the growth and interaction of microorganisms limited by the short supply of some nutrient or nutrients. Here we are interested in the case where there is a single, nonreproducing, growth limiting nutrient. All other factors influencing growth are assumed to be in abundant supply.

Many of the mathematical models of microbial growth in the literature were constructed under the simplifying assumption that nutrient uptake and cellular

* Research supported by NSF grant DMS-90-96279

** Research supported by NSERC grant A-9358

growth are directly coupled. Growth is often assumed to be proportional to uptake of external nutrient and the conversion process is assumed to be instantaneous. (See, for example, [2, 7, 8, 9, 15, 16].) In [8, 9], for the Monod growth model, where response functions are modeled by Michaelis–Menten kinetics, and in [2] for any reasonable monotone increasing response functions, the models predict that the concentration of a single population growing in the chemostat will either approach a positive steady state, or the population will be completely washed out of the system. The outcome for a particular species can be predicted from the relative values of the concentration of the nutrient supply in the feed bottle and the break-even concentrations of the nutrient for cell growth of each species. These break-even concentrations depend directly on the dilution rate. If several populations compete for the same growth limiting nutrient, according to these models, only one species has a chance of surviving, the population with the lowest relative break-even concentration. Again a steady state is approached. In both the single species model and the competition model the outcomes are completely initial condition independent.

The assumption that the external nutrient supply is instantaneously converted to biomass is a broad simplification of a series of very complicated chemical reactions. Very often the chemical structure of the nutrient is not even in a form that can be directly absorbed and assimilated by the microorganisms. Secretion of extracellular enzymes is one of the various mechanisms with which many species of bacteria, e.g. several strains of the *Streptococcus* family and of the *Bacillus* family, can utilize such nutrient supply for growth. (See, for example, [5, 11].) In the presence of such enzymes, the external nutrient is first converted to an intermediate product before being absorbed into the cells, e.g. many strains of oral streptococci which cause dental plaque can utilize dietary sucrose by secreting extracellular glucosyltransferases and fructosyltransferases which convert sucrose to dextrans and fructans respectively [14]. The growth rate of the microorganisms is therefore directly related to the concentration of the intermediate product and depends only indirectly on the concentration of the nutrient supply. For convenience sake, microorganisms which can directly utilize the external nutrient supply for growth are referred to as type I, and those which can only assimilate some modified form of the external nutrient are referred to as type II.

For type II microorganisms, there is obviously a delay between the rate of uptake of the external nutrient and the growth rate of the species. There are many models in which growth is dependent on previous consumption history. In one approach [1, 6], fixed time delays are introduced into the model in the form of retarded functional differential equations. Our approach in this paper is to actually model a delay mechanism.

Among type II microorganisms which secrete extracellular enzymes to convert the nutrient to an intermediate product, there are several mechanisms with which the conversion is accomplished. In some species, the enzymes remain attached to the cell wall after being secreted; formation of the intermediate product occurs when the external nutrient comes into contact with the cells. Penicillinase produced by *Bacillus licheniformis* [12] and α -amylase produced by *Bacillus subtilis* [10] are two examples of cell-bound extracellular enzymes. The intermediate product thus formed either becomes detached from the cells and diffuses into the environment, or remains attached and is eventually absorbed by the same cell. In other species, the enzymes are completely detached from the cells and are mixed with the medium. The intermediate product is formed when the nutrient comes into contact with the enzyme molecules.

We study here the case when the extracellular enzymes are cell-bound and the intermediate product becomes detached from the cells after being formed and is assumed to be homogeneously distributed in the chemostat. The rate of production of the intermediate product, which is assumed to be proportional to the rate of conversion of the nutrient, obviously depends on the concentration of the extracellular enzymes. However, there is experimental indication that there is a uniform distribution of binding sites of the enzymes to the cell membrane [10]. We therefore assume that the concentration of the extracellular enzymes is roughly proportional to the concentration of the microorganisms, and consider the per-capita rate of production of the intermediate product as a function of nutrient concentration only. On the other hand, the per-capita growth rate of the microorganisms is a function of the concentration of the intermediate product. Consequently, it is not necessary to explicitly include the enzyme concentration in the model equations. In our model, general monotone response functions are used to describe the per-capita production rate of intermediate product and the per-capita growth rate. Analysis of the model indicates very different dynamics compared with the usual chemostat models of type I microorganisms as shown in [2, 8, 16]. For example, for type II microorganisms, the asymptotic behavior of the model equations depends on the initial concentrations.

Several modes of competition between two species in the chemostat is also considered. These include: (a) both species are type II and the same intermediate product is produced; (b) both species are type II and they produce distinct intermediate products which cannot be consumed by the other species; (c) one species is type I and one is type II.

Our analysis shows that in cases (b) and (c) coexistence steady states are mathematically possible but nonetheless are always unstable, and in general there is no coexistence steady state in case (a). In all cases, depending upon initial conditions and the parameters of the system, either species can be the sole survivor in the chemostat or both species wash out. It is not clear whether coexistence in the form of oscillation is possible, but no Hopf bifurcation from any equilibrium point can occur. Numerical studies suggest that the solution of the model equations approaches one of the stable equilibrium points corresponding to the washout of one or both of the species.

The following interesting phenomenon is observed in case (a). For certain parameter ranges a one-species stable equilibrium can be destabilized when a small amount of the second species is introduced into the chemostat, even though this second species cannot survive without competition. In numerical simulations both species are eventually washed out from the chemostat. This phenomenon could be exploited in bacterial control and genetic engineering.

This paper is organized as follows. The model equations are presented in Sect. 2. The growth of one species is analyzed in Sect. 3. The three modes of competition between two species are studied in Sects. 4 to 6. The focus is to determine whether any coexistence equilibrium is possible, as well as to determine the local stability of all the equilibrium points. Global asymptotic behavior of the system in some particular cases is also studied. Some concluding remarks are given in Sect. 7.

2 The model

A simple model of the growth of one species in the chemostat is proposed. Growth is assumed to be limited by a single, nonreproducing nutrient and all

other factors influencing growth are in abundant supply. The nutrient is not in a form that can be directly consumed and is chemically transformed to an intermediate product in the presence of cell-bound extracellular enzymes produced by the microorganisms. Molecules of the intermediate product, once they are formed, detach from the cells and mix homogeneously in the culture medium. The growth rate of the microorganisms therefore depends directly on the rate at which the intermediate product is absorbed into the cells. The rate of formation of the intermediate product, on the other hand, depends on the concentration of the extracellular enzymes and of the nutrient in the vessel. Assuming enzyme concentration to be roughly proportional to cell concentration, the per-capita rate of intermediate product produced can be modeled as a function of the nutrient concentration only and so enzyme concentration is not explicitly included in the model. The rate of conversion of the nutrient is proportional to the rate of formation of the intermediate product, and the growth rate is proportional to the consumption rate of the intermediate product. Monotone response functions are used to model both the nutrient-intermediate product conversion process and the growth rate by assimilation of the intermediate product.

Under these assumptions the equations describing one species growth dynamics in the chemostat take the form:

$$\begin{aligned}\frac{dS}{dT} &= S^0D - SD - \frac{1}{\gamma}XF(S), \\ \frac{dP}{dT} &= -PD + XF(S) - \frac{1}{\eta}XQ(P), \\ \frac{dX}{dT} &= -XD + XQ(P),\end{aligned}\tag{2.1}$$

$$S(0) \geq 0, \quad P(0) \geq 0, \quad X(0) > 0,$$

where

$S(T)$ = concentration of nutrient (in the chemostat) at time T ,

$P(T)$ = concentration of intermediate product at time T ,

$X(T)$ = concentration of microorganisms at time T ,

$F(S)$ = per-capita production rate of intermediate product as a function of the concentration of the nutrient,

$Q(P)$ = per-capita growth rate of microorganisms as a function of the concentration of the intermediate product,

γ = yield constant for conversion from nutrient to intermediate product,

η = yield constant for consumption of intermediate product,

S^0 = concentration of nutrient supply in the feed bottle of the chemostat,

D = dilution rate. (Species specific death rates are assumed to be negligible compared to the dilution rate.)

The functions $F(S)$ and $Q(P)$ are assumed to be continuously differentiable, monotone increasing, and satisfy $F(0) = 0$ and $Q(0) = 0$. For example, if the growth rate of the microorganisms is assumed to be modeled by Michaelis-Menten kinetics, then $F(S) = MS/(A + S)$, where M denotes the maximum production rate of the intermediate product, and A denotes the Michaelis-Menten (half-saturation) constant for conversion of the nutrient. (Both M and A are positive.) This is a prototype for a concave uptake function that saturates. Another typical form of monotone dynamics is the so-called sigmoidal or

S-shaped dynamics. These functions are initially convex, and have a single point of inflection where they become concave. They also saturate. An example of a functional expression for such dynamics is $F(S) = MS^2/(S^2 + KS + L)$, where K , L , and M are all positive.

Note that even though there is interdependence between P and X in (2.1), the relationship is neither mutuality nor parasitism. If the term $XF(S)$ in the first two equations is replaced by $PF(S)$, the whole system becomes a model for a food chain in the chemostat which was studied in [3].

3 One species in the chemostat

We first scale (2.1) using the following change of variables and notation:

$$\begin{aligned} s &= S/S^0, & p &= P/\gamma S^0, & x &= X/\gamma\eta S^0, \\ f(s) &= \eta F(S)/D, & q(p) &= Q(P)/D, \\ t &= DT, & ' &= d/dt. \end{aligned}$$

The dimensionless equations thus obtained are

$$\begin{aligned} s' &= 1 - s - xf(s), \\ p' &= -p + xf(s) - xq(p), \\ x' &= -x + xq(p), \\ s(0) &\geq 0, & p(0) &\geq 0, & x(0) &> 0. \end{aligned} \tag{3.1}$$

It is easy to see that \mathbb{R}_+^3 , the closed nonnegative cone in \mathbb{R}^3 , is positively invariant under the solution map of (3.1). Moreover, the system is dissipative. In fact,

$$\lim_{t \rightarrow \infty} (s(t) + p(t) + x(t)) = 1 \tag{3.2}$$

and the convergence is exponential. One can also show that the two-dimensional set

$$\Gamma = \{(s, p, x) \in \mathbb{R}_+^3 \mid s + p + x = 1\} \tag{3.3}$$

is positively invariant. The omega limit set of any trajectory therefore is nonempty, compact, connected and contained in Γ .

As in [2, 3], we define the positive extended real numbers λ and δ as follows:

$$f(\lambda) = 1, \quad q(\delta) = 1. \tag{3.4}$$

The monotonicity and continuity of f and q ensure that λ and δ are uniquely defined. (If $f(s) < 1$ for all $s > 0$ then $\lambda = \infty$, and if $q(p) < 1$ for all $p > 0$ then $\delta = \infty$.) For example, in the case of Michaelis–Menten dynamics, i.e., if $f(s) = m_1 s/(a_1 + s)$ and $q(p) = m_2 p/(a_2 + p)$, then

$$\lambda = \frac{a_1}{m_1 - 1}, \quad \delta = \frac{a_2}{m_2 - 1}. \tag{3.5a}$$

If the dynamics is sigmoidal, for example, if $f(s) = ms^2/(s^2 + Ks + L)$, then

$$\lambda = \frac{K + (K^2 + 4mL - 4L)^{1/2}}{2(m - 1)}. \tag{3.5b}$$

The parameter δ represents the concentration of the intermediate product in the scaled model (3.1) at which the concentration of the microorganisms is neither increasing nor decreasing and so is called the break-even concentration. The interpretation of the parameter λ is not so clear. The motivation for defining λ this way comes from considerations of the related model in which there is no intermediate product (see [2, 8]). In that model $x' = x(f(s) - 1)$ and λ is interpreted as the break-even concentration of the nutrient.

Theorem 3.1 $E_0 = (1, 0, 0)$ is always locally asymptotically stable for (3.1), and is globally asymptotically stable if it is the only equilibrium point.

Proof. Local stability of E_0 follows directly from standard linearization technique. Since the omega limit set of any trajectory is contained in the two-dimensional compact and positively invariant set Γ , and E_0 lies on the boundary of Γ , E_0 must be globally asymptotically stable by the Poincaré–Bendixson theorem and its implications.

An equilibrium point $E = (\bar{s}, \bar{p}, \bar{x})$ of (3.1) is an interior equilibrium point if $\bar{s} > 0$, $\bar{p} > 0$ and $\bar{x} > 0$.

Lemma 3.2 If an equilibrium point $E \neq E_0$ exists, then E is an interior equilibrium and it satisfies $\bar{p} = \delta$, $\lambda < \bar{s} < 1 - \delta$.

Proof. If $\bar{x} = 0$ it is clear that E must equal E_0 . Suppose $\bar{x} > 0$, then $\bar{p} = \delta$ and \bar{x} must satisfy:

$$\bar{x} = 1 - \bar{s} - \delta, \quad \bar{x} = \frac{1 - \bar{s}}{f(\bar{s})}, \quad \bar{x} = \frac{\delta}{f(\bar{s}) - 1}. \quad (3.6)$$

(Note that any two of the above conditions imply the third.) Now $\bar{x} = 1 - \bar{s} - \delta > 0$ if and only if $\bar{s} < 1 - \delta$. On the other hand, $1 - \bar{s} > 1 - \bar{s} - \delta = \bar{x} = (1 - \bar{s})/f(\bar{s})$, which implies that $f(\bar{s}) > 1$ so $\lambda < \bar{s}$.

Theorem 3.3 If $\lambda + \delta \geq 1$, E_0 is the only equilibrium point of (3.1) and hence globally asymptotically stable.

Proof. Let $E = (\bar{s}, \bar{p}, \bar{x})$ be any arbitrary equilibrium point of (3.1). If $E \neq E_0$, $\lambda < \bar{s} < 1 - \delta$ by Lemma 3.2. But this implies that $\lambda + \delta < 1$, a contradiction. Global stability follows from Theorem 3.1.

For the rest of this section we study the asymptotic behavior of trajectories of (3.1) when $\lambda + \delta < 1$. We begin by considering the equilibrium points. By Lemma 3.2, E_0 is the only possible boundary equilibrium point. All other equilibria must be in the interior of \mathbb{R}_+^3 . The next theorem gives necessary and sufficient conditions for the existence of such an interior equilibrium. Define

$$\begin{aligned} g(s) &= 1 - \delta - s, \\ h(s) &= \frac{1 - s}{f(s)}, \\ W(s) &= g(s) - h(s), \\ V(s) &= g(s) - \frac{\delta}{f(s) - 1}. \end{aligned} \quad (3.7)$$

An interior equilibrium $E = (\bar{s}, \bar{p}, \bar{x})$ exists if and only if there exists \bar{s} such that $W(\bar{s}) = 0$ and $V(\bar{s}) = 0$.

Theorem 3.4 *With respect to system (3.1), the following are equivalent:*

- (a) *There exists at least one interior equilibrium point.*
- (b) *There exists $s \in (\lambda, 1 - \delta)$ such that $W(s) \geq 0$.*
- (c) *There exists $s \in (\lambda, 1 - \delta)$ such that $W(s) \geq 0$ and $f(s) = 1 + f'(s)(1 - s)/f(s)$.*
- (d) *There exists $s \in (\lambda, 1 - \delta)$ such that $V(s) \geq 0$.*
- (e) *There exists $s \in (\lambda, 1 - \delta)$ such that $V(s) \geq 0$ and $(f(s) - 1)^2 = \delta f'(s)$.*

Proof. Let $E = (\bar{s}, \bar{p}, \bar{x})$ be any equilibrium point of (3.1). If $E \neq E_0$, by Lemma 3.2 it is an interior equilibrium, hence $\lambda < \bar{s} < 1 - \delta$. Note that $W(\lambda) = -\delta$ by (3.4) and $W(1 - \delta) = -\delta/f(1 - \delta) < 0$. Therefore (b) is equivalent to (a). Since $W'(s) = -1 + [f(s) + f'(s)(1 - s)]/f^2(s)$, (c) implies that there exists an $s \in (\lambda, 1 - \delta)$ such that $W'(s) = 0$ and $W(s) \geq 0$. Also, W is continuous and differentiable on $(\lambda, 1 - \delta)$ and negative at the end points of the interval, therefore (b) implies (c). Clearly (c) implies (b). The proofs for (d) and (e) are similar to the above arguments using the last definition of \bar{x} in (3.6).

Corollary 3.5 (a) *If the inequality in Theorem 3.4(b), (c), (d) or (e) is strict then (3.1) has at least two interior equilibrium points.*

(b) *If $f(s)$ is a concave function for $s \in (\lambda, 1 - \delta)$, then (3.1) has at most two interior equilibrium points.*

(c) *If $f(s)$ is S-shaped for $s \in (\lambda, 1 - \delta)$, (i.e. there exists $\tilde{s} \in (\lambda, 1 - \delta)$ such that $f''(s) > 0$ if $\lambda < s < \tilde{s}$ and $f''(s) < 0$ if $\tilde{s} < s < 1 - \delta$), and $f'''(s) < 0$ if $\lambda < s < \tilde{s}$, then (3.1) has at most two interior equilibrium points.*

(d) *If $\lambda < 1$ and δ is sufficiently small then (3.1) has at least two interior equilibrium points.*

Proof. (a) is obvious.

(b) Note that the graph of $g(s)$ is a straight line passing through $(0, 1 - \delta)$ and $(1 - \delta, 0)$, and the graph of $h(s)$ is a curve passing through $(1, 0)$ and satisfies $h(s) > 0$ for $0 < s < 1$ as well as $h(s) \rightarrow \infty$ as $s \rightarrow 0^+$. Since

$$h''(s) = \frac{2(1 - s)(f'(s))^2 + 2f(s)f'(s) - (1 - s)f''(s)f(s)}{f^3(s)}, \tag{3.8}$$

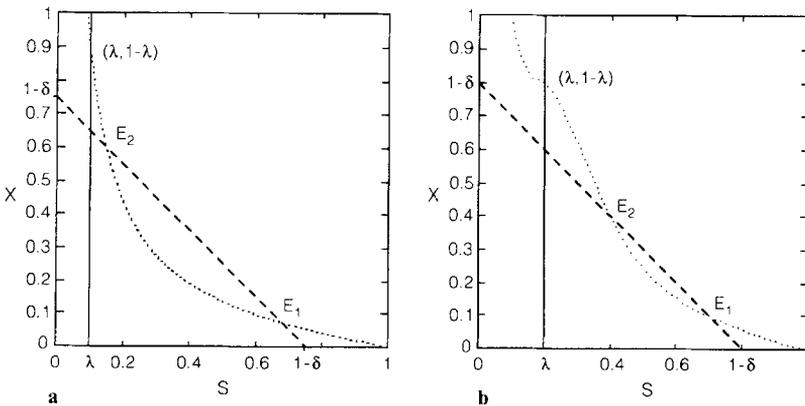


Fig. 3.1. Intersection of $g(s)$ and $h(s)$ when $f(s)$ is **a** concave and **b** S-shaped, for $s \in (\lambda, 1 - \delta)$. $---$ is the graph of $g(s)$ and \cdots is the graph of $h(s)$

if $f(s)$ is concave for $s \in (\lambda, 1 - \delta)$ then $h(s)$ is strictly convex (i.e. $h''(s) > 0$) there, and hence there can be at most two points where g and h intersect such that $W(s) = 0$ (see Fig. 3.1(a)).

(c) Since $h'(s) = -[f(s) + (1-s)f'(s)]/f^2(s)$, h is decreasing on $(\lambda, 1 - \delta)$. Denote the numerator in (3.8) by $k(s)$. Since $k'(s) = 3(1-s)f'(s)f''(s) + 3f(s)f''(s) - (1-s)f'''(s)f(s) \geq 0$ for $\lambda < s < \tilde{s}$, $k(s)$ is increasing for $\lambda < s < \tilde{s}$ and is positive for $\tilde{s} < s < 1 - \delta$. Therefore h can change concavity at most once in $(\lambda, 1 - \delta)$ (from concave to convex), and remains strictly convex on the entire interval $(\lambda, 1 - \delta)$ if $k(\lambda) \geq 0$. Thus there can be at most two points where h and g intersect such that $W(s) = 0$ (see Fig. 3.1(b)).

(d) follows from (a) and Theorem 3.4(d).

Remark 3.6 Most realistic monotone response functions (e.g. Michaelis–Menten or sigmoidal of the form (3.5b)) satisfy the hypotheses in either (b) or (c) of the above corollary. However, we have not ruled out the possibility that for some monotone response functions there might be more than two interior equilibrium points (see Fig. 3.2(d)).

Example 3.7 If $f(s) = ms/(a + s)$, i.e. $f(s)$ is a Michaelis–Menten response function, with $m > 1$ and $a > 0$, then $\lambda = a/(m - 1) > 0$, and if in addition to $\lambda + \delta < 1$,

- (i) $\delta > \delta_0$, there is no interior equilibrium;
- (ii) $\delta < \delta_0$, there are exactly two interior equilibria:

$$E_1 = (c_1, \delta, 1 - \delta - c_1) \quad \text{and} \quad E_2 = (c_2, \delta, 1 - \delta - c_2),$$

where $\delta_0 = (1 - \sqrt{\lambda})^2 a/m\lambda$, $c_1 = \frac{1}{2}[-\beta + (\beta^2 - 4\lambda)^{1/2}]$, $c_2 = \frac{1}{2}[-\beta - (\beta^2 - 4\lambda)^{1/2}]$, and $\beta = -1 - \lambda + m\lambda\delta/a$. The number of equilibrium points follows from Corollary 3.5(b) noting that f is concave. The actual components of E_1 and E_2 are found by setting $W(s) = 0$ and solving the resulting quadratic equation $s^2 + \beta s + \lambda = 0$. In the unlikely case of $\delta = \delta_0$, there is exactly one interior equilibrium $E_1 = (\sqrt{\lambda}, \delta, 1 - \delta - \sqrt{\lambda})$.

Example 3.8 If $f(s) = ms^2/(s^2 + Ks + L)$, $m > 1$, K and L are nonnegative, then $\lambda > 0$ is finite and $f(s)$ is S-shaped on $(0, \infty)$. If the point of inflection $\tilde{s} \leq \lambda$, it is easy to see that the hypotheses of Corollary 3.5(b) are satisfied. If $\tilde{s} > \lambda$, first note that

$$f'''(s) = \frac{6m(Ks^4 + 4Ls^3 - 4L^2s - L^2K)}{(s^2 + Ks + L)^4}.$$

Since $f''(\tilde{s}) = 0$, $f''(s) > 0$ if $s < \tilde{s}$, and $f''(s) < 0$ if $s > \tilde{s}$, it follows that $f'''(\tilde{s}) < 0$. Denote the numerator of $f'''(s)$ by $n(s)$. Note that $n'(s) = 6m(4Ks^3 + 12Ls^2 - 4L^2)$ and $n''(s) = 6m(12Ks^2 + 24Ls) > 0$, therefore $n'(s)$ is increasing. As $n'(0) < 0$, $n(s)$ initially decreases and then increases. Since $n(0) < 0$ and $n(\tilde{s}) < 0$, it follows that $n(s) < 0$ and hence $f'''(s) < 0$ for all $\lambda < s < \tilde{s}$. This shows that the hypotheses of Corollary 3.5(c) are satisfied in this case. In every case then, for dynamics of this form, there are at most two interior equilibrium points.

A more direct method of observing that there are at most two interior equilibria is to note that $h''(s) = (2Ks + 6L - 2sL)/ms^4$. Clearly $h''(s) > 0$ for $s \in (0, 3)$ and so $h(s)$ is strictly convex for $s \in (\lambda, 1 - \delta)$. Thus there can be at most two points at which $W(s) = 0$.

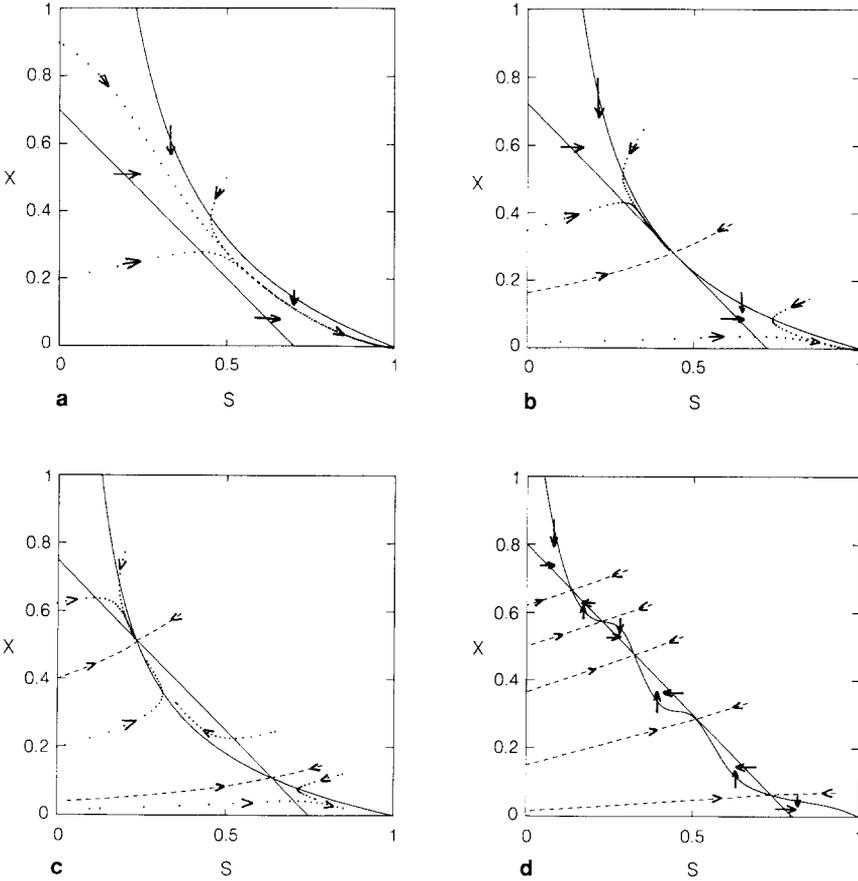


Fig. 3.2. Phase plane analysis of (3.9) for different intersections of $g(s)$ and $h(s)$. —: isoclines $g(s)$ and $h(s)$, - - -: the stable manifold of each equilibrium transverse to the line $g(s)$, \cdots : sample trajectories. **a** $g(s)$ and $h(s)$ do not intersect, E_0 is the global attractor. **b** $g(s)$ and $h(s)$ intersect exactly once. The stable manifold of E_1 forms the separatrix. All trajectories above the separatrix converge to E_1 , and those below converge to E_0 . **c** $g(s)$ and $h(s)$ intersect twice, E_0 and E_2 are locally asymptotically stable and E_1 is a saddle. The stable manifold of E_1 forms the separatrix. All trajectories above (below) the separatrix converge to E_2 (E_0). **d** $g(s)$ and $h(s)$ intersect many times at $E_i = (\bar{s}_i, \bar{x}_i)$. Local stability of each equilibrium point is given by (3.10). The stable manifold of the saddle points and of the semi-stable equilibria partition the space

The interior equilibria, when they exist, are denoted by $E_j = (c_j, \delta, 1 - \delta - c_j)$, where $W(c_j) = V(c_j) = 0$ (by (3.6)), $1 \leq j \leq n$. The ordering of the E_j 's is such that $c_j > c_{j+1}$, $1 \leq j \leq n - 1$. Note that the number of interior equilibria, n , is generically even.

We continue to study model (3.1) under the assumption that $\lambda < 1 - \delta$ by means of a phase plane analysis. By (3.2) and (3.3), we can analyze the flow of (3.1) restricted to the two-dimensional set Γ :

$$\begin{aligned} s' &= 1 - s - xf(s), \\ x' &= -x + xq(1 - s - x). \end{aligned} \tag{3.9}$$

If $E = (\bar{s}, \bar{p}, \bar{x})$ is an equilibrium of (3.1), then $E = (\bar{s}, \bar{x})$ denotes an equilibrium of (3.9) with $\bar{s} + \bar{x} = 1 - \delta$. From the phase portrait of (3.9) (see Fig. 3.2), it can be seen that if

- (i) $h'(\bar{s}) < -1$, E is an asymptotically stable node,
 - (ii) $h'(\bar{s}) > -1$, E is an unstable saddle point,
- (3.10)

where $h(s)$ is given in (3.7). (The eigenvalues of the variational matrix of (3.9) at any equilibrium are real and for case (i) are both negative, while for case (ii) they are of opposite sign.) E_0 is always an asymptotically stable node. The one-dimensional stable manifold of each of the unstable critical points form the separatrices. All solutions converge to one of the asymptotically stable equilibrium points. (E is semi-stable for the nongeneric case of $h'(\bar{s}) = -1$.)

From this analysis of (3.9) we can see that the indirect nutrient-biomass conversion modeled in (2.1) gives rise to growth dynamics very different from that in [2, 8]. In particular, the initial concentration of the species is an important factor for survival in the chemostat. Since E_0 is always asymptotically stable, even when there exists an asymptotically stable interior equilibrium, washout is possible if the initial concentration of the species is too low. This might be an alternative explanation for the washout observed occasionally in experiments and usually assumed to be due to a problem with the equipment.

Another feature of model (3.1) is that the nutrient "uptake" rate is not directly correlated with the growth rate of the species. This is illustrated in Fig. 3.3 where $s(1) > s(0)$, while $x(t)$ increases at $t = 0$ but decreases at $t = 1$. Thus the species concentration can be decreasing at a nutrient concentration which is higher than a level at which it is increasing.

If $\delta \rightarrow 0$, the equilibrium concentration of $p \rightarrow 0$ for all possible equilibria. Since

$$(x + p)' = -(x + p) + \bar{x}f(s),$$

if $\delta \rightarrow 0$, one would expect the dynamics of (3.1) to eventually approach that of the system

$$\begin{aligned} s' &= 1 - s - xf(s), \\ p' &= 0, \\ x' &= -x + xf(s), \\ s(0) &\geq 0, \quad p(0) = 0, \quad x(0) > 0, \end{aligned}$$

which is basically the system studied in [2]. Recall that for that system, when $f(s)$ is monotone increasing and $\lambda < 1$, the washout equilibrium is always unstable and the interior equilibrium $(\lambda, 1 - \lambda)$ is globally attracting. Indeed, if $\delta \rightarrow 0$ in (3.6), either $\bar{x} = 0$ or $\bar{x} = 1 - \lambda$, so $E_1 \rightarrow E_0$ as $\delta \rightarrow 0$, and all trajectories of (3.9) converge to E_2 . (See Fig. 3.1.) Note that there is a change of stability of E_0 at $\delta = 0$. We can therefore regard δ as an indicator of the "significance" of the delay caused by the indirect nutrient uptake process. Specifically, for small enough δ , a low initial concentration of the species is a less detrimental factor, and in the limiting case as $\delta \rightarrow 0$, the species survives as long as $\lambda < 1$.

The parameter δ is also related to the growth rate of the species upon consumption of the intermediate product. A small δ means a relatively small concentration of the intermediate product is sufficient for the species to break

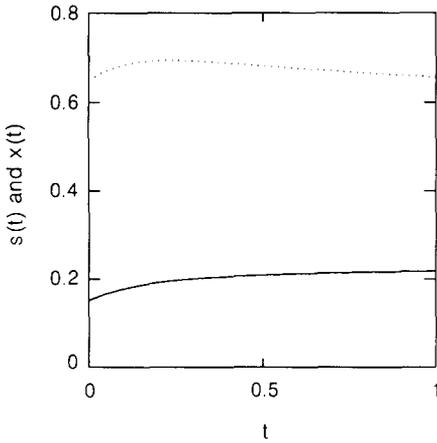


Fig. 3.3. Time evolution of (3.1) illustrating that $s(t)$ and $x(t)$ are not directly correlated.

—: $s(t)$, \cdots : $x(t)$; $f(s) = 9s^2/(s^2 + s + 0.1)$,

$q(p) = 85p^2/(9p^2 + 7.2p + 0.63)$, $\lambda = 0.1906$,

$\delta = 0.15$, $s(0) = 0.15$, $p(0) = 0.25$, $x(0) = 0.65$.

Note that $s(1) > s(0)$, while $x(t)$ is increasing at $t = 0$ but decreasing at $t = 1$

even, whereas a large δ means a much higher concentration of the intermediate product is necessary in order for the species to break even. From this perspective the above analysis has the following biological interpretation. If δ is not negligible and the initial concentration of the species is low, then the conversion of the nutrient to the intermediate product proceeds at a low rate also. This could result in the concentration of the intermediate product decreasing for a long period of time. Consequently growth of the species by consumption of the intermediate product is not fast enough to replenish loss of population by washout.

On the other hand, the fact that the nutrient is only indirectly utilized makes it more difficult for the species to survive in the chemostat. This is more apparent when $f(s)$ is given by Michaelis–Menten kinetics as in Example 3.7, where $\delta < \delta_0(\lambda)$, or

$$m > m_0(\delta) = \left(\frac{\sqrt{a\delta} + \sqrt{1 - \delta + a}}{1 - \delta} \right)^2$$

is a necessary condition for the species to survive in the chemostat. If no intermediate product is involved, i.e., $\delta = 0$, then $\lambda < 1$, or $m > m_0(0) = a + 1$, is sufficient to prevent washout. Since $m_0(\delta)$ is increasing for $0 < \delta < 1$, the range of m (with a fixed) for which the species can survive decreases as δ increases.

4 Competition – same intermediate product

We consider in this section the mode of competition between two species in the chemostat when both species are of type II and the extracellular enzymes they produce transform the nutrient to the same intermediate product. The model equations with the same assumptions as in Sects. 2 and 3 are:

$$\begin{aligned} s' &= 1 - s - \frac{1}{\gamma_1} x_1 f_1(s) - \frac{1}{\gamma_2} x_2 f_2(s), \\ p' &= -p + x_1 f_1(s) + x_2 f_2(s) - x_1 q_1(p) - x_2 q_2(p), \\ x_1' &= -x_1 + x_1 q_1(p), \\ x_2' &= -x_2 + x_2 q_2(p), \\ s(0) &\geq 0, \quad p(0) \geq 0, \quad x_1(0) > 0, \quad x_2(0) > 0, \end{aligned} \tag{4.1}$$

where the scaled quantities are obtained as in Sect. 3, except here $p = P/S^0$, $x_i = X/\eta_i S^0$, $i = 1, 2$. The subscripted quantities satisfy all the analogous properties of the corresponding quantities in the previous section. In particular, $f_i(\lambda_i) = 1$ and $q_i(\delta_i) = 1$, $i = 1, 2$. Note that since the intermediate product transformed from the nutrient by the extracellular enzymes secreted by one species can be consumed by the other species, the interaction between the two species in this case is actually a combination of competition and cooperation.

It is easily seen that the nonnegative cone \mathbb{R}_+^4 is positively invariant under the solution map of (4.1). Boundedness of the solution can be shown by the following argument. Let $\bar{\gamma} = \max(\gamma_1, \gamma_2)$, then $s' \leq 1 - s - x_1 f_1(s)/\bar{\gamma} - x_2 f_2(s)/\bar{\gamma}$. Denote $\bar{\gamma}s + p + x_1 + x_2$ by u . Since $u' \leq \bar{\gamma} - u$, $s(t)$, $p(t)$, $x_1(t)$ and $x_2(t)$ remain bounded for all $t \geq 0$.

It is quite obvious from the equations in (4.1) that no coexistence equilibrium exists except for the nongeneric case of $\delta_1 = \delta_2$. The set of equilibrium points of (4.1) are therefore quite simple in general. It includes $E_0 = (1, 0, 0, 0)$, corresponding to the washout of both species, $E_{1j} = (c_{1j}, \delta_1, 1 - \delta_1 - c_{1j}, 0)$, $1 \leq j \leq n_1$, corresponding to only the x_1 -species survives, and $E_{2k} = (c_{2k}, \delta_2, 0, 1 - \delta_2 - c_{2k})$, $1 \leq k \leq n_2$, corresponding to only the x_2 -species survives. Conditions for the existence of $E_{i\zeta}$, $i = 1, 2$, $1 \leq \zeta \leq n_i$, are given in Theorem 3.4. Note that $c_{i\zeta}$ is the nutrient concentration of the corresponding equilibrium, i.e., $W_i(c_{i\zeta}) = V_i(c_{i\zeta}) = 0$, where W_i and V_i are as given in (3.7).

The variational matrix of (4.1) at any equilibrium point is

$$J = \begin{bmatrix} -1 - u_1/\gamma_1 - u_2/\gamma_2 & 0 & -f_1/\gamma_1 & -f_2/\gamma_2 \\ u_1 + u_2 & -1 - v_1 - v_2 & f_1 - q_1 & f_2 - q_2 \\ 0 & v_1 & -1 + q_1 & 0 \\ 0 & v_2 & 0 & -1 + q_2 \end{bmatrix}$$

where

$$\begin{aligned} f_i &= f_i(s), & q_i &= q_i(p) \\ u_i &= x_i f'_i(s), & v_i &= x_i q'_i(p), \\ & & i &= 1, 2. \end{aligned} \tag{4.2}$$

The stability of all the equilibria, if they exist, is summarized in the next theorem.

Theorem 4.1 *Suppose without loss of generality $\delta_1 < \delta_2$, and all equilibria of (4.2) are hyperbolic.*

- (a) E_0 is always an asymptotically stable node.
- (b) E_{1j} , $1 \leq j \leq n_1$, if they exist, are stable in the x_2 -direction. Each E_{1j} is an asymptotically stable node if $h'_1(c_{1j}) < 1$, and a saddle point if $h'_1(c_{1j}) > -1$, where $h_1(s) = 1 - s/f(s)$.
- (c) E_{2k} , $1 \leq k \leq n_2$, if they exist, are unstable in the x_1 -direction and therefore are saddle points.

Proof. (a) At E_0 , $u_i = v_i = 0$, and all eigenvalues of J are -1 .

(b) If E_{1j} , $1 \leq j \leq n_1$, exist, $q_1 = q_1(\delta_1) = 0$ and $q_2 = q_2(\delta_1) < 1$, so each E_{1j} is stable in the x_2 -direction. Stability of each E_{1j} is given by (3.10).

(c) If E_{2k} , $1 \leq k \leq n_2$, exist, $q_1 > 1$ and $q_2 = 0$, so each E_{2k} is unstable in the x_1 -direction.

Note that the stability of each one-species equilibrium is determined independently of whether or not the other species can survive in the chemostat without competition.

Numerical studies of (4.1), with both f_i and q_i , $i = 1, 2$, being Michaelis–Menten terms ($n_1 = n_2 = 2$) suggest that all trajectories converge to some equilibrium. If the initial concentration of any species is small, then that species will be washed out of the chemostat. If only one of the two species, say x_1 , can survive in the absence of competition, then provided that the initial concentration is high enough, the solution will approach E_{12} if $\delta_1 < \delta_2$, and will approach E_0 if $\delta_1 > \delta_2$. Apparently the x_2 -species, which cannot survive even in the absence of competition, is always washed out from the chemostat eventually. This suggests that if a species cannot survive in the chemostat without competition, it will also be unable to survive when the competitor is present. This observation is not obvious from the model equations, since the intermediate product is also transformed from the nutrient by the competing species. If there are equilibrium points of the form E_{1j} and E_{2k} , then it seems that the species with the lower δ value will be the sole survivor in the chemostat, provided that its initial concentration is high enough.

A significant feature in this mode of competition is the possibility of a “kamikaze” effect observed in numerical simulation. A species with both δ and λ satisfying any one of the conditions in Theorem 3.4, and an initial concentration high enough so that it can live indefinitely in the chemostat by itself, can be eventually washed out from the chemostat when a small amount of another species, which produces and consumes the same intermediate product but with a lower δ value, is introduced into the chemostat. This is the case even if this other species has a λ value which does not allow the species to survive by itself in the chemostat. (See Fig. 4.1.)

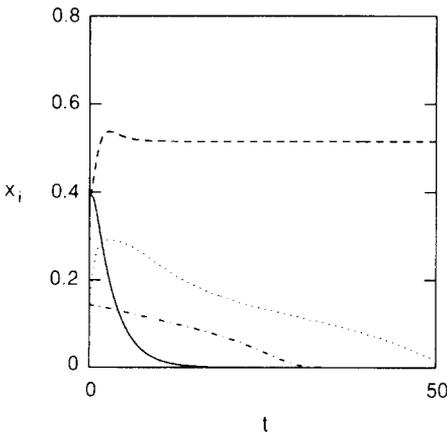


Fig. 4.1. Outcome of competition in model (4.2) illustrating the “kamikaze” effect.
 $f_1(s) = 3.5s/(2.5\lambda_1 + s)$, $q_1(p) = 2p/(\delta_1 + p)$,
 $f_2(s) = 10s/(9\lambda_2 + s)$, $q_2(p) = 16p/(15\lambda_2 + p)$,
 $\lambda_1 = 0.4$, $\delta_1 = 0.04$, $\lambda_2 = 0.75$, $\delta_2 = 0.02$,
 $s(0) = 0.875$, $p(0) = 0.01$, $x_1(0) = 0.4$,
 $x_2(0) = 0.15$. —: $x_1(t)$ when x_2 is present,
 - - - : $x_1(t)$ when x_2 is absent, · · · : $x_2(t)$
 when x_1 is present, - · - · : $x_2(t)$ when x_1 is absent. Note that x_2 dies out more slowly when x_1 is present than when x_1 is absent – there is initially more intermediate product when x_1 is present

5 Competition – distinct intermediate product

The equations describing competition between two species when the nutrient is converted to two different intermediate products each of which cannot be

assimilated by the competitor are:

$$\begin{aligned}
 s' &= 1 - s - x_1 f_1(s) - x_2 f_2(s) \\
 p_1' &= -p_1 + x_1 f_1(s) - x_1 q_1(p_1) \\
 x_1' &= -x_1 + x_1 q_1(p_1) \\
 p_2' &= -p_2 + x_2 f_2(s) - x_2 q_2(p_2) \\
 x_2' &= -x_2 + x_2 q_2(p_2) \\
 s(0) &\geq 0, \quad p_i(0) \geq 0, \quad x_i(0) > 0, \quad i = 1, 2.
 \end{aligned} \tag{5.1}$$

The parameters λ_i and δ_i , $i = 1, 2$, are defined as before. Also it can be shown that the four-dimensional set $\Delta \subset \mathbb{R}_+^4$ satisfying

$$\Delta = \{(s, p_1, x_1, p_2, x_2) \in \mathbb{R}_+^5 \mid s + p_1 + x_1 + p_2 + x_2 = 1\}$$

is positively invariant under the solution map of (5.1) and contains the omega limit set of all trajectories. We therefore consider the flow of (5.1) restricted to Δ :

$$\begin{aligned}
 p_1' &= -p_1 + x_1 f_1(1 - p_1 - x_1 - p_2 - x_2) - x_1 q_1(p_1) \\
 x_1' &= -x_1 + x_1 q_1(p_1) \\
 p_2' &= -p_2 + x_2 f_2(1 - p_1 - x_1 - p_2 - x_2) - x_2 q_2(p_2) \\
 x_2' &= -x_2 + x_2 q_2(p_2) \\
 p_i(0) &\geq 0, \quad x_i(0) > 0, \quad i = 1, 2.
 \end{aligned} \tag{5.2}$$

In this case one can show that if a species cannot survive in the absence of the competition, it will not be able to survive when the competing species is introduced.

Theorem 5.1 *In (5.2), if there is no equilibrium of the form $(\delta_1, \bar{x}_1, 0, 0)$, where $\bar{x}_1(t) > 0$, then $p_1(t) \rightarrow 0$ and $x_1(t) \rightarrow 0$ as $t \rightarrow \infty$. A similar statement holds for the second species.*

Proof. Define $r(x_1) = -\delta_1 + x_1 f_1(1 - \delta_1 - x_1) - x_1$, which is just p_1' when $p_1 = \delta_1$ and $p_2 = x_2 = 0$. Note that $r(0) < 0$ and $r(1 - \delta_1) < 0$. Since there is no equilibrium of the form $(\delta_1, \bar{x}_1, 0, 0)$, $r(x_1) < 0$ for all $x_1 \in [0, 1 - \delta_1]$. If $p_1(t) > \delta_1$ for all $t \geq 0$, $x_1' > 0$ for all $t \geq 0$ and so $x_1(t) \rightarrow \hat{x}_1 > 0$ monotonically. But then $x_1'(t) \rightarrow 0$ and thus $p_1(t) \rightarrow \delta_1$ as $t \rightarrow \infty$, i.e. $(\delta_1, \hat{x}_1, 0, 0)$ is an equilibrium point, a contradiction. Hence there exists $\tau > 0$ such that $p_1(\tau) \leq \delta_1$. Note that if $p_1(\tau) = \delta_1$, $p_1'(\tau) \leq r(x_1) < 0$, therefore $p_1(t) < \delta_1$ and $x_1'(t) < 0$ for all $t > \tau$. In that case $x_1(t) \rightarrow \hat{x}_1 \geq 0$ monotonically and thus $x_1'(t) \rightarrow 0$ as $t \rightarrow \infty$. If $\hat{x}_1 \neq 0$, $p_1(t) \rightarrow \delta_1$ as $t \rightarrow \infty$ and we have the same contradiction that $(\delta_1, \hat{x}_1, 0, 0)$ is an equilibrium point. Thus it must be the case that $x_1(t) \rightarrow 0$ and hence $p_1(t) \rightarrow 0$ as $t \rightarrow \infty$.

Corollary 5.2 *For $i = 1, 2$, if $\lambda_i + \delta_i \geq 1$, or if $W_i(s) < 0$ for $V_i(s) < 0$ for all $s \in (\lambda_i, 1 - \delta_i)$, ($W_i(s)$ and $V_i(s)$ are as defined in (3.7)), then $p_i(t) \rightarrow 0$ and $x_i(t) \rightarrow 0$ as $t \rightarrow \infty$.*

Coexistence of the two species in the chemostat therefore is only possible when each species can survive in the absence of a competitor. We will develop criteria that guarantee the existence of coexistence equilibria. It is more convenient to carry out the analysis with (5.1) than with (5.2).

Let $\hat{E} = (\hat{s}, \hat{p}_1, \hat{x}_1, \hat{p}_2, \hat{x}_2)$ denote an equilibrium point of (5.1). If \hat{E} is a coexistence equilibrium, then

$$\hat{p}_i = \delta_i, \quad \hat{x}_i = \frac{\delta_i}{f_i(\hat{s}) - 1}, \quad i = 1, 2, \quad (5.3)$$

where $\hat{s} > \bar{\lambda} = \max(\lambda_1, \lambda_2)$, so that $\hat{x}_1 > 0$ and $\hat{x}_2 > 0$, and \hat{s} satisfies

$$\hat{s} = 1 - \sum_{i=1}^2 \frac{\delta_i f_i(\hat{s})}{f_i(\hat{s}) - 1}. \quad (5.4)$$

For $s > \bar{\lambda}$, define

$$z(s) = \sum_{i=1}^2 \frac{\delta_i f_i(s)}{f_i(s) - 1}. \quad (5.5)$$

Theorem 5.3 (a) If $\bar{\lambda} \geq 1 - \delta_1 - \delta_2$, there is no interior equilibrium of (5.1).

(b) A necessary and sufficient condition for at least one interior equilibrium to exist is that $1 - s - z(s) \geq 0$ for some $s \in (\bar{\lambda}, 1 - \delta_1 - \delta_2)$. If strict inequality holds, there exist at least two interior equilibria.

(c) If $f_i(s)$, $i = 1, 2$, satisfy $f_i''(s)(f_i(s) - 1) - 2(f_i'(s))^2 < 0$ for all $s \in (\bar{\lambda}, 1 - \delta_1 - \delta_2)$ (for example if both f_i are concave), then $z(s)$ is strictly convex for the same values of s and hence there exist at most two interior equilibria.

(d) If $\bar{\lambda} < 1$ and δ_i , $i = 1, 2$, are both sufficiently small then there exist at least two interior equilibria.

(e) A necessary condition for an interior equilibrium to exist is that $z(1 - \delta_1 - \delta_2) < 1 - \bar{\lambda}$.

Proof. (a) By (5.3), $\hat{s} < 1 - \delta_1 - \delta_2$ and $\hat{s} > \bar{\lambda}$ so that both $\hat{x}_1 > 0$ and $\hat{x}_2 > 0$.

(b) This follows from (a), (5.4) and (5.5) and the observation that $z(s)$ is continuous for $s > \bar{\lambda}$ and $z(s) \rightarrow \infty$ as $s \rightarrow \bar{\lambda}^+$.

(c) Since

$$z'(s) = \sum_{i=1}^2 \frac{-\delta_i f_i'(s)}{(f_i(s) - 1)^2} < 0,$$

$z(s)$ is a decreasing function of s . Note that

$$z''(s) = \sum_{i=1}^2 -\delta_i \left(\frac{f_i''(s)(f_i(s) - 1) - 2(f_i'(s))^2}{(f_i(s) - 1)^3} \right) > 0$$

for $s \in (\bar{\lambda}, 1 - \delta_1 - \delta_2)$ by the hypothesis, so $z(s)$ is strictly convex for s in the same interval. Thus there can be at most two intersections of the curve $z(s)$ and the line $1 - s$, and hence at most two interior equilibria.

(d) follows from (b).

(e) follows from the fact that $\bar{\lambda} < \hat{s} < 1 - \delta_1 - \delta_2$, that $z(s)$ is a decreasing function, and that the line $1 - s < 1 - \bar{\lambda}$ for all $s > \bar{\lambda}$.

In the case that the response functions $f_i(s)$, $i = 1, 2$, are Michaelis–Menten, parts (c) and (d) of the above theorem imply that if $\bar{\lambda} < 1$ and δ_i , $i = 1, 2$, are sufficiently small, there are exactly two interior equilibria of (5.1). In fact we can be more specific.

Theorem 5.4 Assume that $f_i(s) \equiv m_i s / (a_i + s)$, $m_i > 1$ and $a_i > 0$, $i = 1, 2$, and that $\lambda_1 < \lambda_2 < 1$ and $\delta_2 < (1 - \sqrt{\lambda_2})^2 a_2 / m_2 \lambda_2$ (i.e. there are exactly two equilibria of the form E_{2k} . See Example 3.7.) If $\sqrt{\lambda_2} < 1 - \delta_1 - \delta_2$, then $1 - \sqrt{\lambda_2} - \delta_2 g_2(\sqrt{\lambda_2}) > 0$. If $\delta_1 < [1 - \sqrt{\lambda_2} - \delta_2 g_2(\sqrt{\lambda_2})] / g_1(\sqrt{\lambda_2})$, where $g_i(s) = f_i(s) / (f_i(s) - 1)$, $i = 1, 2$, then there exist exactly two solutions s_1^* and s_2^* of (5.4).

Proof. Define $F(s) = z(s) - (1 - s) = \delta_1 g_1(s) + \delta_2 g_2(s) - (1 - s)$. By (5.4), if $(s^*, p_1^*, x_1^*, p_2^*, x_2^*)$ is an interior equilibrium, $F(s^*) = 0$ and $\lambda_2 < s^* < 1 - \delta_1 - \delta_2$. Since $\lambda_2 < 1$, $\lambda_2 < \sqrt{\lambda_2} < 1 - \delta_1 - \delta_2$, and $(1 - \sqrt{\lambda_2})/g_2(\sqrt{\lambda_2}) = (1 - \sqrt{\lambda_2})^2 a_2/m_2 \lambda_2 > \delta_2$, so that $\delta_2 g_2(\sqrt{\lambda_2}) < 1 - \sqrt{\lambda_2}$. If $\delta_1 < [1 - \sqrt{\lambda_2} - \delta_2 g_2(\sqrt{\lambda_2})]/g_1(\sqrt{\lambda_2})$, $F(\sqrt{\lambda_2}) < 0$. Since $F(s) \rightarrow \infty$ as $s \rightarrow \lambda_2^+$ and $F(1 - \delta_1 - \delta_2) > 0$, there must be at least two values of s , s_1^* and s_2^* , such that $F(s_1^*) = F(s_2^*) = 0$. Lastly, $F''(s) > 0$ for $s > \lambda_2$, hence $F(s)$ is convex and there must be exactly two interior equilibria.

Next we determine the stability of the equilibrium points of (5.2): $E_0 = (0, 0, 0, 0)$, $E_{1j} = (\delta_1, 1 - \delta_1 - c_{1j}, 0, 0)$, $1 \leq j \leq n_1$, $E_{2k} = (0, 0, \delta_2, 1 - \delta_2 - c_{2k})$, $1 \leq k \leq n_2$, $i = 1, 2$. There is also, as we have seen, the potential for coexistence equilibria E^* .

The variational matrix of (5.2) is

$$J = \begin{pmatrix} J_1 & M_1 \\ M_2 & J_2 \end{pmatrix},$$

where J_i and M_i , $i = 1, 2$, are 2×2 matrices. J_i has the form

$$J_i = \begin{pmatrix} -1 - u_i - v_i & -u_i + f_i - q_i \\ v_i & -1 + q_i \end{pmatrix}$$

and M_i has the form

$$M_i = \begin{pmatrix} -u_i & -u_i \\ 0 & 0 \end{pmatrix},$$

where u_i and v_i are as defined in (4.2), except here $s = 1 - p_1 - x_1 - p_2 - x_2$ and $q_i = q_i(p_i)$, $i = 1, 2$.

It is easily seen that the local stability of E_0 and of E_{ij} is determined by the eigenvalues of J_1 and J_2 , and the stability of each E_{ij} is the same as the stability of the corresponding one-species equilibrium of (3.1). The next theorem summarizes local stability of these equilibrium points.

Theorem 5.5 *Suppose all equilibria of (5.2) are hyperbolic.*

- (a) E_0 is always locally asymptotically stable.
- (b) Each E_{1j} , $1 \leq j \leq n_1$, is stable in the p_2 - and x_2 -directions, and each E_{2k} , $1 \leq k \leq n_2$, is stable in the p_1 - and x_1 -directions.
- (c) Each E_{ij} , $i = 1, 2$, $1 \leq j \leq n_i$, is asymptotically stable if $h'_i(c_{ij}) < -1$, unstable if $h'_i(c_{ij}) > -1$, where $h_i(s) = (1 - s)/f_i(s)$.

The above theorem asserts that competitive exclusion holds if the initial concentrations of the two species is in the basin of attraction of some E_{ij} for which $h'_i(s_{ij}) < -1$. Washout occurs if they are in the basin of attraction of E_0 . Therefore the outcome is initial concentration dependent.

Finally we consider the interior equilibria $E^* = (\delta_1, x_1^*, \delta_2, x_2^*)$ of (5.2). Direct substitution shows that at E^* , $q_i = 1$ and $f_i - q_i = \delta_i/x_i^*$, $i = 1, 2$. The eigenvalues of J evaluated at E^* are solutions of the equation

$$P(\mu) = P_1(\mu)P_2(\mu) + P_3(\mu) = 0 \quad (5.6)$$

where

$$\begin{aligned}
 P_1(\mu) &= \mu^2 + (1 + u_1 + v_1)\mu + v_1(1 + u_1 - f_1), \\
 P_2(\mu) &= \mu^2 + (1 + u_2 + v_2)\mu + v_2(1 + u_2 - f_2), \\
 P_3(\mu) &= -u_1u_2(v_1 + \mu)(v_2 + \mu).
 \end{aligned}$$

Theorem 5.6 *All solutions of (5.6) are real, at least two of them are negative and at least one of them is positive. Thus any coexistence equilibrium of (5.2), if it exists, must be unstable.*

The theorem is obtained by estimating the roots of $P(\mu)$ relative to the roots of $P_1(\mu)$ and $P_2(\mu)$. We first prove several lemmas concerning the polynomials $P_1(\mu)$ and $P_2(\mu)$.

Since $P_i(\mu) \rightarrow \infty$ as $\mu \rightarrow \pm \infty$ and $P_i(-v_i) = -v_i f_i$, $i = 1, 2$, it is clear that the roots of $P_i(\mu)$ are real and that at least one of them is negative. Denote the roots by r_i and R_i where $r_i < R_i$.

Lemma 5.7 $r_i < -v_i < \min(0, R_i)$, $i = 1, 2$.

Lemma 5.8 *If $1 + u_i - f_i < 0$, then $P_i(0) < 0$ and therefore $R_i > 0$, $i = 1, 2$.*

Lemma 5.9 *Assume that $-v_2 < -v_1$. Then there exists μ such that $-v_2 \leq \mu \leq -v_1$ and $P_1(\mu)P_2(\mu) > 0$. The result is also true if the subscripts are interchanged.*

Proof. First assume that $R_2 < R_1$. There are three different orderings of the roots: (i) $r_2 < r_1 < R_2 < R_1$; (ii) $r_2 < R_2 < r_1 < R_1$; (iii) $r_1 < r_2 < R_2 < R_1$. In case (i), $P_i(\mu) < 0$, $i = 1, 2$, if $r_1 < \mu < R_2$. Therefore it suffices to show that $[-v_2, -v_1] \cap (r_1, R_2) \neq \emptyset$. This must be the case, otherwise either $-v_1 \leq r_1$ or $R_2 \leq -v_2$, contradicting Lemma 5.10. In case (ii), $P_i(\mu) > 0$, $i = 1, 2$, for $R_2 < \mu < r_1$ and $(R_2, r_1) \subset [-v_2, -v_1]$. In case (iii), $P_2(-v_2) < 0$ and $P_1(-v_2) < 0$ since $r_1 < -v_2 < R_1$. In all of the three cases, there exists μ such that $-v_2 \leq \mu \leq -v_1$ and $P_1(\mu)$ and $P_2(\mu)$ are of the same sign.

If $R_1 < R_2$, then there are only two possible orderings of the roots: (i) $r_1 < r_2 < R_1 < R_2$ and (ii) $r_2 < r_1 < R_1 < R_2$. (The ordering $r_1 < R_1 < r_2 < R_2$ is not possible by Lemma 5.7.) Case (i) is similar to (i) above, and case (ii) is similar to case (iii) above.

The proof is similar if the subscripts are interchanged.

Lemma 5.10 *There exist γ_i , $i = 1, 2, 3$, such that $\gamma_1 < \gamma_2 < 0 < \gamma_3$, and $P(\gamma_1) < 0$, $P(\gamma_2) > 0$ and $P(\gamma_3) < 0$.*

Proof. Let $\gamma_1 = \min(r_1, r_2) < 0$. Then $P_1(\gamma_1)P_2(\gamma_1) = 0$ and $P_3(\gamma_1) < 0$ since $\gamma_1 < \min(-v_1, -v_2)$ by Lemma 5.7. Hence $P(\gamma_1) = P_3(\gamma_1) < 0$. Let γ_2 be the value of μ in Lemma 5.9. Then $P_1(\gamma_2)P_2(\gamma_2) > 0$, $P_3(\gamma_2) > 0$ and hence $P(\gamma_2) > 0$. Lastly, if $1 + u_i - f_i < 0$, $i = 1$ or 2 , Lemma 5.8 asserts that there exists $\gamma_3 = \max(R_1, R_2) > 0$ such that $P_1(\gamma_3)P_2(\gamma_3) = 0$. Therefore $P(\gamma_3) = P_3(\gamma_3) < 0$. If $1 + u_i - f_i \geq 0$, $i = 1, 2$, then since $f_i - 1 = \delta_i/x_i^* > 0$, $P(0) = -v_1v_2[(1 + u_2 - f_2)(f_1 - 1) + u_1(f_2 - 1)] < 0$. So there must exist $\gamma_3 > 0$ such that $P(\gamma_3) < 0$.

Proof of Theorem 5.6 Since $P(\mu) \rightarrow \infty$ as $\mu \rightarrow \pm \infty$, by the Intermediate Value Theorem there exists $\mu_1 < \gamma_1 < 0$ and $\mu_4 > \gamma_3 > 0$ such that $P(\mu_1) = P(\mu_4) = 0$. Similarly, there exist μ_2 and μ_3 , $\gamma_1 < \mu_2 < \gamma_2 < \mu_3 < \gamma_3$, such that $P(\mu_2) = P(\mu_3) = 0$. Hence all solutions of (5.6) are real, and at least one of them, μ_4 , is positive, and at least two of them, μ_1 and μ_2 , are negative.

In all of our numerical simulations, the solution of (5.2) approaches one of the stable equilibrium points on the boundary of the state space. We conjecture that the solution of (5.2) approaches a stable equilibrium on the boundary.

Finally we consider how the dynamics exhibited in this competition model is related to that in the standard model in [2, 8]. Assume that $\lambda_1 < \lambda_2 < 1$, and δ_1 and δ_2 are sufficiently small so there are at least two interior equilibrium points by Theorem 5.3(d). To simplify our discussion, assume that there are exactly two, E_1^* and E_2^* , and let $s_1^* > s_2^*$, where s_i^* , $i = 1, 2$, denotes the corresponding equilibrium concentration of the nutrient. Also by Corollary 3.5(d), if δ_i is sufficiently small, there are at least two equilibria at which species i is present and species j is absent, $i, j = 1, 2, i \neq j$. Again assume that there are exactly two, E_{i1} and E_{i2} , $i = 1, 2$. (See Fig. 5.1(a).)

If $\delta_1 > 0$ is fixed (small) and $\delta_2 \rightarrow 0$, the model (5.1) approaches a model of competition of mode (c) in which x_2 is of type I. (This will be further discussed in the next section.) In that case $E_1^* \rightarrow E_{11}$ and $E_{21} \rightarrow E_0$ (see Fig. 5.1(b)). If $\delta_1 \rightarrow 0$ as well, $E_{11} \rightarrow E_0$ and $E_2^* \rightarrow E_{22}$ (see Fig. 5.1(d)) and one gets the standard chemostat model as in [2, 8] in which E_{12} is the global attractor.

On the other hand if we fix δ_2 (small) and allow $\delta_1 \rightarrow 0$, then $E_1^* \rightarrow E_{21}$, $E_2^* \rightarrow E_{22}$ and $E_{11} \rightarrow E_0$, and there is no interior equilibrium (see Fig. 5.1(c)).

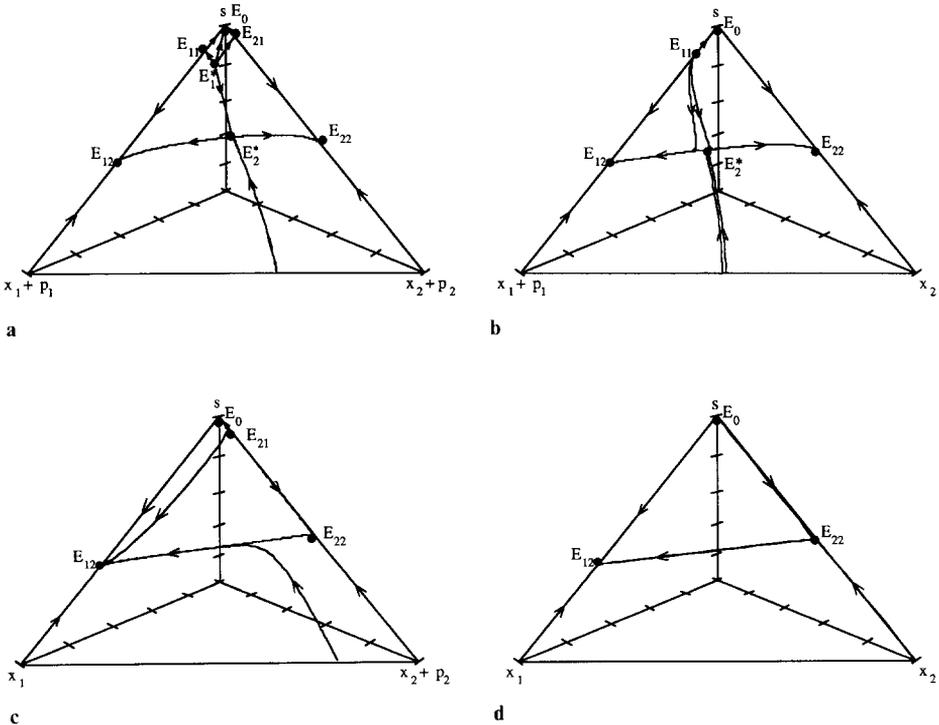


Fig. 5.1. Change of the phase portrait of (5.1) restricted to the simplex Δ when $\delta_1 \rightarrow 0$ and/or $\delta_2 \rightarrow 0$, with $f_1(s) = 3.5s/(2.5\lambda_1 + s)$, $\lambda_1 = 0.4$, $f_2(s) = 10s/(9\lambda_2 + s)$, $\lambda_2 = 0.5 > \lambda_1$. **a** $q_1(p_1) = 2p_1/(\delta_1 + p_1)$, $\delta_1 = 0.04$, $q_2(p_2) = 16p_2/(15\delta_2 + p_2)$, $\delta_2 = 0.02$. The outcome is initial condition dependent. **b** $\delta_2 \rightarrow 0$, x_2 is type I, the outcome is still initial condition dependent. **c** $\delta_1 \rightarrow 0$, x_1 is type I, E_{12} is the global attractor. **d** $\delta_1 \rightarrow 0$ and $\delta_2 \rightarrow 0$, both x_1 and x_2 are type I, E_{12} is the global attractor

$\delta_1 \rightarrow 0$ as well, then $E_{21} \rightarrow E_0$, and we again obtain the standard model represented in Fig. 5.1(d).

In both of the above cases, as δ_i , $i = 1, 2$, decreases the basin of attraction of E_{i2} increases. Thus the species has a better chance of survival if it has a lower break-even concentration.

6. Competition – one species is of type I

Finally we consider the case when one of the competing species, x_2 say, is of type I and can directly assimilate the nutrient supply:

$$\begin{aligned} s' &= 1 - s - x_1 f_1(s) - x_2 f_2(s) \\ p_1' &= -p_1 + x_1 f_1(s) - x_1 q_1(p_1) \\ x_1' &= -x_1 + x_1 q_1(p_1) \\ x_2' &= -x_2 + x_2 f_2(s) \end{aligned} \tag{6.1}$$

$$s(0) \geq 0, \quad p_1(0) \geq 0, \quad x_i(0) > 0, \quad i = 1, 2.$$

As mentioned in the last section, model (6.1) can be considered as the limiting case of (5.1) when $\delta_2 \rightarrow 0$. See Fig. 5.1(b).

The solution of (6.1) remains bounded in the nonnegative cone of \mathbb{R}^4 . Similar to previous sections, since $s + p_1 + x_1 + x_2 \rightarrow 1$ as $t \rightarrow \infty$, we can study the following system instead of (6.1):

$$\begin{aligned} p_1' &= -p_1 + x_1 f_1(1 - p_1 - x_1 - x_2) - x_1 q_1(p_1) \\ x_1' &= -x_1 + x_1 q_1(p_1) \\ x_2' &= -x_2 + x_2 f_2(1 - p_1 - x_1 - x_2) \\ p_1(0) &\geq 0, \quad x_i(0) > 0, \quad i = 1, 2. \end{aligned} \tag{6.2}$$

This system has the following boundary equilibria: $E_0 = (0, 0, 0)$, $E_{1j} = (\delta_1, 1 - \delta_1 - c_{1j}, 0)$, $1 \leq j \leq n_1$, and $E_2 = (0, 0, 1 - \lambda_2)$. E_2 exists if and only if $\lambda_2 < 1$, and the criteria for the existence of E_{1j} are given in Theorem 3.4. Using a proof similar to the one for Theorem 5.1 as well as in [2, Theorem 3.2], it can be shown that a necessary condition for the two species to coexist is that each species can survive in the absence of the competitor:

Theorem 6.1 (a) *If there is no equilibrium of the form $(\delta_1, \bar{x}_1, 0)$, where $\bar{x}_1 > 0$, then $p_1(t) \rightarrow 0$ and $x_1(t) \rightarrow 0$ as $t \rightarrow \infty$.*

(b) *If $\lambda_2 \geq 1$, $x_2(t) \rightarrow 0$ as $t \rightarrow \infty$.*

Henceforth we assume that there are boundary equilibria of the form E_{1j} and E_2 . We first determine the conditions under which there are coexistence equilibria of (6.2). Recall from Sect. 3 that n_1 is in general even and $c_{1j} > c_{1,j+1}$, $1 \leq j \leq n_1 - 1$.

Theorem 6.2 *Suppose E_{1j} , $1 \leq j \leq n_1$, where n_1 is even, and E_2 exist. Then (6.2) has a coexistence equilibrium if and only if $\lambda_2 \in (c_{1,2j}, c_{1,2j-1})$ for some j , $1 \leq j \leq n_1/2$. The coexistence equilibrium, if it exists, must be unique.*

Proof. Direct calculation shows that the interior equilibrium (δ_1, x_1^*, x_2^*) , if it exists, must be unique with $x_1^* = \delta_1 / (f_1(\lambda_2) - 1)$ and $x_2^* = 1 - \lambda_2 - \delta_1 - x_1^*$. Note that $0 < x_1^* < \infty$ if and only if $\lambda_1 < \lambda_2$, and $x_2^* > 0$ only if $\lambda_2 < 1 - \delta_1$. Moreover,

$x_2^* > 0$ if and only if $1 - \lambda_2 - \delta_1 - \delta_1/(f_1(\lambda_2) - 1) > 0$, i.e., $V_1(\lambda_2) > 0$, where V_1 is as defined in (3.7). The necessary and sufficient condition on λ_2 for the existence of E^* follows from the fact that for $s \in (\lambda_1, 1 - \delta_1)$, $V_1(s) > 0$ if and only if $s \in (c_{1,2j}, c_{1,2j-1})$ for some j , $1 \leq j \leq n_1/2$.

The variational matrix of (6.2) at any equilibrium is of the form

$$J = \begin{pmatrix} -1 - u_1 - v_1 & f_1 - u_1 - q_1 & -u_1 \\ v_1 & -1 + q_1 & 0 \\ -u_2 & -u_2 & -1 + f_2 - u_2 \end{pmatrix}$$

where u_1 and v_1 are as defined in (4.3) with p replaced by p_1 . Local stability of the boundary equilibria is summarized in the next theorem.

Theorem 6.3 *Suppose all equilibria of (6.2) are hyperbolic.*

- (a) E_0 is a saddle point.
- (b) E_{1j} , $1 \leq j \leq n_1$, is stable in the x_2 -direction if $f_2(c_{1j}) < 1$, and is unstable if $f_2(c_{1j}) > 1$.
- (c) E_2 is always an asymptotically stable node.

Corollary 6.4 *Suppose all equilibria of (6.2) are hyperbolic. Then $\lambda_2 \neq c_{1j}$, $1 \leq j \leq n_1$, and*

- (a) if $\lambda_2 < c_{1n_1}$, E_{1j} is a saddle point for all $1 \leq j \leq n_1$.
- (b) If $\lambda_2 > c_{11}$, each E_{1j} , $1 \leq j \leq n_1$, is either an asymptotically stable node or a saddle point as determined by (3.10).
- (c) if $\lambda_2 \in (c_{1n_1}, c_{11})$, there exists β , $1 \leq \beta \leq n_1 - 1$, such that $c_{1\beta} < \lambda_2 < c_{1,\beta+1}$. Then E_{1j} is a saddle point if $j > \beta$, and is either an asymptotically stable node or a saddle point, as determined by (3.10), if $1 \leq j \leq \beta$.

It is interesting to note that in cases (b) and (c) of the above corollary, the x_2 -species, even though it has the more efficient mechanism to utilize the nutrient for growth (see Sect. 3), will still vanish from the chemostat if its initial concentration is not high enough.

If an interior equilibrium E^* exists, the eigenvalues of the variational matrix J at E^* are roots of the characteristic polynomial

$$P_1(\mu)(u_2 + \mu) - u_1 u_2 (v_1 + \mu),$$

where $P_1(\mu)$ is the same as in (5.6). Using similar arguments as in the proof of Theorem 5.6, it can be shown that all the eigenvalues are real and one of them is positive, thus E^* is always a saddle point.

Numerical simulations suggest that if none of the E_{1j} 's is asymptotically stable, the solution of (6.2) approaches E_2 , (of course except when $(p(0), x_1(0), x_2(0))$ is in the stable manifold of E^* , if it exists). Otherwise competitive exclusion holds and which one of the two species is the winner depends on the initial concentrations. The phase portrait when E^* exists and $n_1 = 2$ is as given in Fig. 5.1(b).

In the case when $\lambda_2 < \lambda_1$, one can obtain a global result on the asymptotic behavior of trajectories of (6.2).

Theorem 6.5 *If $\lambda_2 < \lambda_1$, $p_1(t) \rightarrow 0$ and $x_1(t) \rightarrow 0$ while $x_2(t) \rightarrow 1 - \lambda_2$.*

The proof of the theorem makes use of a version of Theorem 8 in [4, p. 28] for generalized *type K* functions on \mathbb{R}^2 . We follow the same notation as in [13]. A function $F: B \rightarrow \mathbb{R}^2$, where $B \subset \mathbb{R}^2$, has property π_K if

(i) $F_1(u) \leq F_1(v)$ for any $u = (u_1, u_2)$, $v = (v_1, v_2)$ in B with $u_1 = v_1$ and $u_2 \geq v_2$, and

(ii) $F_2(u) \leq F_2(v)$ for any u, v in B with $u_1 \geq v_1$ and $u_2 = v_2$.

The next proposition, which is similar to Theorem 8 in [4], is required for the proof of Theorem 6.5. The following partial ordering on \mathbb{R}^2 is assumed: for any u, v in \mathbb{R}^2 , $u \leq_K v$ if $u_1 \leq v_1$ and $u_2 \geq v_2$.

Proposition 6.6 *Suppose $F(t, u) : \mathbb{R} \times B \rightarrow \mathbb{R}^2$ has property π_K for each fixed value of t and let $u(t)$ be a solution of the differential equation $u' = F(t, u)$ on $[0, \infty)$.*

(a) *If $v(t)$ is continuous and satisfies the differential inequality $v' \geq_K F(t, v)$ for $t \geq 0$, and $v(0) \geq_K u(0)$, then $v(t) \geq_K u(t)$ for $t \geq 0$.*

(b) *If $v(t)$ is continuous and satisfies the differential inequality $v' \leq_K F(t, v)$ for $t \geq 0$, and $v(0) \leq_K u(0)$, then $v(t) \leq_K u(t)$ for $t \geq 0$.*

Proof of Theorem 6.5 Let $u \in \mathbb{R}^2$ and

$$F(t, u) = \begin{pmatrix} F_1(t, u) \\ F_2(t, u) \end{pmatrix} = \begin{pmatrix} -u_1 + u_1 f_1(1 - u_1 - u_2) \\ -u_2 + u_2 f_2(1 - u_1 - u_2) \end{pmatrix},$$

which has property π_K . Define $y(t) = p_1(t) + x_1(t)$. Then $v(t) = (y(t), x_2(t))^T$ satisfies the differential inequality $v'(t) \leq_K F(t, v)$ for $t \geq 0$. Consider the equation

$$\begin{aligned} u' &= F(t, u) \\ u_1(0) &= p_1(0) + x_1(0) > 0, \quad u_2(0) = x_2(0) > 0. \end{aligned} \tag{6.3}$$

If $\lambda_2 < \lambda_1$, the equilibrium point $(0, 1 - \lambda_2)$ is globally asymptotically stable [2, Corollary 3.5]. By Proposition 6.6, $v(t) \leq_K u(t)$ for all $t \geq 0$, thus $v_1(t) = p_1(t) + x_1(t) \rightarrow 0$ as $t \rightarrow \infty$. Since the solution of (6.2) is nonnegative for all $t \geq 0$, $p_1(t) \rightarrow 0$ and $x_1(t) \rightarrow 0$ as $t \rightarrow \infty$. As E_2 is globally asymptotically stable on the plane $p_1 = x_1 = 0$ whenever $x_2(0) > 0$, all trajectories of (6.2) must therefore approach E_2 as $t \rightarrow \infty$.

The phase portrait for the case of $\lambda_2 < \lambda_1$ is as given in Fig. 5.1(c), with the subscripts 1 and 2 interchanged.

7 Conclusions

We have proposed and analyzed a simple model to describe the growth dynamics of microorganisms which secrete cell-bound extracellular enzymes to transform the nutrient to an intermediate product of a form that can be assimilated into the cells. Similar to the standard chemostat model studied in [2, 8], the species concentration will reach some equilibrium. However, the initial concentration of the species, in addition to the vital parameters, determines whether the species can survive in the chemostat.

For the three modes of competition between two species considered here, the following features are of interest:

(1) When both species transform the nutrient to the same intermediate product (mode (a)), under certain circumstances a one-species stable equilibrium can be destabilized when a small amount of the missing species is introduced into the chemostat, even if the new species is unable to survive when the first species is absent. This will obviously be the case when one of the species, x_2 say, cannot convert the nutrient to an intermediate product, i.e., $f_2(s) = 0$ in (4.1). The

species x_2 could be, for example, a mutation of x_1 which cannot secrete the necessary enzymes. In the absence of x_1 there is no intermediate product in the chemostat and the mutated species x_2 will eventually vanish. The crucial factor is that the second species has a smaller δ , the break-even concentration of the intermediate product for cell growth. This results in all the equilibria on the face $x_2 = 0$, except for E_0 , being unstable in the x_2 -direction, i.e., stable equilibria corresponding to the survival of x_1 only are destabilized when a small amount of x_2 is introduced into the chemostat. In numerical simulations both species are eventually washed out. Thus an inferior species, when sharing the same intermediate product with another species better adapted to the environment, can drive both of them to extinction. This “kamikaze” phenomenon could be exploited in bacterial control and genetic engineering.

(2) When each of the two species transforms the nutrient to an intermediate product distinct from the other one (mode (b)), all the boundary equilibria, if they exist, are locally stable. It is interesting to note that even though one species may have both the lower λ and δ , the outcome is still initial condition dependent.

(3) In mode (c) where one of the species can directly consume the nutrient, the washout equilibrium is a saddle whenever the type I species can survive in the absence of the competitor. The equilibrium corresponding to the survival of only the type I species can either be a global attractor or a local one. However, the type I species, even though it has the more efficient mechanism to utilize the nutrient for growth, under certain circumstances will still vanish from the chemostat when competing with a type II species.

(4) In modes (b) and (c), the model predicts that it is possible to have coexistence equilibria, even though these equilibria are always unstable and therefore cannot be observed in natural ecosystems. However, their existence suggests that environmental factors that were neglected in the model, or modifications of the nutrient consumption mechanism, might make it possible to stabilize the coexistence equilibria. Knowledge of the location of these equilibria also can help to estimate the basin of attraction of the boundary equilibria.

(5) In all the competition models we consider, even though in numerical simulations the solution always approaches one of the stable equilibrium points on the boundary, coexistence in some other form, for example, periodic orbits or strange attractors, has not been ruled out. However, the possibility of a periodic orbit resulting from a Hopf bifurcation has been eliminated since we have shown that all of the eigenvalues of the variational matrix evaluated at any equilibrium point are real.

Acknowledgements. We would like to thank E. Berge, D. Lauffenburger, M. Moo-Young and C. Schnaitman for various discussions, and to S. P. Daoussis for preparation of the figures while being supported by the NSERC Summer Research Scholarship Program.

References

1. Bush, A. W., Cook, A. E.: The effect of time delay and growth rate inhibition in the bacterial treatment of wastewater. *J. Theor. Biol.* **63**, 385–395 (1975)
2. Butler, G. J., Wolkowicz, G. S. K.: A mathematical model of the chemostat with a general class of functions describing nutrient uptake. *SIAM J. Appl. Math.* **45**, 138–151 (1985)

3. Butler G. J., Wolkowicz, G. S. K.: Predator-mediated competition in the chemostat. *J. Math. Biol.* **24**, 167–191 (1986)
4. Coppel, W. A.: *Stability and Asymptotic Behavior of Differential Equations*. Boston: D. C. Heath 1965
5. Chaloupka, J., Krumphanzl, V. (eds.): *Extracellular Enzymes of Microorganisms*. New York: Plenum 1987
6. Freedman, H. I., So, J. W.-H., Waltman, P.: Coexistence in a model of competition in the chemostat incorporating discrete delays. *SIAM J. Appl. Math.* **49**, 859–870 (1989)
7. Herbert, D., Elsworth, R., Telling, R. C.: The continuous culture of bacteria: a theoretical and experimental study. *J. Gen. Microb.* **4**, 601–622 (1956)
8. Hsu, S. B., Hubbell, S. P., Waltman, P.: A mathematical model for single-nutrient competition in continuous cultures of microorganisms. *SIAM J. Appl. Math.* **32**, 366–383 (1977)
9. Hsu, S. B.: Limiting behavior for competing species. *SIAM J. Appl. Math.* **34**, 760–763 (1978)
10. Nagata, Y., Yamaguchi, K., Maruo, B.: Genetic and biochemical studies on cell-bound α -amylase in *Bacillus subtilis*. *Marburg J. Bacteriol.* **119**, 425–430 (1974)
11. Priest, F. G.: *Extracellular Enzymes*. Berkshire: Van Nostrand Reinhold 1984
12. Sargent, M. G., Ghosh, B. K., Lampen, J. O.: Localization of cell-bound penicillinase in *Bacillus licheniformis*. *J. Bacteriol.* **96**, 1329–1338 (1968)
13. Smith, H. L.: Competing subcommunities of mutualists and a generalized Kamke theorem. *SIAM J. Appl. Math.* **46**, 856–874 (1986)
14. Walker, G. J., Jacques, N. A.: Polysaccharides of oral streptococci, In: Raider, J., Peterkofsky, A., (eds.) *Sugar Transport and Metabolism in Gram-positive Bacteria*. Chichester: Ellis Horwood Limited 1987
15. Waltman, P., Hsu, S. B., Hubbell, S.: Theoretical and experimental investigations of microbial competition in continuous culture, In: Bjurton, T. (ed.) *Modelling and Differential Equations in Biology*. New York: Marcel Dekker 1980
16. Wolkowicz, G. S. K., Lu, Z.: Global dynamics of a mathematical model of competition in the chemostat: general response functions and differential death rates. *SIAM J. Appl. Math.* **52**, 222–233 (1992)