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Global stability in a chemostat with multiple nutrients

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Abstract. We study a single species in a chemostat, limited by two nutrients, and separate nutrient uptake from growth. For a broad class of uptake and growth functions it is proved that a nontrivial equilibrium may exist. Moreover, if it exists it is unique and globally stable, generalizing a result in [15].

1. Introduction

In 1950, Monod [21] proposed his now classic model of the nutrient-limited growth of microorganisms. In this model, a single nutrient limits growth and growth is directly coupled to nutrient uptake. Two separate modifications of this model have been made. The first accounts for the observation that nutrient uptake and growth are often decoupled. Nutrient uptake increases the internal stores of nutrients upon which growth depends [2, 4]. The second extends the model to include multiple potentially limiting nutrients [16, 32]. When both nutrients are essential for growth, typically the nutrient in shortest supply limits growth [5], known as Liebig's law of the minimum [5, 25]. The mathematical theory and biological implications of both of these modifications of Monod's model have been studied extensively, both in terms of the growth of a single species and competition between two species (decoupling of uptake and growth: [6, 29]; multiple limiting nutrients: [16, 18, 19, 8, 32]).

Only recently have these two modifications of the Monod model been jointly examined. Legović and Cruzado [15] studied a chemostat model with Michaelis-Menten uptake functions, Droop's function relating growth rate to the internal store

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of the limiting nutrient, and Liebig's law of the minimum. They solved for equilibria and showed that if a nontrivial equilibrium exists, it is unique with a stable linearization. In [12] this model was further analyzed during the exponential growth phase and at equilibrium, and extensively related the model results to chemostat studies. This model has also been used as the basis of an evolutionary model determining the optimal chemical stoichiometry of phytoplankton [13].

Here, we further analyze a more general class of models of the nutrient-limited growth of microorganisms that includes the models studied by [15, 12]. Our techniques borrow from the theory on monotone dynamical systems. In general, solutions of systems in this class converge to equilibria and more complicated behavior—such as oscillations—is rare and typically unobservable [27]. In fact, a global mathematical analysis of many chemostat models in the literature, has been very successful, largely due to the availability of the theory of monotone systems, see [29] for a review. For the chemostat model studied here, we will prove uniqueness and global stability of the nontrivial equilibrium for a broad class of uptake and growth functions. From the mathematical point of view, the key idea is to transform the system into a monotone system by means of a nonlinear state transformation. A particular global stability result due to J.F. Jiang [10] is then used to prove the main result.

Our results extend the previous results of [15] and [12, 13] in the following directions.

1. If a nontrivial equilibrium exists, it is not only locally, but also globally stable. Assuming that it is not a co-limitation equilibrium, this implies that ultimately only one nutrient will be growth limiting for the species. Switches in the nutrient that determines growth will not occur after some transient time.
2. Our stability results are shown to be valid under less restrictive assumptions on the uptake and growth rate functions and this suggests that they are robust with respect to certain changes in these functions as long as the changes do not violate a crucial monotonicity assumption. For example, the assumption that growth rates saturate at the same value for different nutrients has been assumed in previous models [12, 13, 15] but questioned in experiments [33].

2. Chemostat model

We will consider the following chemostat model which is operated at a constant dilution rate a :

$$\begin{aligned}
 \dot{R}_i &= a(R_{in,i} - R_i) - f_i(R_i)B, \quad i = 1, 2 \\
 \dot{Q}_i &= f_i(R_i) - Q_i \min_j (\mu_j(Q_j)), \quad i = 1, 2 \\
 \dot{B} &= B[\min_j (\mu_j(Q_j)) - a]
 \end{aligned} \tag{1}$$

where R_i is the nutrient concentration of the i -th nutrient, Q_i is the cell quota of the i -th nutrient (this is the average amount of the i -th nutrient per cell) and B is the concentration of the organism (number of cells per unit volume), feeding on both

nutrients. Note that loss of organism is only due to washout from the chemostat. Death of the organism inside the chemostat is neglected.

Nutrient uptake is governed by the nutrient uptake rate functions $f_i(R_i)$, both of which are assumed to satisfy the following hypotheses:

1. (*smoothness*) The functions $f_i : \mathbb{R}_+ \rightarrow \mathbb{R}$ are continuously differentiable and $f_i(0) = 0$.
2. (*strict monotonicity*) $f_i' > 0$ on \mathbb{R}_+ .

A typical choice for f_i would be a Monod (or Michaelis-Menten) function:

$$f_i(R_i) = \frac{v_i R_i}{K_i + R_i}$$

for certain positive constants v_i and K_i .

Growth of the organism is assumed to follow ‘the law of the minimum’, a standard assumption in multiple nutrient models [5, 25]. This is reflected in the model by the presence of the minimum function, where the minimum is taken over both growth rate functions $\mu_j(Q_j)$, which are assumed to satisfy the following:

1. (*smoothness*) $\mu_j(Q_j) : [Q_{\min,j}, \infty) \rightarrow \mathbb{R}$ for some positive constant $Q_{\min,j}$, is continuously differentiable and $\mu_j(Q_{\min,j}) = 0$.
2. (*strict monotonicity*) $\mu_j' > 0$ on $[Q_{\min,j}, \infty)$.

A typical choice for μ_j has been proposed by Droop:

$$\mu_j(Q_j) = \mu_j \left(1 - \frac{Q_{\min,j}}{Q_j} \right) \text{ for } Q_j \in [Q_{\min,j}, \infty) \quad (2)$$

for certain positive constants μ_j and $Q_{\min,j}$. The quota Q_j is the total nutrient concentration of nutrient j per cell, which can be divided into two components: stored nutrients awaiting assembly into cellular structure and nutrients in those cellular structures. The minimum quota $Q_{\min,j}$ is the nutrient stored in cellular structures, so that growth ceases when $Q_j = Q_{\min,j}$ (i.e. there are no stored nutrients to assemble).

The model studied in [15, 12] assumes that the uptake functions are Monod functions and that the growth functions take Droop’s form.

Notice that :

1. Assuming continuity for f_i and μ_j seems natural, while continuity of their derivatives is assumed to facilitate the mathematical analysis. For instance, a simple linearization argument may become impossible if we do not make this assumption. Of course, the same problem arises for linearizations at equilibria where μ_1 and μ_2 are equal (so-called “co-limitation equilibria”), due to the minimum in (1). But we will see later that such technical complications can be avoided by our approach (no linearization arguments will be required at such equilibria).
2. The assumption that f_i and μ_j are increasing is far less trivial or technically motivated. In fact, this assumption may well fail to hold for certain organisms. For instance, it is possible that when the nutrient concentration reaches some threshold value, they become toxic and inhibit further growth. For results on models dealing with this case, see [1, 34, 29, 9].

Biologically meaningful initial conditions for system (1) are given by:

$$R_i(0) \geq 0, \quad Q_i(0) \geq Q_{\min,i}, \quad B(0) > 0, \quad i = 1, 2$$

but we will analyze this system on the larger set

$$\mathcal{P} = \{(R_1, R_2, Q_1, Q_2, B) \in \mathbb{R}_+^5 \mid R_i \geq 0, \quad Q_i \geq Q_{\min,i}, \quad B \geq 0, \quad i = 1, 2\}$$

Note that \mathcal{P} is a positively invariant set for (1). The constraints on R_i and B are obvious since these are concentrations. Notice also that the set where $B = 0$ is invariant for the system (1) and that the resulting dynamics is less interesting from biological point of view. Nevertheless it plays an important role in the global analysis of the full model.

We start the analysis by rescaling the system:

$$\bar{t} = at, \quad \bar{R}_i = R_i/R_{in,i}, \quad \bar{Q}_i = Q_i/Q_i^*, \quad \bar{B} = B/B^*, \quad i = 1, 2$$

where Q_i^* and B^* are positive constants satisfying $B^*Q_i^* = R_{in,i}$ for $i = 1, 2$. Defining new uptake functions and growth rate functions as follows:

$$\bar{f}_i(\bar{R}_i) = \frac{B^*}{aR_{in,i}} f_i(R_{in,i}\bar{R}_i), \quad \bar{\mu}_i(\bar{Q}_i) = \frac{1}{a}\mu(Q_i^*\bar{Q}_i)$$

noting that these functions satisfy the exact same hypotheses as their corresponding unbarred relatives, and dropping bars, leads to the following scaled system:

$$\begin{aligned} \dot{R}_i &= 1 - R_i - f_i(R_i)B, \quad i = 1, 2 \\ \dot{Q}_i &= f_i(R_i) - Q_i \min_j (\mu_j(Q_j)), \quad i = 1, 2 \\ \dot{B} &= B[\min_j (\mu_j(Q_j)) - 1] \end{aligned} \quad (3)$$

Notice that the state space \mathcal{P} is unaffected by this rescaling operation (with $Q_{\min,i}$ now equal to $Q_{\min,i}/Q_i^*$).

3. Equilibria

We show that system (3) has at most 2 equilibria, one corresponding to extinction of the organism which always exists, and possibly a second one corresponding to the presence of the organism.

3.1. Unique extinction equilibrium point

Consider the following equations:

$$\begin{aligned} f_1(1) - Q_1 \min_j (\mu_j(Q_j)) &= 0 \\ f_2(1) - Q_2 \min_j (\mu_j(Q_j)) &= 0 \end{aligned} \quad (4)$$

Solutions of (4) determine the Q_1 and Q_2 values of extinction equilibria of system (3) for which $R_1 = R_2 = 1$ and $B = 0$.

There are two cases:

Case 1. $f_2(1)/f_1(1) \geq Q_{\min,2}/Q_{\min,1}$.

In this case we find that for every $Q_1 \geq Q_{\min,1}$, there holds that $[f_2(1)/f_1(1)] Q_1 \geq Q_{\min,2}$ and therefore (4) is equivalent to:

$$\begin{aligned} Q_1 \min \left(\mu_1(Q_1), \mu_2 \left(\frac{f_2(1)}{f_1(1)} Q_1 \right) \right) &= f_1(1) \\ Q_2 &= \frac{f_2(1)}{f_1(1)} Q_1 \end{aligned} \quad (5)$$

Now notice that the left hand side of the first equation in (5) is strictly increasing in Q_1 , takes the value 0 at $\bar{Q}_1 = Q_{\min,1}$ and has limit $+\infty$ as $Q_1 \rightarrow \infty$. Therefore there is a unique solution $\bar{Q}_1 \in (Q_{\min,1}, \infty)$ for the first equation in (5). Inserting \bar{Q}_1 in the second equation of (5) yields:

$$\bar{Q}_2 = \frac{f_2(1)}{f_1(1)} \bar{Q}_1 > Q_{\min,2},$$

proving existence as well as uniqueness of the equilibrium point.

Case 2. $f_2(1)/f_1(1) \leq Q_{\min,2}/Q_{\min,1}$.

In this case we find that for every $Q_2 \geq Q_{\min,2}$, there holds that $[f_1(1)/f_2(1)] Q_2 \geq Q_{\min,1}$ and therefore (4) is equivalent to:

$$\begin{aligned} Q_2 \min \left(\mu_1 \left(\frac{f_1(1)}{f_2(1)} Q_2 \right), \mu_2(Q_2) \right) &= f_2(1) \\ Q_1 &= \frac{f_1(1)}{f_2(1)} Q_2 \end{aligned} \quad (6)$$

A similar argument shows that the first equation has a unique solution $\bar{Q}_2 \in (Q_{\min,2}, \infty)$ which can then be inserted into the second to find $\bar{Q}_1 > Q_{\min,1}$, again proving uniqueness and existence of the equilibrium point.

Summarizing,

Proposition 1. *System (3) has a unique extinction equilibrium point:*

$$E_0 = (1, 1, \bar{Q}_1, \bar{Q}_2, 0) \in \mathcal{P}.$$

For the remainder of this paper we assume that $\mu_1(\bar{Q}_1) \neq \mu_2(\bar{Q}_2)$. Then without loss of generality (possibly after relabeling of indices), we assume that:

$$\mu_1(\bar{Q}_1) < \mu_2(\bar{Q}_2) \quad (7)$$

and therefore there holds by (4) that:

$$\begin{aligned} f_1(1) &= \bar{Q}_1 \mu_1(\bar{Q}_1) \\ f_2(1) &= \bar{Q}_2 \mu_1(\bar{Q}_1), \end{aligned} \quad (8)$$

a fact which will be used throughout the rest of this paper.

The local stability behavior of E_0 is determined by a single parameter as we show next.

Lemma 1. *The extinction equilibrium point E_0 is locally asymptotically stable if $\mu_1(\bar{Q}_1) < 1$ and unstable if $\mu_1(\bar{Q}_1) > 1$.*

Proof. Since $\mu_1(\bar{Q}_1) < \mu_2(\bar{Q}_1)$, we can linearize system (3) at E_0 and get the following Jacobian:

$$\begin{pmatrix} -1 & 0 & 0 & 0 & -f_1(1) \\ 0 & -1 & 0 & 0 & -f_2(1) \\ f_1'(1) & 0 & -\mu_1(\bar{Q}_1) - \bar{Q}_1\mu_1'(\bar{Q}_1) & 0 & 0 \\ 0 & f_2'(1) & -\bar{Q}_2\mu_1'(\bar{Q}_1) & -\mu_1(\bar{Q}_1) & 0 \\ 0 & 0 & 0 & 0 & \mu_1(\bar{Q}_1) - 1 \end{pmatrix}$$

Inspection of the Jacobian shows that four of its eigenvalues are real and negative and that its fifth eigenvalue is $\mu_1(\bar{Q}_1) - 1$. This concludes the proof. \square

3.2. Nontrivial equilibrium point

Nontrivial equilibria of system (3), i.e. equilibria with $B \neq 0$, correspond to solutions of:

$$\begin{aligned} \min_j (\mu_j(Q_j)) &= 1 \\ Q_1 &= f_1(R_1), \quad Q_2 = f_2(R_2) \\ B &= (1 - R_1)/f_1(R_1) = (1 - R_2)/f_2(R_2) \end{aligned}$$

with $R_i \in (0, 1)$.

It will prove useful for future reference to notice that the last two equations and strict monotonicity of the f_i imply that B is a strictly decreasing function of $R_1 \in (0, 1)$ or of $R_2 \in (0, 1)$.

The solutions of the above equations are given by all solutions of:

$$\begin{aligned} \mu_1(Q_1) &= 1 \\ f_1(R_1) &= Q_1 \\ B &= (1 - R_1)/f_1(R_1) \\ 1 - R_2 - f_2(R_2)B &= 0 \\ Q_2 &= f_2(R_2) \end{aligned} \tag{9}$$

with the constraints $\mu_1(Q_1) \leq \mu_2(Q_2)$, $R_1, R_2 \in (0, 1)$ and all solutions of

$$\begin{aligned} \mu_2(Q_2) &= 1 \\ f_2(R_2) &= Q_2 \\ B &= (1 - R_2)/f_2(R_2) \\ 1 - R_1 - f_1(R_1)B &= 0 \\ Q_1 &= f_1(R_1) \end{aligned} \tag{10}$$

with the constraints $\mu_2(Q_2) \leq \mu_1(Q_1)$, $R_1, R_2 \in (0, 1)$.

The following fact is useful:

Fact:

Each of the constrained equations (9), respectively (10) have at most one solution.

This follows immediately by an inspection of the equations: the first three equations of (9), (respectively (10)) may be solved for Q_1 , R_1 and B (Q_2 , R_2 , B) which are unique by the strict monotonicity properties of f_1 and μ_1 (f_2 and μ_2). The fourth equation of (9) (respectively (10)) may then be solved for R_2 (R_1). Existence of this solution follows from the fact that the left hand side of this equation takes a positive value at $R_2 = 0$ ($R_1 = 0$) and a negative value at $R_2 = 1$ ($R_1=1$), while uniqueness is inferred from strict monotonicity of the left hand side of this equation. Finally, the last equation may be solved to yield Q_2 (Q_1) which is unique by strict monotonicity of f_2 (f_1).

This fact implies that system (3) has at most two nontrivial equilibria, which are denoted by¹- if they exist:

$$\tilde{E}^1 = (\tilde{R}_1^1, \tilde{R}_2^1, \tilde{Q}_1^1, \tilde{Q}_2^1, \tilde{B}^1), \text{ respectively } \tilde{E}^2 = (\tilde{R}_1^2, \tilde{R}_2^2, \tilde{Q}_1^2, \tilde{Q}_2^2, \tilde{B}^2).$$

where \tilde{E}^1 (\tilde{E}^2) corresponds to the solution of (9) (respectively (10)).

Proposition 2. *System (3) has at most one nontrivial equilibrium point.*

Proof. Suppose there are two different nontrivial equilibria \tilde{E}^1 and \tilde{E}^2 . Then $\tilde{B}^1 \neq \tilde{B}^2$ (for if this would not be true, both equilibria would coincide). Assume that

$$\tilde{B}^1 < \tilde{B}^2$$

Recalling that B is strictly decreasing on R_1 , this implies that:

$$\tilde{R}_1^1 > \tilde{R}_1^2.$$

Strict monotonicity of f_1 then implies that:

$$\tilde{Q}_1^1 = f_1(\tilde{R}_1^1) > f_1(\tilde{R}_1^2) = \tilde{Q}_1^2$$

Strict monotonicity of μ_1 then implies that:

$$1 = \mu_1(\tilde{Q}_1^1) > \mu_1(\tilde{Q}_1^2)$$

But this contradicts that $1 = \mu_2(\tilde{Q}_2^2) \leq \mu_1(\tilde{Q}_1^2)$.

If one assumes that $\tilde{B}^1 > \tilde{B}^2$, a similar proof also leads to a contradiction. \square

The next result relates the existence of a (unique) nontrivial equilibrium point \tilde{E} to the stability properties of E_0 .

Lemma 2. *If system (3) has a nontrivial equilibrium point \tilde{E} (which must be unique by proposition 2), then*

$$\mu_1(\tilde{Q}_1) > 1.$$

It then follows (by lemma 1) that the extinction equilibrium point E_0 is unstable.

¹ Superscripts 1 refer to solutions of (9) while superscripts 2 refer to solutions of (10).

Proof. First assume that $\tilde{E} = \tilde{E}^1$. Then strict monotonicity of f_1 implies that:

$$\tilde{Q}_1^1 \mu_1(\tilde{Q}_1^1) = \tilde{Q}_1^1 \cdot 1 = f_1(\tilde{R}_1^1) < f_1(1) = \bar{Q}_1 \mu_1(\bar{Q}_1),$$

where we have used that \tilde{E}^1 corresponds to a solution of (9) in the first two equalities, and (8) in the last equality. Now the function $Q_1 \mu_1(Q_1)$ is strictly increasing because $\mu_1(Q_1)$ is. This implies that:

$$\tilde{Q}_1^1 < \bar{Q}_1$$

and hence, using monotonicity of μ_1 once more, that:

$$1 = \mu_1(\tilde{Q}_1^1) < \mu_1(\bar{Q}_1)$$

which concludes the proof for this case.

If $\tilde{E} = \tilde{E}^2$, we proceed by assuming that the lemma does not hold, i.e. that $\mu_1(\bar{Q}_1) \leq 1$. This implies that:

$$\bar{Q}_1 = \frac{f_1(1)}{\mu_1(\bar{Q}_1)} \geq f_1(1).$$

On the other hand we have that:

$$\tilde{Q}_1^2 = f_1(\tilde{R}_1^2) < f_1(1)$$

and thus upon combining inequalities that:

$$\tilde{Q}_1^2 < f_1(1) \leq \bar{Q}_1$$

Strict monotonicity of μ_1 and our initial assumption then imply that:

$$\mu_1(\tilde{Q}_1^2) < \mu_1(\bar{Q}_1) \leq 1$$

But this contradicts that $1 = \mu_2(\tilde{Q}_2^2) \leq \mu_1(\tilde{Q}_1^2)$. □

It is possible that there is no nontrivial equilibrium point. For example, if the μ_j are of the Droop form (2) with $\mu_j \leq 1$ for $j = 1, 2$, because then there is no solution to the equation $\min_j (\mu_j(Q_j)) = 1$. Thus, the interesting theoretical problem is when one assumes existence, uniqueness having already been proved. This justifies the following hypothesis, which we assume to hold throughout the remainder of this paper:

System (3) has a unique nontrivial equilibrium point $\tilde{E} \in \mathcal{P}$.

Then obviously, there holds that either $\tilde{E} = \tilde{E}^1$ or $\tilde{E} = \tilde{E}^2$.

Remark 1. Notice that we allow for the possibility that the values of μ_1 and μ_2 coincide at \tilde{E} , i.e. we allow that \tilde{E} is a co-limitation equilibrium point. Mathematically speaking, this may create some technical problems. For instance, it is not possible to linearize system (3) at a co-limitation equilibrium point. However, as will become clear later, our approach to prove global stability does not require linearization arguments and hence avoids such problems.

4. Conservation principle

Consider the dynamics of the following quantities:

$$M_i = R_i + BQ_i, \quad i = 1, 2$$

We interpret the M_i as the total concentration of nutrient i , both in free and stored form. These quantities satisfy:

$$\dot{M}_i = 1 - M_i$$

so $M_i(t) \rightarrow 1$ exponentially as $t \rightarrow \infty$. As a first step in the analysis of system (3), it seems therefore reasonable to replace R_i by $1 - BQ_i$ in the system equations which gives the following reduced system:

$$\begin{aligned} \dot{Q}_1 &= f_1(1 - BQ_1) - Q_1 \min_j (\mu_j(Q_j)), \\ \dot{Q}_2 &= f_2(1 - BQ_2) - Q_2 \min_j (\mu_j(Q_j)), \\ \dot{B} &= B[\min_j (\mu_j(Q_j)) - 1] \end{aligned} \quad (11)$$

We will later justify this reduction.

The state space of this system is:

$$\mathcal{P}^r = \{(Q_1, Q_2, B) \in \mathbb{R}_+^3 \mid Q_1 \geq Q_{\min,1}, Q_2 \geq Q_{\min,2}, BQ_1 \leq 1, BQ_2 \leq 1\}$$

which can be shown to be forward invariant. (A proof of this claim follows easily from the transformed version (20) of this system which we study later)

As before, biologically relevant initial conditions belong to \mathcal{P}^r but also satisfy $B > 0$.

Next we show that all solutions of (11) eventually enter a compact set and remain in it forever after.

Proposition 3. *There is some constant $M > 0$ such that every solution $(Q_1(t), Q_2(t), B(t))$ satisfies:*

$$Q_1(t), Q_2(t), B(t) < M \text{ for all sufficiently large } t.$$

Proof. First, we prove that solutions do not escape in finite time. To that end, consider the dynamics of the variable:

$$V := Q_1^2 + Q_2^2,$$

which obeys:

$$\dot{V} \leq 2(f_1(1)Q_1 + f_2(1)Q_2) \leq 2(f_1(1) + f_2(1)) + 2 \max(f_1(1), f_2(1)) V$$

where we used monotonicity of f_i in the first inequality and the fact that $Q_i \leq 1 + Q_i^2$ in the second. The resulting inequality implies that V - and hence Q_1 and Q_2 - remains bounded in finite time intervals. Moreover, since $BQ_i \leq 1$, we also get a bound for $B(t)$ on finite time intervals.

Next, we introduce the following auxiliary variables:

$$z_i = BQ_i, \quad i = 1, 2,$$

with dynamics given by:

$$\dot{z}_i = -z_i + Bf_i(1-z_i) = -z_i + \frac{z_i}{Q_i} f_i(1-z_i) \leq \left(-1 + \frac{f_i(1-z_i)}{Q_{\min,i}}\right) z_i, \quad i = 1, 2. \quad (12)$$

Then we may pick a sufficiently small $\delta_i \in (0, 1)$, $i = 1, 2$, for which there holds that for all $z_i \in [1 - \delta_i, 1]$:

$$\dot{z}_i \leq -c_i z_i < 0, \quad i = 1, 2$$

for some $c_i > 0$, $i = 1, 2$, by continuity of the f_i . Then with $\Delta = \min\{\delta_1, \delta_2\}$, we obtain:

$$z_i(t) \leq 1 - \Delta \text{ for sufficiently large } t.$$

This bound and monotonicity of the f_i will yield a uniform lower bound for the $Q_i(t)$, $i = 1, 2$. Indeed, first notice that:

$$\dot{Q}_i \geq f_i(\Delta) - Q_i \min_j (\mu_j(Q_j)) \text{ for sufficiently large } t.$$

So for sufficiently small $q > 0$, we find that whenever $Q_i \in [Q_{\min,i}, Q_{\min,i} + q]$:

$$\dot{Q}_i \geq f_i(\Delta) - cQ_i > 0, \quad i = 1, 2,$$

for some sufficiently small $c > 0$ by continuity of the μ_i , and thus that:

$$Q_i(t) \geq Q_{\min,i} + q, \quad i = 1, 2 \text{ for sufficiently large } t. \quad (13)$$

Finally, this lower bound leads to a uniform upper bound for the $Q_i(t)$:

$$\dot{Q}_i \leq f_i(1) - CQ_i, \quad i = 1, 2 \text{ for sufficiently large } t,$$

for some $C > 0$ (using that the f_i are strictly increasing and continuity of the μ_i). This implies that the statement of the proposition holds for the $Q_i(t)$, $i = 1, 2$. To conclude this proof, notice that the statement is trivial for $B(t)$ since $B(t)Q_i(t) \leq 1$ and $Q_i(t) \geq Q_{\min,i}$ for $i = 1, 2$, implying that $B(t) \leq 1/Q_{\min,i}$ for all $t \geq 0$. \square

The assumptions made before imply that system (11) has precisely two equilibria. First, there is an extinction equilibrium

$$E_0^r = (\bar{Q}_1, \bar{Q}_2, 0),$$

see proposition 1. Secondly, there is a nontrivial equilibrium point \tilde{E}^r given by:

$$\tilde{E}^r = (\tilde{Q}_1^1, \tilde{Q}_2^1, \tilde{B}^1) \quad \text{or} \quad (\tilde{Q}_1^2, \tilde{Q}_2^2, \tilde{B}^2).$$

Notice that the set $\mathcal{B}_0 = \{(Q_1, Q_2, B) \in \mathcal{P}^r \mid B = 0\}$ is forward invariant for system (11) and that the dynamics on this set are given by the following planar system:

$$\begin{aligned}\dot{Q}_1 &= f_1(1) - Q_1 \min_j (\mu_j(Q_j)), \\ \dot{Q}_2 &= f_2(1) - Q_2 \min_j (\mu_j(Q_j)),\end{aligned}\tag{14}$$

defined on $\mathcal{Q} = \{(Q_1, Q_2) \in \mathbb{R}_+^2 \mid Q_i \geq Q_{\min,i}\}$. The asymptotic behavior of this system (both in forward and backward time) will later prove to play an important role and is investigated next.

Proposition 4. *System (14) has a globally asymptotically stable equilibrium point in $E_0^{r,0} = (\bar{Q}_1, \bar{Q}_1)$. Every backward solution, except for the equilibrium $E_0^{r,0}$, leaves \mathcal{Q} in finite time or is unbounded.*

Proof. First notice that (forward) solutions are bounded by proposition 3. Next consider:

$$V = \left(\frac{f_2(1)}{f_1(1)} Q_1 - Q_2 \right)^2.$$

Taking the time derivative of V along solutions of (14) shows that:

$$\dot{V} = -2 \left[\frac{f_2(1)}{f_1(1)} Q_1 - Q_2 \right]^2 \min_j (\mu_j(Q_j)) \leq 0.$$

Lasalle's invariance principle implies that solutions converge to the largest invariant set in the set where $\dot{V} = 0$. The latter consists of three straight lines given by the equations $Q_1 = Q_{\min,1}$, $Q_2 = Q_{\min,2}$ and $Q_2 = [f_2(1)/f_1(1)]Q_1$.

From the system equations (14), it follows that the vector field is transversal to the first two lines, implying that solutions starting here leave the lines instantaneously. The third line is invariant for (14) and contains the unique equilibrium point $E_0^{r,0}$. Suppose that a point l on this line different from $E_0^{r,0}$ is an ω limit point. Then by backward invariance of ω limit sets, the ω limit set is unbounded or contains a point outside the state space. But this is impossible by Proposition 3 and hence $E_0^{r,0}$ is the only possible ω limit point.

To prove the statement regarding the backward solutions we consider the backward time system:

$$\begin{aligned}\dot{Q}_1 &= -f_1(1) + Q_1 \min_j (\mu_j(Q_j)), \\ \dot{Q}_2 &= -f_2(1) + Q_2 \min_j (\mu_j(Q_j)),\end{aligned}\tag{15}$$

defined on \mathcal{Q} . Let us suppose that the statement does not hold. Then there is a solution $(Q_1(t), Q_2(t))$ of system (15) which is in \mathcal{Q} and bounded for all $t \geq 0$. Thus there is some $M > 0$ such that:

$$Q_{\min,i} \leq Q_i(t) \leq M, \quad i = 1, 2, \quad \forall t \geq 0.\tag{16}$$

Pick $\epsilon > 0$ small enough such that for $i = 1, 2$ there holds:

$$-f_i(1) + Q_i \min_j (\mu_j(Q_j)) \leq -\alpha < 0, \quad \forall Q_i \in [Q_{\min,i}, Q_{\min,i} + \epsilon]. \quad (17)$$

for some $\alpha > 0$.

Then we claim that the lower bound in (16) can be strengthened to:

$$Q_{\min,i} + \epsilon < Q_i(t), \quad i = 1, 2, \quad \forall t \geq 0. \quad (18)$$

If this were not the case, then there would exist a time $t^* \geq 0$ and some index i^* such that $Q_{i^*}(t^*) \in [Q_{\min,i^*}, Q_{\min,i^*} + \epsilon]$. Then by (17) we obtain:

$$\dot{Q}_{i^*} = -f_{i^*}(1) + Q_{i^*} \min_j (\mu_j(Q_j)) \leq -\alpha$$

implying that there exists some time $T > t^*$ such that $Q_{i^*}(T) < Q_{\min,i^*}$, contradicting (16).

Let us now introduce the following auxiliary variable:

$$q_2 = Q_2 - \frac{f_2(1)}{f_1(1)} Q_1$$

Along the solution $(Q_1(t), Q_2(t))$ this variable obeys the following equation:

$$\dot{q}_2 = q_2 \min_j (\mu_j(Q_j(t))) \geq cq_2$$

for some $c > 0$, using (18). There are two cases to consider. If $q_2(0) \neq 0$, then $q_2(t)$ will diverge, which contradicts boundedness of the solution $(Q_1(t), Q_2(t))$. If $q_2(0) = 0$, then $q_2(t) = 0$ for all $t \geq 0$. In other words, the solution $(Q_1(t), Q_2(t))$ evolves on the invariant line given by the equation $Q_2 = [f_2(1)/f_1(1)]Q_1$. But it is easy to see from the system equations (15) that a solution on this line (and different from the solution at the equilibrium $E_0^{r,0}$) either leaves \mathcal{Q} in finite time or diverges. This concludes the proof. \square

5. Transformation to a monotone system

This section contains the key step in the global analysis of the reduced system (11). We will show that by means of a nonlinear state transformation, the reduced system can be transformed in a monotone system. Consider new state variables for system (11):

$$z_1 = BQ_1, \quad z_2 = BQ_2, \quad B = B \quad (19)$$

The interpretation for z_i is the concentration of nutrient i stored in the organism. In terms of the variables (z_1, z_2, B) we get:

$$\begin{aligned} \dot{z}_i &= -z_i + Bf_i(1 - z_i), \quad i = 1, 2, \\ \dot{B} &= B[\min_j (\mu_j(z_j/B)) - 1]. \end{aligned} \quad (20)$$

Some caution should be taken in defining the state space for this system. First, notice that the state transformation (19) is not one-to-one since every point $(Q_1, Q_2, 0) \in$

\mathcal{P}^r is mapped to $(0, 0, 0)$. So it makes sense only for the biologically relevant initial conditions corresponding to $B \neq 0$ where it is one-to-one. But notice that the function $B \min_j \mu_j(z_j/B)$ is locally Lipschitz continuous in the region where $0 < Q_{\min, j} < z_j/B < C$ (for arbitrarily large C), if we set it zero for $z_1 = z_2 = B = 0$. Therefore, the state space for the transformed system is:

$$\mathcal{P}^t = \{(z_1, z_2, B) \in \mathbb{R}_+^3 \mid z_i \in [0, 1], Q_{\min, i} B \leq z_i, i = 1, 2, B > 0\} \cup \{(0, 0, 0)\}.$$

Notice that system (20) has 2 equilibria, one at $(0, 0, 0)$ and a second one at \tilde{E}^t , which is the image of \tilde{E}^r under the transformation (19).

We show next that this system is monotone [27]. First recall that a system $\dot{x} = f(x)$ with f locally Lipschitz in some open set U , having some forward invariant subset $X \subset U \subset \mathbb{R}^n$, is called monotone (with respect to the standard order \leq on \mathbb{R}^n , generated by the nonnegative orthant \mathbb{R}_+^n) if for any two solutions $x(t)$ and $y(t)$ with $x(0) \leq y(0)$, defined on some interval $[0, T]$ for some $T > 0$, there holds that $x(t) \leq y(t)$ for all $t \in [0, T]$. It is well-known that if the state space X is p -convex (meaning that whenever $x, y \in X$ with $x \leq y$, then the line segment connecting x and y is also contained in X), a sufficient condition for this to happen is that the system is of type K, see e.g. chapter 3, proposition 1.1 in [27]. A system $\dot{x} = f(x)$ is of type K if whenever $x \leq y$, and $x_i = y_i$ for some i , then $f_i(x) \leq f_i(y)$.

Lemma 3. *System (20) is of type K on the p -convex set \mathcal{P}^t and hence monotone.*

Proof. It is easily checked that \mathcal{P}^t is p -convex. Denote the vector field of system (20) by $F(z_1, z_2, B)$ and pick two states $(z_1^a, z_2^a, B^a) \leq (z_1^b, z_2^b, B^b)$ with $B^a = B^b$. (The proof is trivial when $z_1^a = z_1^b$ or $z_2^a = z_2^b$) Then

$$\begin{aligned} F_3(z_1^a, z_2^a, B^a) &= B^a [\min_j (\mu_j(z_j^a/B^a)) - 1] \\ &\leq B^a [\min_j (\mu_j(z_j^b/B^a)) - 1] \\ &= B^b [\min_j (\mu_j(z_j^b/B^b)) - 1] = F_3(z_1^b, z_2^b, B^b) \end{aligned}$$

where the middle inequality holds because the functions μ_j are increasing. \square

We will need the following result from the theory of monotone systems. The result is due to J.F. Jiang [10] and stated next.

Theorem 1. *Suppose that a system $\dot{x} = f(x)$ is monotone on the state space $X = \prod_{i=1}^n I_i \subset \mathbb{R}^n$ where I_i are intervals (i.e. $I_i = (a_i, b_i)$, $[a_i, b_i]$, $[a_i, b_i)$ or $(a_i, b_i]$) for – possibly extended – real numbers $a_i < b_i$). Assume that*

1. *Every forward orbit has compact closure in X .*
2. *The system has a unique equilibrium point $\bar{x} \in X$.*

Then, \bar{x} is globally asymptotically stable.

The main result of this section is the following.

Theorem 2. *The equilibrium point \tilde{E}^t of system (20) is globally asymptotically stable with respect to initial conditions in $\mathcal{P}^t \setminus \{(0, 0, 0)\}$. Equivalently, the equilibrium point \tilde{E}^r of system (11) is globally asymptotically stable with respect to initial conditions in \mathcal{P}^r for which $B \neq 0$.*

Proof. The idea of the proof is to extend the state space of system (20) and delete the equilibrium at the origin, in such a way that Theorem 1 is applicable. First, for $i = 1, 2$ pick arbitrary continuously differentiable extensions μ_i^e of the μ_i functions such that:

$$\begin{aligned} \mu_i^e : \mathbb{R}_+ &\rightarrow \mathbb{R}, \quad \mu_i^e(Q_i) < 0 \text{ for } Q_i \in [0, Q_{\min,i}), \\ \mu_i^e(Q_i) &= \mu_i(Q_i) \text{ for } Q_i \geq Q_{\min,i}, \quad \mu_i^e > 0 \text{ on } \mathbb{R}_+. \end{aligned}$$

For example, we may pick $\mu_i^e(Q_i) = \mu_i(Q_i)$ when $Q_i \geq Q_{\min,i}$, and $\mu_i^e(Q_i) = (Q_i - Q_{\min,i})\mu_i'(Q_{\min,i})$ for $Q_i < Q_{\min,i}$.

Next define the following system:

$$\begin{aligned} \dot{z}_i &= -z_i + Bf_i(1 - z_i), \quad i = 1, 2, \\ \dot{B} &= B[\min_j (\mu_j^e(z_j/B)) - 1] \end{aligned} \tag{21}$$

with state space

$$X = \{(z_1, z_2, B) \in \mathbb{R}_+^3 \mid z_i \in [0, 1], i = 1, 2, B \in (0, \infty)\}$$

Notice that system (21) is monotone since it is of type K on X (the same proof as in Lemma 3 holds for system (21)), that it has a *unique* equilibrium point at \tilde{E}^t and that the state space is of the form described in Theorem 1. Clearly, if we can prove that forward orbits have compact closure in X , then it follows from Theorem 1 that \tilde{E}^t is globally asymptotically stable for system (21) and hence also for system (20) provided initial conditions are in $\mathcal{P}^t \setminus \{(0, 0, 0)\}$, so we are done.

Before doing just that, we introduce one more system, namely an extended version of system (11):

$$\begin{aligned} \dot{Q}_i &= f_i(1 - BQ_i) - Q_i \min_j (\mu_j^e(Q_j)), \quad i = 1, 2, \\ \dot{B} &= B[\min_j (\mu_j^e(Q_j)) - 1] \end{aligned} \tag{22}$$

with state space $\mathcal{P}^{r,e} = \{(Q_1, Q_2, B) \in \mathbb{R}_+^3 \mid Q_i \geq 0, BQ_i \leq 1, i = 1, 2\}$. Notice that this system has two equilibria, one at E_0^r and a second one at \tilde{E}^r . A careful inspection of the proofs of Proposition 3 and Proposition 4, reveals that both propositions remain valid for this extended system. Let us start by re-examining the proof of Proposition 3. First, we show that there are no finite escape times for solutions of system (22). To that end we introduce – without loss of generality – the following additional assumption for the μ_i^e : there exists some $\beta > 0$ such that $\mu_i^e(Q_i) \geq -\beta$ for $Q_i \in \mathbb{R}_+$. Now re-consider the dynamics of the variable $V = Q_1^2 + Q_2^2$ along solutions of system (22):

$$\dot{V} \leq 2(f_1(1)Q_1 + f_2(1)Q_2) + 2\beta V \leq 2(f_1(1) + f_2(1)) + \beta^* V$$

for some $\beta^* > 0$. This shows that $V(t)$ and hence $Q_1(t)$ and $Q_2(t)$ remain bounded on bounded time intervals. Then the equation for B in (22) shows that on bounded time intervals $\dot{B} \leq B(c - 1)$ for some $c > 0$ and hence the same conclusion holds for $B(t)$ as well.

Next we prove that solutions of (22) are bounded. First notice that the system equations imply that $Q_i(t) > 0$ for all $t > 0$ and $i = 1, 2$. Now there exists $\epsilon > 0$ small enough such that for all $Q_i \in (0, \epsilon]$ holds that:

$$\dot{Q}_i \geq \alpha Q_i, \quad i = 1, 2,$$

for some $\alpha > 0$, implying that for all sufficiently large t , we have that:

$$Q_i(t) \geq \epsilon, \quad i = 1, 2.$$

This and the fact that $BQ_i \leq 1$, imply in particular that for all sufficiently large t , $B(t) \leq 1/\epsilon$, which establishes a lower bound for the B -component of solutions of (22). The whole argument in the proof of Proposition 3 involving the variables $z_i = BQ_i$ for $i = 1, 2$ can now be repeated if one replaces $Q_{\min,i}$ by ϵ in the inequality (12). Then as before, there exists some $\Delta > 0$ such that $z_i(t) \leq 1 - \Delta$ for $i = 1, 2$ and all sufficiently large t . Moreover, one obtains a uniform lower bound for the $Q_i(t)$ by noticing that for all sufficiently large t , there holds that:

$$\dot{Q}_i \geq f_i(\Delta) - Q_i \min_j \mu_j^e(Q_j), \quad i = 1, 2.$$

But then there is some sufficiently small $q > 0$, such that whenever $Q_i \in [0, Q_{\min,i} + q]$, we have that:

$$\dot{Q}_i \geq +\alpha^*, \quad i = 1, 2,$$

for some $\alpha^* > 0$ and hence that (13) holds for all sufficiently large t and $i = 1, 2$. Then the same argument as in the proof of Proposition 3 leads to a uniform upper bound for the $Q_i(t)$. The lower bound (13) also plays a significant role in showing the validity of Proposition 4. Indeed, it implies that the ω limit set of every solution of system (22) starting in the invariant set $\{(Q_1, Q_2, B) \in \mathcal{P}^{r,e} \mid B = 0\}$, must belong to the state space \mathcal{Q} of system (14). But Proposition 4 shows that there is only one possible ω limit set, namely the equilibrium point $E_0^{r,0}$.

Finally, the assertion regarding backward solutions of system (22), restricted to the invariant set $\{(Q_1, Q_2, B) \in \mathcal{P}^{r,e} \mid B = 0\}$ (except for the unique equilibrium point \tilde{E}^t) is proved using a similar argument as in the proof of Proposition 4. Reconsider system (15), but replace μ_j by μ_j^e and the state space \mathcal{Q} by the (extended) state space \mathbb{R}_+^2 . It is clear from the proof of Proposition 4 that a possibly bounded solution of the extended version of system (15) enters the subset of \mathbb{R}_+^2 where for at least one i , $Q_i \in [0, Q_{\min,i})$. But then $\dot{Q}_i < -f_i(1)$, so there exists some time T such that $Q_i(T) < 0$, implying that the solution has left the state space, a contradiction.

Let us return now to the issue of proving that forward orbits of system (21) have compact closure in X . First of all, we have shown above that $B(t)$ is bounded for solutions of system (22), and hence also for solutions of system (21). This proves

boundedness of solutions of system (21). So, what remains to be shown is that for all $x \in X$, the omega limit set $\omega(x)$ does not meet the set $\{(z_1, z_2, B) \in \mathbb{R}_+^3 \mid B = 0\}$. Now, from proposition 3 applied to system (22), it follows that solutions of system (21) will reside in a wedge-shaped region:

$$Q_i(t) = z_i(t)/B(t) < M \text{ for all large } t. \quad (23)$$

This implies that the only possible ω limit point with $B = 0$ for solutions of system (21) is $(0, 0, 0)$ (for if $(\bar{z}_1, \bar{z}_2, 0)$ would be another limit point with $\bar{z}_i \neq 0$ for at least one i , then there would be a sequence of times $\{t_k\} \rightarrow \infty$ such that $B(t_k) \rightarrow 0$ and $z_i(t_k) \rightarrow \bar{z}_i$; but then for at least one i the inequality (23) would be violated) and we are left with proving that it is *not* an ω limit point.² In terms of system (22), this means that we need to show that no ω limit point of a solution starting in the subset of $\mathcal{P}^{r,e}$ where $B \neq 0$, belongs to $\mathcal{B}_0 = \{(Q_1, Q_2, B) \in \mathcal{P}^{r,e} \mid B = 0\}$. (recall that the single point $(0, 0, 0)$ is the image of the set \mathcal{B}_0 under transformation (19)) Suppose this is not true, then for some $x \in \mathcal{P}^{r,e}$ with nonzero B -value, we have that $p \in \omega(x)$ for some $p \in \mathcal{B}_0$. If $p \neq E_0^r$, then the backward solution through p also belongs to $\omega(x)$ (by backward invariance of ω limit sets). But this backward solution leaves the state space in some finite time, or is unbounded by Proposition 4, applied to system (22). So we should only consider the case that $p = E_0^r$. But this case can be reduced to the previous one by means of the Butler-McGehee lemma, see e.g. [29] p. 12.

Indeed, a simple linearization argument shows that E_0^r is a hyperbolic equilibrium point with 2-dimensional stable and 1-dimensional unstable manifold (see lemmas 1 and 2). Then the Butler-McGehee lemma implies that $\omega(x)$ should contain some point $q \in W^s(E_0^r)$, the stable manifold of E_0^r , such that $q \neq E_0^r$. Since $W^s(E_0^r)$ is 2-dimensional and in view of the stability result in Proposition 4, applied to the 2-dimensional system (22), we conclude that $q \in \mathcal{B}_0$. So we have reduced this case to the previous one and therefore the proof is finished. \square

6. Global stability for the original system

In this section we justify why the global stability result for the reduced system (11) implies a global stability result for the original system. In turn, this leads to the main result of this paper.

Theorem 3. *The nontrivial equilibrium point \tilde{E} of system (3) is globally asymptotically stable with respect to all initial conditions in \mathcal{P} for which $B \neq 0$.*

Proof. The proof relies on a global stability result for cascaded systems. First, notice that by introducing the new variables:

$$M_i = R_i + BQ_i, \quad i = 1, 2,$$

² Strictly speaking we should *add* the point $(0, 0, 0)$ to the state space X of system (21), if it were to be an ω limit point.

system (3) can be rewritten as a cascaded system:

$$\begin{aligned}\dot{M}_i &= 1 - M_i \\ \dot{Q}_i &= f_i(M_i - BQ_i) - Q_i \min_j (\mu_j(Q_j)) \\ \dot{B} &= B[\min_j (\mu_j(Q_j)) - 1]\end{aligned}\tag{24}$$

with state space $\mathcal{P}^c = \{(M_1, M_2, Q_1, Q_2, B) \in \mathbb{R}_+^5 \mid M_i \geq 0, Q_i \geq Q_{\min,i}, B \geq 0, i = 1, 2\}$. Here we are only interested in solutions with initial conditions satisfying $B \neq 0$.

If solutions of (24) are bounded, then the global asymptotically stable equilibrium point of the first subsystem $\dot{M}_i = 1 - M_i$, $i = 1, 2$ at $(1, 1)$, and Theorem 2, imply that system (24) has a global asymptotically stable equilibrium point, see e.g. Appendix F in [29] or [30, 31]. From this we conclude that the theorem is proved.

So we are left with proving that solutions of (24) are bounded. We will show the equivalent statement that solutions of (3) are bounded instead. First, notice that the definition and the dynamics of the auxiliary variables M_i imply in particular that there is an arbitrarily small $\epsilon > 0$ such that:

$$R_i(t), B(t)Q_i(t) \leq 1 + \epsilon \text{ for all sufficiently large } t \text{ and } i = 1, 2.$$

which already establishes a bound for $R_i(t)$. Now, since $Q_i(t) \geq Q_{\min,i} > 0$ for $i = 1, 2$ and all $t \geq 0$, this implies that:

$$B(t) \leq \alpha \text{ for all sufficiently large } t$$

for some $\alpha > 0$. This establishes the bound on B . Then for all sufficiently large t we have that:

$$\dot{R}_i = 1 - R_i - B(t)f_i(R_i) \geq 1 - R_i - \alpha f_i(R_i), \quad i = 1, 2$$

and then continuity of the f_i implies that there exists some $\delta > 0$ such that if $R_i \in [0, \delta]$, then $\dot{R}_i \geq \rho$ for some $\rho > 0$ and thus we infer that:

$$R_i(t) > \delta \text{ for all sufficiently large } t \text{ and } i = 1, 2.$$

This, and strict monotonicity of the f_i , imply that for sufficiently large t :

$$\dot{Q}_i \geq f_i(\delta) - Q_i \min_j (\mu_j(Q_j)), \quad i = 1, 2$$

which by a similar argument as in the proof of Proposition 3 results in a uniform lower bound for the $Q_i(t)$, see (13).

Finally we find a uniform upper bound for the $Q_i(t)$ as follows. First notice that for all sufficiently large t :

$$\dot{Q}_i \leq f_i(1 + \epsilon) - CQ_i, \quad i = 1, 2$$

for some $C > 0$. This can be inferred using strict monotonicity of the f_i , the bound $R_i(t) \leq 1 + \epsilon$ given above, the lower bound (13) and continuity of the μ_j . Then there is some $M > 0$ such that for all sufficiently large t and $i = 1, 2$, there holds that $Q_i(t) < M$. \square

7. Discussion

The introduction of the notion of cell quota in Droop's model [4] to mimic decoupling of nutrient uptake and growth has led to a number of theoretical investigations of chemostat models under different assumptions, see [14, 22] for a single-nutrient, single-species model and then in [26] for a single-nutrient, two-species competition model. The study of two-nutrients, single-species models has been initiated in [15] and followed-up more recently by [12, 13]. The local stability results in those papers have been extended to global ones here. Moreover, the class of uptake and growth rate functions has been enlarged reflecting robustness of the stability properties.

Global stability does not seem to be the rule in chemostat models. Under periodic forcing for instance, oscillatory behavior has been shown to occur in [23, 28, 29] and chaotic behavior has been observed in [3]. Oscillations are also possible in autonomous chemostat models, for instance when there is a predator that feeds on the primary consumer [11], or when there are three or more populations competing for three or more limiting resources [7, 17, 20]. The closest situation to the one we consider here was investigated by [24], who showed that limit cycles were possible in an unforced variable internal stores model that explicitly followed the size-structure of the population. This does not occur under the assumptions that nutrient uptake is proportional to biomass and continuous with time.

Chemostat models with multiple, *locally stable* equilibria are also possible. (Clearly, in this case, the chemostat cannot be globally stable.) This can happen for instance when uptake functions are not always increasing, but are decreasing past some threshold value for the nutrient concentration. This situation has been studied by [1, 34] where it was shown that bi-stability and even multi-stability may occur. Those models involved competition between n species for a single nutrient, but did not assume that uptake and growth are decoupled. The equilibria are always boundary equilibria where at most one species has nonzero concentration. Depending on the initial condition, a particular solution converges to one of them. Notice that this case is not in conflict with the competitive exclusion principle since at most one species survives in the long run, although the survivor may differ for distinct solutions.

The main result of our paper is that these exotic phenomena (limit cycles, chaos, and multi-stability) do not occur for a broad range of biologically realistic models of growth on two essential resources in a chemostat without inhibitory effects of resources.

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