

Stability and Stabilization for Models of Chemostats with Multiple Limiting Substrates *

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Abstract

We study chemostat models in which multiple species compete for two or more limiting nutrients. First we consider the case where the nutrient flow and species removal rates and input nutrient concentrations are all given positive constants. In that case, we use Brouwer degree theory to give conditions guaranteeing that the models admit globally asymptotically stable componentwise positive equilibrium points, from all componentwise positive initial states. Then we use the results to develop stabilization theory for a class of controlled chemostats with two or more limiting nutrients. For cases where the dilution rate and input nutrient concentrations can be selected as controls, we prove that many different componentwise positive equilibria can be made globally asymptotically stable. This extends the existing control results for chemostats with one limiting nutrient. We demonstrate our methods in simulations.

1 Introduction

Chemostat models play a crucial role in bioengineering and population biology. The chemostat is a laboratory bioreactor in which fresh medium is continuously added and culture liquid is continuously removed, so that the culture volume remains constant. It has important industrial applications, including the commercial production of genetically altered organisms. Also, chemostat models play a key role for experimentally reproducing and understanding the behaviors of interacting organisms in lakes and waste-water treatment plants. The basic mathematical model for the chemostat was first derived in [40, 41]. See [9, 10, 18, 19, 20, 28, 39, 46] for more recent discussions on the chemostat and its role in microbial ecology. For well-mixed chemostats, the competitive exclusion principle [2] specified conditions on the growth rates under which only one species can persist generically. This led to a large literature whose aim is to explain the discrepancy between the competitive exclusion principle, and the fact that it is common for multiple competing species to survive in nature on one limiting substrate; see [1, 8, 25, 50] and [29]-[37] and the references therein.

By contrast, fewer studies have been devoted to the important case of chemostats with two or more limiting nutrients. The case of two species and two limiting nutrients was studied by MacArthur, Tilman, and others using graphical methods, leading to co-called resource competition theory [21, 26, 27, 38, 47, 48]. Tilman's method was based on information at potential coexistence equilibria. See also [6] for graphical methods for ensuring coexistence of two species in chemostats with two limiting nutrients based on considering isoclines and the locations of single species equilibria. One of the key testable predictions of resource competition theory is an extension of the competitive exclusion principle [22] that states that generically, the number of coexisting species cannot exceed the number of limiting resources. The conclusions of resource competition theory have been validated in experiments; see, e.g., [12] for a review. Moreover, there are several available global stability results for chemostats with two limiting substrates and two competing species. For example, stable periodic solutions were reported for Monod kinetics [14] and later for interacting

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resources [4, 5, 7, 42]. There are numerical studies for chemostats with more than two competing species and more than two limiting nutrients that illustrate the possibility of chaotic or oscillatory dynamics [15, 16]. See also [3, 23, 24] for theoretical results on limit cycles in chemostats with multiple competing species and several limiting nutrients, which are very different from our work owing to our stability and stabilization analyses for equilibrium points.

In this work, we further advance the theory of chemostats in which more than two species compete for more than two limiting nutrients. The general model for N species competing for M resources is [11]

$$\begin{cases} \dot{s}_j &= D_j^s(s_j^{in} - s_j) - \sum_{i=1}^N \mathcal{G}_{i,j}(S)x_i, \quad 1 \leq j \leq M \\ \dot{x}_i &= \left[-D_i^x + \sum_{j=1}^M \eta_{i,j} \mathcal{G}_{i,j}(S) \right] x_i, \quad 1 \leq i \leq N, \end{cases} \quad (1)$$

where $S = (s_1, s_2, \dots, s_M)$, s_j is the concentration of the j th substrate, x_i is the concentration of the i th species, the constant $s_j^{in} > 0$ is the concentration of substrate j at the inlet (i.e., the j th input nutrient concentration), the constant $D_j^s s_j^{in} > 0$ is the input flux of substrate s_j , $\mathcal{G}_{i,j}(S)$ is the rate of consumption of substrate j by species i per unit of biomass of species i as a function of the substrate concentrations, and the constant $\eta_{i,j} > 0$ is the yield coefficient of the conversion of substrate j to biomass of species i .

The problem of determining the set of all componentwise nonnegative equilibrium points for (1) in the closure of $\mathcal{X} = (0, \infty)^{M+N}$ is difficult in general, because we must ensure that some of the terms in brackets are zero, and that the \dot{s}_j 's are zero. The implications of the extended competitive exclusion principle lead us to first consider the particular and crucial case where $M = N$. In Section 3, we use Brouwer degree theory [13, 44] to prove the existence of componentwise positive equilibrium points for (1) when $M = N$, under rather general assumptions. In Section 4, we establish the existence of a globally asymptotically stable equilibrium point for particular families of growth functions $\mathcal{G}_{i,j}$, where the stability properties must be understood relative to componentwise positive initial states. Our global asymptotic stability result is valid in cases where $M \neq N$, but it only applies when the componentwise nonnegative equilibria of the system are known, which is not guaranteed in general. In Section 5, we combine the results of Sections 3 and 4 to establish global asymptotic stability of componentwise positive equilibrium points for systems with $N = M$.

While our stability results require more structure for the $\mathcal{G}_{i,j}$'s than we require for existence of componentwise positive equilibria, we can prove global asymptotic stability of equilibrium points in the important case of Monod uptake functions, which are widely used in the chemostat literature. Moreover, when a componentwise nonnegative equilibria is known, we allow the constants D_j^s and D_i^x to be distinct. This contrasts with [45] which proves stability properties of coexistence equilibria for $N = 2$ or $N = 3$ when $D_j^s = D_i^x = D$ for all $i, j \in \{1, 2, \dots, N\}$. See also [50] for coexistence of multiple species in chemostats with one limiting substrate where the species and substrate levels do not necessarily converge to an equilibrium point but where the species levels instead are guaranteed to stay between two given positive bounds, and [1] for coexistence of any number of species along a periodic orbit in chemostats with four limiting resources.

Throughout Sections 3-5, we take D_i^x , D_j^s , and s_{in}^j as given constants, so there are no controls. However, our results for the case of given constant D_i^x , D_j^s , and s_{in}^j are key to proving our results for the controlled case. Specifically, we show in Section 6 how if we take the dilution rate and input nutrient concentrations as controllers, then there are many different componentwise positive equilibria that can be made globally asymptotically stable. This significantly extends our work [8], [25],[29]-[37] on control mechanisms that generate coexistence of multiple competing species in models of well mixed chemostats, which only cover models with one limiting substrate. We illustrate our work in simulations.

2 Definitions and Notation

We omit the arguments of our functions when they are clear. A point $(z_1, \dots, z_n) \in \mathbb{R}^n$ is *weakly positive* provided $z_i \geq 0$ for all $i \in \{1, 2, \dots, n\}$, and *positive* if $z_i > 0$ for all $i \in \{1, 2, \dots, n\}$. We adopt the convention that $\{p, \dots, q\} = \emptyset$ when $p > q$, and $\mathcal{B}_\varepsilon(y)$ is the open ball of radius $\varepsilon > 0$ centered at y in a Euclidean space whose dimension will be clear from the context. By C^1 of a function on a closed set \mathcal{S} , we mean C^1 on some open set containing \mathcal{S} .

Given a system $\dot{x} = \mathcal{F}(x)$ with state space $\mathcal{X} = (0, \infty)^p$ for some $p \in \mathbb{N}$, where \mathcal{F} is locally Lipschitz on the closure $\text{clos}(\mathcal{X})$ of \mathcal{X} , and a weakly positive equilibrium point Y_* (meaning $\mathcal{F}(Y_*) = 0$), we say that Y_* is *globally asymptotically stable relative to \mathcal{X}* provided (i) for each constant $\varepsilon > 0$, there is a constant $\delta > 0$ such that all trajectories of the system starting in $\mathcal{X} \cap \mathcal{B}_\delta(Y_*)$ remain in $\mathcal{B}_\varepsilon(Y_*)$ for all nonnegative times and (ii) all trajectories of the system starting in \mathcal{X} converge to Y_* asymptotically, i.e., the stability and attractiveness properties hold for all trajectories in \mathcal{X} .

Let ξ_* be any non-negative real number. If $\xi_* > 0$, then we define the function $\varphi_{\xi_*} : (-\xi_*, \infty) \rightarrow \mathbb{R}$ by

$$\varphi_{\xi_*}(\xi) = \xi - \xi_* \ln\left(1 + \frac{\xi}{\xi_*}\right) \quad (2)$$

and we define $\varphi_0 : (0, \infty) \rightarrow \mathbb{R}$ by $\varphi_0(\xi) = \xi$. The φ_{ξ_*} 's are all C^1 and radially unbounded (meaning $\lim_{\xi \rightarrow +\infty} \varphi_{\xi_*}(\xi) = \lim_{\xi \rightarrow -\xi_*} \varphi_{\xi_*}(\xi) = +\infty$ for all $\xi_* > 0$, while $\lim_{\xi \rightarrow +\infty} \varphi_0(\xi) = +\infty$). Also, since

$$\varphi'_{\xi_*}(\xi) = \frac{\xi}{\xi + \xi_*} \quad \forall \xi_* > 0 \text{ and } \xi \in (-\xi_*, \infty), \quad (3)$$

the φ_{ξ_*} 's for $\xi_* > 0$ are all positive definite (meaning 0 at 0, and positive at all other points in their domains). We use the positive points

$$\nu = (1, \dots, 1)^\top \in \mathbb{R}^N, \quad \Delta = (D_1^x, \dots, D_N^x)^\top, \quad \text{and} \quad \Theta = (D_1^s s_1^{in}, \dots, D_M^s s_M^{in})^\top. \quad (4)$$

For any $a, b \in \mathbb{R}^N$, we use $a \leq b$ to mean $a_i \leq b_i$ for all $i \in \{1, 2, \dots, N\}$. For each $i \in \{1, 2, \dots, N\}$, we let $P_i : \mathbb{R}^N \rightarrow \mathbb{R}^N$ be the function $P_i(a) = (p_1^i(a), \dots, p_N^i(a))$ whose components are defined by $p_k^i(a) = 0$ if $k \neq i$ and $p_i^i(a) = a_i$ for all $a = (a_1, \dots, a_N) \in \mathbb{R}^N$. Let $Q_i : \mathbb{R}^N \rightarrow \mathbb{R}^N$ be the function defined by $Q_i(a) = a - P_i(a)$. We use $C = [c_{i,j}]$ to denote the matrix with generic entry $c_{i,j}$ in its i th row and j th column. The following well known result is called Barbalat's lemma [44, p.205]: If $\lambda : [0, \infty) \rightarrow \mathbb{R}$ is uniformly continuous and $\lim_{p \rightarrow \infty} \int_0^p \lambda(r) dr$ exists and is finite, then $\lambda(t) \rightarrow 0$ as $t \rightarrow \infty$.

Some of what follows uses Brouwer degree theory, which we review next; see [13, pp. 202-207] or [44, pp. 101-105] for more on degree theory. Consider a C^1 function $f : \text{clos}(\mathcal{S}) \rightarrow \mathbb{R}^n$ where $\mathcal{S} \subseteq \mathbb{R}^n$ is bounded and open, and a point $p \in \mathbb{R}^n$. If there does not exist a point in the boundary $x \in \partial\mathcal{S}$ such that $f(x) = p$, and if the determinant $\det\{J_f\}$ of the Jacobian of f is nonzero at all points $x \in f^{-1}(p)$, then the *Brouwer degree* of f with respect to p is

$$d(f, p, \mathcal{S}) = \sum_{x \in f^{-1}(p) \cap \mathcal{S}} \text{sgn}(\det\{J_f\}(x)), \quad (5)$$

where sgn is defined by $\text{sgn}(q) = 1$ if $q > 0$ and $\text{sgn}(q) = -1$ if $q < 0$. The Inverse Function Theorem guarantees that the sum is over a finite set, so the degree is well defined. One can extend the definition of degree to points p that admit values $x \in f^{-1}(p)$ such that $\det\{J_f\}(x) = 0$, as follows. If f admits a value $x \in f^{-1}(p)$ such that $\det\{J_f\}(x) = 0$, then set $d(f, p, \mathcal{S}) = \lim_{p_j \rightarrow p} d(f, p_j, \mathcal{S})$ where $\{p_j\}$ is any sequence of points in \mathcal{S} converging to p such that $\det\{J_f\}(x) \neq 0$ for all $x \in f^{-1}(p_j)$. Such sequences $\{p_j\}$ exist by Sard's Theorem. This gives the desired extension of degree, and $f(x) = p$ admits a solution $x \in \mathcal{S}$ when $d(f, p, \mathcal{S}) \neq 0$. We also use the *homotopy invariance* property for C^1 functions $H : \text{clos}(\mathcal{S}) \times [0, 1] \rightarrow \mathbb{R}^n$, which states that if $p \in \mathbb{R}^n$ is such that there is no pair $(x, t) \in (\partial\mathcal{S}) \times [0, 1]$ such that $H(x, t) = p$, then the function $\mathcal{L} : [0, 1] \rightarrow \mathbb{R}$ defined by $\mathcal{L}(t) = d(H(\cdot, t), p, \mathcal{S})$ is constant.

3 Existence of Positive Equilibrium Points

3.1 Statement of Result

We first consider the special case

$$\begin{cases} \dot{s}_j &= D_j^s (s_j^{in} - s_j) - \sum_{i=1}^N \mathcal{G}_{i,j}(S) x_i, \quad 1 \leq j \leq N \\ \dot{x}_i &= \left[-D_i^x + \sum_{j=1}^N \eta_{i,j} \mathcal{G}_{i,j}(S) \right] x_i, \quad 1 \leq i \leq N \end{cases} \quad (6)$$

of (1) where $N = M$. We introduce these assumptions:

Assumption 1 For all $i, j, k \in \{1, 2, \dots, N\}$, the function $\mathcal{G}_{i,j}$ is C^1 on $[0, \infty)^N$, $\mathcal{G}_{i,j}(S) > 0$ for all $S \in (0, \infty)^N$, $(\partial\mathcal{G}_{i,j}/\partial s_k)(S) \geq 0$ for all $S \in [0, \infty)^N$, and $(\partial\mathcal{G}_{i,i}/\partial s_i)(mP_i(\nu)) > 0$ for all $m > 0$. Also, $\mathcal{G}_{i,j}(Q_j(S)) = 0$ for all i, j , and $S \in [0, \infty)^N$. \square

Assumption 2 There exist constants

$$B \in \left(0, \min_{i \in \{1, 2, \dots, N\}} s_i^{in}\right) \quad \text{and} \quad \epsilon \in (0, B) \quad (7)$$

such that

$$\sum_{j=1}^N \eta_{i,j} \mathcal{G}_{i,j}(BP_i(\nu)) > D_i^x \quad (8)$$

and

$$\sum_{j=1}^N \eta_{i,j} \mathcal{G}_{i,j}(BQ_i(\nu) + \epsilon P_i(\nu)) < D_i^x \quad (9)$$

hold for all $i \in \{1, 2, \dots, N\}$. Also,

$$\sum_{i=1, i \neq k}^N \frac{\mathcal{G}_{i,k}(S) D_i^s (s_i^{in} - \epsilon)}{\mathcal{G}_{i,i}(S)} < D_k^s (s_k^{in} - B) \quad (10)$$

holds for all $k \in \{1, 2, \dots, N\}$ and all $S \in [\epsilon, B]^N$. \square

We prove the following:

Theorem 1 *If (6) satisfies Assumptions 1-2, then it admits a positive equilibrium point.* \square

Remark 1 Assumption 1 includes the important cases where each $\mathcal{G}_{i,j}$ takes the Monod form $\mathcal{G}_{i,j}(S) = c_{i,j} s_j / (1 + g_j s_j)$ or the Tessier form

$$\mathcal{G}_{i,j}(S) = c_{i,j} s_j (1 - \exp(-s_j/g_j)) \quad (11)$$

for positive constants $c_{i,j}$ and g_j . Roughly speaking, conditions (8)-(9) mean that the growth of each species x_i depends primarily on the substrate s_i . Similarly, condition (10) basically says that each substrate s_i is consumed primarily by species x_i because $\mathcal{G}_{i,i}$ is larger relative to $\mathcal{G}_{i,k}$ for $i \neq k$. Assumption 2 resembles a perturbation result that would say the the model is close to the juxtaposition of N models with one species and one nutrient, but it is not a perturbation condition because there is no stipulation that B must be small. \square

3.2 Proof of Theorem 1

We first outline the steps of the proof. We first prove that there exists a point $S^s = (s_1^s, \dots, s_N^s) \in (\epsilon, B)^N$ such that

$$\sum_{j=1}^N \eta_{i,j} \mathcal{G}_{i,j}(S^s) = D_i^x \quad \forall i \in \{1, 2, \dots, N\}. \quad (12)$$

Then we prove that the system of equations

$$\sum_{i=1}^N \mathcal{G}_{i,j}(S^s) x_i + D_j^s s_j^s = D_j^s s_j^{in}, \quad 1 \leq j \leq N \quad (13)$$

has a solution $X^s = (x_{s1}, x_{s2}, \dots, x_{sN}) \in (0, \infty)^N$. This will give the positive equilibrium $Z^s = (S^s, X^s)$ of (6).

First Step. Existence of S^s . Consider the compact set $\mathcal{C} = [\epsilon, B]^N$ and the C^1 function $H : \mathcal{C} \times [0, 1] \rightarrow \mathbb{R}^N$ defined by $H(S, l) = (H_1(S, l), \dots, H_N(S, l))^\top$, where

$$H_i(S, l) = \sum_{j=1}^N \eta_{i,j} \mathcal{G}_{i,j}(lQ_i(S) + P_i(S)) . \quad (14)$$

One easily checks that there is no pair $(S, l) \in (\partial\mathcal{C}) \times [0, 1]$ such that $H(S, l) = \Delta$, where Δ is from (4). To see why, notice that if $S_a = (s_{a1}, \dots, s_{aN}) \in \partial\mathcal{C}$ were any point that admits an $i \in \{1, 2, \dots, N\}$ such that $s_{ai} = \epsilon$, then $lQ_i(S_a) + P_i(S_a) \leq BQ_i(\nu) + \epsilon P_i(\nu)$ componentwise for all $l \in [0, 1]$. Since the $\mathcal{G}_{i,j}$'s are non-decreasing in each component of S , it follows from (9) that $H_i(S_a, l) < D_i^x$. Therefore, $H(S_a, l) \neq \Delta$. Next, consider a point $S_b = (s_{b1}, \dots, s_{bN}) \in \partial\mathcal{C}$ that admits an $i \in \{1, 2, \dots, N\}$ such that $s_{bi} = B$. Then $BP_i(\nu) \leq lQ_i(S_b) + P_i(S_b)$ for each $l \in [0, 1]$. Since the $\mathcal{G}_{i,j}$'s are non-decreasing in each component, (8) gives $H_i(S_b, l) > D_i^x$, so $H(S_b, l) \neq \Delta$.

Since there is no pair $(S, l) \in (\partial\mathcal{C}) \times [0, 1]$ such that $H(S, l) = \Delta$, it follows from the homotopy invariance property that the Brouwer degrees satisfy

$$d(H(\cdot, 0), \Delta, (\epsilon, B)^N) = d(H(\cdot, 1), \Delta, (\epsilon, B)^N) . \quad (15)$$

Also, $H(S, 0) = (\gamma_1(s_1), \dots, \gamma_N(s_N))^\top$, where $\gamma_i(m) = \sum_{j=1}^N \eta_{i,j} \mathcal{G}_{i,j}(mP_i(\nu))$ for $i = 1, 2, \dots, N$. Since Assumption 1 gives $\gamma'_i(r) > 0$ for all $r > 0$ and all $i \in \{1, 2, \dots, N\}$, and since (8)-(9) give $\gamma_i(B) > D_i^x > \gamma_i(\epsilon)$ for all $i \in \{1, 2, \dots, N\}$, it follows that the equation $H(S, 0) = \Delta$ admits a unique solution $S_p \in (\epsilon, B)^N$. Since $\gamma'_i(r) > 0$ for all $r > 0$ and all $i \in \{1, 2, \dots, N\}$, the determinant of the Jacobian matrix of $H(\cdot, 0)$ at the point S_p is positive, so $d(H(\cdot, 0), \Delta, (\epsilon, B)^N) = 1$. It follows from (15) that there is a solution $S^s \in (\epsilon, B)^N$ of the equation $H(S, 1) = \Delta$, which satisfies (12).

Second Step. Existence of X^s . We introduce the set $\mathcal{E} = [0, A]^N$, where

$$A = \max_{m \in \{1, 2, \dots, N\}} \frac{D_m^s s_m^{in}}{\mathcal{G}_{m,m}(S^s)} + 1 . \quad (16)$$

We define $F : \mathcal{E} \times [0, 1] \rightarrow \mathbb{R}^N$ by $F(X, l) = (F_1(X, l), \dots, F_N(X, l))^\top$ and

$$F_k(X, l) = \sum_{i=1, i \neq k}^N l \mathcal{G}_{i,k}(S^s) x_i + \mathcal{G}_{k,k}(S^s) x_k + D_k^s s_k^s \quad (17)$$

for $k = 1, 2, \dots, N$ and $X = (x_1, \dots, x_N)$, and we proceed by contradiction.

Suppose that there were a pair $(k, l) \in \{1, 2, \dots, N\} \times [0, 1]$, and a point $X_e \in \mathcal{E}$ whose k th component is equal to A , such that $F(X_e, l) = \Theta$, where Θ be the constant vector in (4). Since Assumption 1 ensures that $\mathcal{G}_{k,k}(S^s) > 0$, it follows from (16) that $F_k(X_e, l) \geq \mathcal{G}_{k,k}(S^s)A > D_k^s s_k^{in}$. Therefore $F(X_e, l) \neq \Theta$. Next suppose that there were a pair $(k, l) \in \{1, 2, \dots, N\} \times [0, 1]$, and a point $X_f = (x_{f1}, \dots, x_{fN}) \in \mathcal{E}$ whose k th component is 0, such that $F(X_f, l) = \Theta$. Then

$$\begin{aligned} F_k(X_f, l) &= \sum_{i=1, i \neq k}^N l \mathcal{G}_{i,k}(S^s) x_{fi} + D_k^s s_k^s \quad \text{and} \\ F_m(X_f, l) &= \sum_{i=1, i \neq m}^N l \mathcal{G}_{i,m}(S^s) x_{fi} + \mathcal{G}_{m,m}(S^s) x_{fm} + D_m^s s_m^s \end{aligned} \quad (18)$$

for all $m \in \{1, 2, \dots, N\} \setminus \{k\}$. Hence, $D_m^s s_m^{in} = F_m(X_f, l) \geq \mathcal{G}_{m,m}(S^s) x_{fm} + D_m^s s_m^s$ for all $m \in \{1, 2, \dots, N\} \setminus \{k\}$. Since $S^s \in (\epsilon, B)^N$, Assumptions 1-2 imply that $\mathcal{G}_{m,m}(S^s) > 0$ and $s_m^{in} > B > s_m^s > \epsilon$ for all $m \in \{1, 2, \dots, N\} \setminus \{k\}$. This gives $x_{fm} \leq \{D_m^s s_m^{in} - D_m^s s_m^s\} / \mathcal{G}_{m,m}(S^s)$ for all $m \in \{1, 2, \dots, N\} \setminus \{k\}$, which we can combine with (18) to get

$$F_k(X_f, l) \leq \sum_{i=1, i \neq k}^N \mathcal{G}_{i,k}(S^s) \frac{D_i^s s_i^{in} - D_i^s \epsilon}{\mathcal{G}_{i,i}(S^s)} + D_k^s B . \quad (19)$$

Hence, (10) gives $F_k(X_f, l) < D_k^s s_k^{in}$, so $F(X_f, l) \neq \Theta$, so there is no pair $(X, l) \in (\partial\mathcal{E}) \times [0, 1]$ such that $F(X, l) = \Theta$.

We deduce from the homotopy invariance property that

$$d(F(\cdot, 0), \Theta, (0, A)^N) = d(F(\cdot, 1), \Theta, (0, A)^N). \quad (20)$$

Next, observe that for all $j \in \{1, 2, \dots, N\}$, we have $F_j(X, 0) = \mathcal{G}_{j,j}(S^s)x_j + D_j^s s_j^s = D_j^s s_j^{in}$ when $x_j = D_j^s(s_j^{in} - s_j^s)/\mathcal{G}_{j,j}(S^s)$. Since $\mathcal{G}_{j,j}(S^s) > 0$ for all j , it follows that the equation $F(X, 0) = \Theta$ admits exactly one solution in $(0, A)^N$. Arguing as we did in the first step of our proof, one can easily prove that $d(F(\cdot, 0), \Theta, (0, A)^N) = 1$, so (20) gives $d(F(\cdot, 1), \Theta, (0, A)^N) = 1$. Hence, (13) admits a solution $X^s \in (0, A)^N$, as claimed.

4 Lyapunov Approach to Prove Global Asymptotic Stability

4.1 Assumptions and Result

We establish a global asymptotic stability result for a specific family of systems (1). We do not assume that $N = M$, but do assume that (i) a stability condition holds for a known weakly positive equilibrium point, (ii) the functions $\mathcal{G}_{i,j}$ are all Monod functions depending only on s_j , (iii) the yield coefficients $\eta_{i,j}$ are all equal to 1 (but see Remark 3 for analogous results for cases where the yield factors are not necessarily all equal 1), and (iv) the half saturation constants $1/g_j$ are all identical for all the consumption rates of a given substrate by all species. Condition (iv) is not very restrictive when the species are not too dissimilar. In particular, we assume in this section that the resources are non-interacting.

Therefore, we assume that

$$\mathcal{G}_{i,j}(S) = \frac{c_{i,j}s_j}{1+g_j s_j} \quad (21)$$

where $g_j > 0$ and $c_{i,j} > 0$ are constants for all i and j . The system we consider is then

$$\begin{cases} \dot{s}_j &= D_j^s(s_j^{in} - s_j) - \sum_{i=1}^N c_{i,j} \frac{s_j x_i}{1+g_j s_j}, \quad 1 \leq j \leq M \\ \dot{x}_i &= \left[-D_i^x + \sum_{j=1}^M c_{i,j} \frac{s_j}{1+g_j s_j} \right] x_i, \quad 1 \leq i \leq N. \end{cases} \quad (22)$$

To ease the analysis of its stability properties, we introduce some notation. We use the functions

$$\Gamma_k(S) = D_k^x - \sum_{l=1}^M c_{k,l} \frac{s_l}{1+g_l s_l}, \quad 1 \leq k \leq N, \quad (23)$$

which gives the net decay rate of species x_k . Let L_k denote the k th row of $C = [c_{i,j}] \in \mathbb{R}^{N \times M}$ and C_{j_1, \dots, j_a}^b denote the submatrix of C that is obtained by keeping only the rows L_{j_1}, \dots, L_{j_a} . For instance,

$$C_{1,2}^b = \begin{bmatrix} L_1 \\ L_2 \end{bmatrix}.$$

We give sufficient conditions that ensure that (22) has a weakly positive globally asymptotically stable equilibrium point relative to $(0, \infty)^{M+N}$. Recall that a *bipartition* $\{E_1, E_2\}$ of $\{1, 2, \dots, N\}$ is any pair of sets E_1 and E_2 (one of which could be empty) such that $E_1 \cup E_2 = \{1, 2, \dots, N\}$ and $E_1 \cap E_2 = \emptyset$. Also, a matrix M is *right invertible* provided there is a matrix T such that MT is an identity matrix. We assume:

Assumption 3 There are a weakly positive equilibrium point $E_* = (S_*, X_*) \in \mathbb{R}^M \times \mathbb{R}^N$ for (22) and a bipartition $\{E_1, E_2\}$ of $\{1, 2, \dots, N\}$ such that (i) $\Gamma_k(S_*) = 0$ for all $k \in E_1$, and $\Gamma_k(S_*) > 0$ for all $k \in E_2$ and (ii) the matrix C_{j_1, \dots, j_q}^b with $E_1 = \{j_1, \dots, j_q\}$ is right invertible. \square

We can prove:

Theorem 2 Let (22) satisfy Assumption 3. Then E_* is a globally asymptotically stable equilibrium point for (22) relative to $(0, \infty)^{M+N}$. \square

Remark 2 If Assumption 3 holds, and if we set $S_* = (s_{1*}, \dots, s_{M*})$, then $s_{j*} > 0$ for all $j \in \{1, 2, \dots, M\}$, because $D_j^s s_j^{in} > 0$ for all $j \in \{1, 2, \dots, M\}$. Also, $x_{k*} = 0$ for all $k \in E_2$, since $\Gamma_k(S_*) > 0$ and $\dot{x}_k = -\Gamma_k(S_*)x_k$ for all $k \in E_2$. Numerical simulations may help determine whether Assumption 3 holds. Indeed, if simulations suggest that (22) has a globally asymptotically stable equilibrium point relative to $(0, \infty)^{2N}$, then they suggest where approximately the equilibrium point is in $[0, \infty)^N$. Then one can guess the corresponding sets E_1 and E_2 and check whether Assumption 3 holds for this bipartition. \square

4.2 Proof of Theorem 2

By renumbering the i 's as necessary, we assume without loss of generality that there exists $q \in \{1, 2, \dots, N\}$ such that $E_1 = \{1, 2, \dots, q\}$ and $E_2 = \{q+1, \dots, N\}$. We set

$$K_j(p) = D_j^s + \sum_{i=1}^N c_{i,j} \frac{x_{i*}}{1+g_j s_{j*}} \frac{1}{1+g_j p}, \quad 1 \leq j \leq M. \quad (24)$$

Set $\tilde{x}_j = x_j - x_{j*}$ for $j = 1, \dots, N$; $\tilde{X} = (\tilde{x}_1, \dots, \tilde{x}_N)$; $\tilde{s}_j = s_j - s_{j*}$ for $j = 1, 2, \dots, M$; and $\tilde{S} = (\tilde{s}_1, \dots, \tilde{s}_M)$. Since E_* is an equilibrium point of (22), we easily get

$$\dot{\tilde{s}}_j = -D_j^s \tilde{s}_j + \sum_{i=1}^N c_{i,j} \left(x_{i*} \frac{s_{j*}}{1+g_j s_{j*}} - x_i \frac{s_j}{1+g_j s_j} \right) = -K_j(s_j) \tilde{s}_j - \sum_{i=1}^N c_{i,j} \frac{s_j}{1+g_j s_j} \tilde{x}_i \quad (25)$$

for all $j \in \{1, 2, \dots, M\}$. Hence, simple calculations give

$$\begin{cases} \dot{\tilde{s}}_j = -K_j(s_j) \tilde{s}_j - \sum_{i=1}^N c_{i,j} \frac{s_j \tilde{x}_i}{1+g_j s_j}, & 1 \leq j \leq M, \\ \dot{\tilde{x}}_k = \left[-\Gamma_k(S_*) + \sum_{l=1}^M \frac{c_{k,l}}{1+g_l s_{l*}} \frac{\tilde{s}_l}{1+g_l s_l} \right] x_k, & 1 \leq k \leq N. \end{cases} \quad (26)$$

Set

$$U_f(\tilde{S}, \tilde{X}) = \sum_{j=1}^M \frac{1}{1+g_j s_{j*}} \varphi_{s_{j*}}(\tilde{s}_j) + \sum_{k=1}^N \varphi_{x_{k*}}(\tilde{x}_k), \quad (27)$$

where the functions φ_{ξ_*} are defined in (2). Then U_f is continuously differentiable on its domain

$$\mathcal{X} = \{(\tilde{S}, \tilde{X}) : \tilde{s}_i > -s_{i*} \forall i \in \{1, 2, \dots, M\} \text{ and } \tilde{x}_m > -x_{m*} \forall m \in \{1, 2, \dots, N\}\}.$$

Also, \mathcal{X} is a positively invariant set for (26) because $(0, \infty)^{M+N}$ is positively invariant for (22). Recalling (3), it follows that the time derivative of U_f along all trajectories of (26) in \mathcal{X} is

$$\begin{aligned} \dot{U}_f &= \sum_{j=1}^M \frac{1}{1+g_j s_{j*}} \frac{\tilde{s}_j \dot{\tilde{s}}_j}{s_j} + \sum_{k=1}^N \frac{\tilde{x}_k \dot{\tilde{x}}_k}{x_k} \\ &= -\sum_{j=1}^M \frac{K_j(s_j)}{(1+g_j s_{j*}) s_j} \tilde{s}_j^2 - \sum_{j=1}^M \frac{1}{1+g_j s_{j*}} \frac{\tilde{s}_j}{1+g_j s_j} \sum_{i=1}^N c_{i,j} \tilde{x}_i - \sum_{k=1}^N \Gamma_k(S_*) \tilde{x}_k + \sum_{k=1}^N \tilde{x}_k \sum_{l=1}^M \frac{c_{k,l}}{1+g_l s_{l*}} \frac{\tilde{s}_l}{1+g_l s_l} \\ &= -\sum_{j=1}^M \frac{K_j(s_j)}{(1+g_j s_{j*}) s_j} \tilde{s}_j^2 - \sum_{k=q+1}^N \Gamma_k(S_*) \tilde{x}_k, \end{aligned} \quad (28)$$

where the last equality follows because Assumption 3 and our renumbering imply that $\Gamma_k(S_*) = 0$ for all $k \in E_1 = \{1, 2, \dots, q\}$. As we saw in Remark 2,

$$x_{m*} = 0 \quad \forall m \in E_2 = \{q+1, \dots, N\}. \quad (29)$$

It follows from (28) and the forward invariance of \mathcal{X} for (26) that $\dot{U}_f \leq 0$ for all $t \geq 0$ along all trajectories of (26) starting in \mathcal{X} . This condition resembles the assumptions of LaSalle Invariance, but we cannot apply LaSalle Invariance directly, because we do not necessarily have $0 \in \mathcal{X}$. However, our stability proof is strongly reminiscent of LaSalle Invariance.

We integrate $\dot{U}_f \leq 0$ over $[0, t]$ for any $t \geq 0$ to get

$$U_f(\tilde{S}(t), \tilde{X}(t)) \leq U_f(\tilde{S}(0), \tilde{X}(0)) . \quad (30)$$

This gives local stability of E_* . Hence, the global asymptotic stability property will follow once we prove attractivity of the equilibrium. To prove the attractivity, we first use (28) and Barbalat's Lemma to show that

$$\lim_{t \rightarrow +\infty} \tilde{s}_j(t) = 0, \quad \lim_{t \rightarrow +\infty} \tilde{x}_i(t) = 0, \quad \text{and} \quad \lim_{t \rightarrow +\infty} \dot{\tilde{s}}_j(t) = 0 \quad \forall j \in \{1, 2, \dots, M\} \quad \text{and} \quad \forall l \in \{q+1, \dots, N\} \quad (31)$$

for all trajectories of (26) in \mathcal{X} . Then we use the right invertibility of $C_{1, \dots, q}^b$ to prove that the remaining components $\tilde{x}_1(t), \dots, \tilde{x}_q(t)$ all converge to zero. The details are as follows.

By integrating (28) and using the fact that U_f is nonnegative valued, we deduce that for all $t \geq 0$,

$$U_f(\tilde{S}(0), \tilde{X}(0)) \geq \int_0^t \left(\sum_{j=1}^M \frac{K_j(s_j(\ell)) \tilde{s}_j(\ell)^2}{(1 + g_j s_{j*}) s_j(\ell)} + \sum_{k=q+1}^N \Gamma_k(S_*) \tilde{x}_k(\ell) \right) d\ell. \quad (32)$$

The inequality (30) and the structure of (26) imply that $\dot{\tilde{S}}, \dot{\tilde{X}}$ and \tilde{S} are uniformly continuous for each trajectory $(\tilde{S}, \tilde{X})(\ell)$ of (26), and that there is a constant $c_o > 0$ such that

$$\frac{K_j(s_j(\ell))}{(1 + g_j s_{j*}) s_j(\ell)} \geq c_o \quad \forall \ell \geq 0 \quad \text{and} \quad j \in \{1, 2, \dots, M\}.$$

Since $\Gamma_k(S_*) > 0$ for all $k \in \{q+1, \dots, N\}$, it follows from (29), (32), and Barbalat's lemma that (31) holds. Next observe that the first equation in (26) gives

$$\tilde{\Xi}(t) C_{1, \dots, q}^b = \left(\sum_{i=1}^q c_{i,1} \tilde{x}_i(t), \dots, \sum_{i=1}^q c_{i,M} \tilde{x}_i(t) \right) = W(t), \quad (33)$$

where $\tilde{\Xi}(t) = [\tilde{x}_1(t), \dots, \tilde{x}_q(t)] \in \mathbb{R}^{1 \times q}$, $W(t) = [w_1(t), \dots, w_M(t)] \in \mathbb{R}^{1 \times M}$, and

$$w_j(t) = \frac{1 + g_j s_j(t)}{s_j(t)} \left[-K_j(s_j(t)) \tilde{s}_j(t) - \dot{\tilde{s}}_j(t) \right] - \sum_{i=q+1}^N c_{i,j} \tilde{x}_i(t) \quad (34)$$

for all $j \in \{1, 2, \dots, M\}$. Applying the right inverse $\eta \in \mathbb{R}^{M \times q}$ from Assumption 3 to (33) gives $\tilde{\Xi}(t) = W(t)\eta$. Since (31) implies that $\lim_{t \rightarrow +\infty} \|W(t)\| = 0$, we get $\lim_{t \rightarrow +\infty} \|\tilde{\Xi}(t)\| = 0$. This equality, the definition of $\tilde{\Xi}$, and (31) give the attractivity, hence global asymptotic stability of the equilibrium E_* point of (22) relative to $(0, \infty)^{M+N}$.

Remark 3 If the positive yield constants $\eta_{i,j}$ in (6) can all be written in the form $\eta_{i,j} = \chi_i \lambda_j$ where χ_i and λ_j are positive constants (which is equivalent to requiring that all rows of $[\eta_{i,j}]$ are constant multiples of each other, and where we can assume that $\chi_1 = 1$ by scaling the λ_j 's), then we can transform (6) into a new system for which the yield constants in the new coordinates are all equal to one. In fact, if $\eta_{i,j} = \chi_i \lambda_j$ for all i and j in (6), and if we set $y_i = x_i / \chi_i$, $r_j = \lambda_j s_j$, $r_j^{in} = \lambda_j s_j^{in}$, $r = (r_1, \dots, r_M)^\top$, and $\mathcal{F}_{i,j}(r) = \chi_i \lambda_j \mathcal{G}_{i,j}(r_1 / \lambda_1, \dots, r_M / \lambda_M)$, then we get

$$\begin{cases} \dot{r}_j &= D_j^s (r_j^{in} - r_j) - \sum_{i=1}^N \mathcal{F}_{i,j}(r) y_i, \quad 1 \leq j \leq M \\ \dot{y}_i &= \left[-D_i^x + \sum_{j=1}^M \mathcal{F}_{i,j}(r) \right] y_i, \quad 1 \leq i \leq N. \end{cases} \quad (35)$$

The system (35) has the form (1) with $\eta_{i,j} = 1$ for all i and j , and therefore is covered by the preceding global asymptotic stability result. \square

5 Globally Asymptotically Stable Positive Equilibrium

5.1 Statement of Result

In this section, we combine Theorems 1-2 to establish the existence of a globally asymptotically stable positive equilibrium point for a family of systems of the form (22).

Theorem 3 Consider the system (22). Assume that $N = M$, that $C = [c_{i,j}]$ is invertible, and that there exist a constant $D > 0$ such that $D_j^s = D_i^x = D$ for all $i, j \in \{1, 2, \dots, N\}$ and positive constants B and ϵ satisfying (7) such that

$$\frac{c_{i,i}B}{1 + g_i B} > D \quad \forall i \in \{1, 2, \dots, N\}, \quad (36)$$

$$\frac{c_{i,i}\epsilon}{1 + g_i \epsilon} + \sum_{j=1, j \neq i}^N \frac{c_{i,j}B}{1 + g_j B} < D \quad \forall i \in \{1, 2, \dots, N\}, \text{ and} \quad (37)$$

$$\sum_{i=1, i \neq k}^N \frac{c_{i,k}(1 + g_i \epsilon)}{c_{i,i}(1 + g_k B)} \frac{s_i^{in} - \epsilon}{s_k^{in} - B} < \frac{\epsilon}{B} \quad \forall k \in \{1, 2, \dots, N\}. \quad (38)$$

Then (22) admits a globally asymptotically stable positive equilibrium point relative to $(0, \infty)^{2N}$. \square

Remark 4 Under the assumptions of Theorem 3, we can use the expressions for the growth functions (21) to derive the components of the positive equilibrium point for (22). In fact, we can use the formulas for \dot{x}_i and the invertibility of C to solve for $s_l / \{1 + g_l s_l\}$ and therefore also for s_l for $l = 1, \dots, N$ that make the terms in brackets in (22) all equal to zero. Putting these values in the formulas for \dot{s}_j and again using the invertibility of C gives the equilibrium values of the x_i 's that make all of the \dot{s}_j 's equal to zero. \square

5.2 Proof of Theorem 3

To prove Theorem 3, first check Assumptions 1-2. Then Theorem 1 gives a positive equilibrium point (S_*, X_*) for (22). Then apply Theorem 2 to show that (S_*, X_*) is globally asymptotically stable relative to $(0, \infty)^{2N}$. The details are as follows.

One checks that Assumptions 1-2 hold with $\eta_{i,j} \equiv 1$. Indeed, Assumption 1 holds because of the Monod structure (21) of the growth functions $\mathcal{G}_{i,j}$. Also, (36) implies that

$$\sum_{j=1}^N \mathcal{G}_{i,j}(BP_i(\nu)) = \mathcal{G}_{i,i}(BP_i(\nu)) > D \quad (39)$$

for all $i \in \{1, 2, \dots, N\}$. It follows that (8) is satisfied. Also, the inequality (37) and our choices of the $\mathcal{G}_{i,j}$'s and Q_i 's give

$$\mathcal{G}_{i,i}(\epsilon\nu) + \sum_{j=1, j \neq i}^N \mathcal{G}_{i,j}(Q_i(B\nu)) < D \quad (40)$$

for all $i \in \{1, 2, \dots, N\}$. Hence, since the functions $\mathcal{G}_{i,k}$ only depend on s_k , (9) holds.

The inequality (38) ensures that

$$\sum_{i=1, i \neq k}^N \frac{\frac{c_{i,k}B}{1+g_k B} D(s_i^{in} - \epsilon)}{\frac{c_{i,i}\epsilon}{1+g_i \epsilon}} = \sum_{i=1, i \neq k}^N \frac{c_{i,k}(1 + g_i \epsilon) B D(s_i^{in} - \epsilon)}{c_{i,i}\epsilon(1 + g_k B)} < D(s_k^{in} - B) \quad (41)$$

for $k = 1, 2, \dots, N$. We easily deduce that (10) is satisfied. Therefore, Assumption 2 is satisfied. Consequently, Theorem 1 implies that (22) admits a positive equilibrium point (S_*, X_*) . For all $k \in \{1, 2, \dots, N\}$, we have $\Gamma_k(S_*) = 0$, and C is invertible. It follows that Assumption 3 is satisfied. We deduce from Theorem 2 that (S_*, X_*) is a globally asymptotically stable equilibrium point of (22) relative to $(0, \infty)^{2N}$.

5.3 Simulation for Theorem 3

The assumptions of Theorem 3 hold with $M = N = 3$,

$$D = 2, \quad s_k^{in} = \frac{17}{4} \quad \forall k \in \{1, 2, 3\}, \quad (42)$$

$$c_{k,k} = 2 \quad \forall k \in \{1, 2, 3\}, \quad c_{i,k} = \frac{1}{12} \quad \text{for } i \neq k, \quad g_k = \frac{1}{4} \quad \forall k \in \{1, 2, 3\}, \quad B = 2, \quad \text{and } \epsilon = \frac{1}{4}. \quad (43)$$

We simulated (22) with (42)-(43) and the initial state $(0.5, 1, 1.5, 0.5, 1, 1.5)$, and obtained the curves in Figure 1. Our simulation illustrates the rapid convergence of the species and nutrient levels to the positive equilibrium point whose existence is guaranteed by Theorem 3.

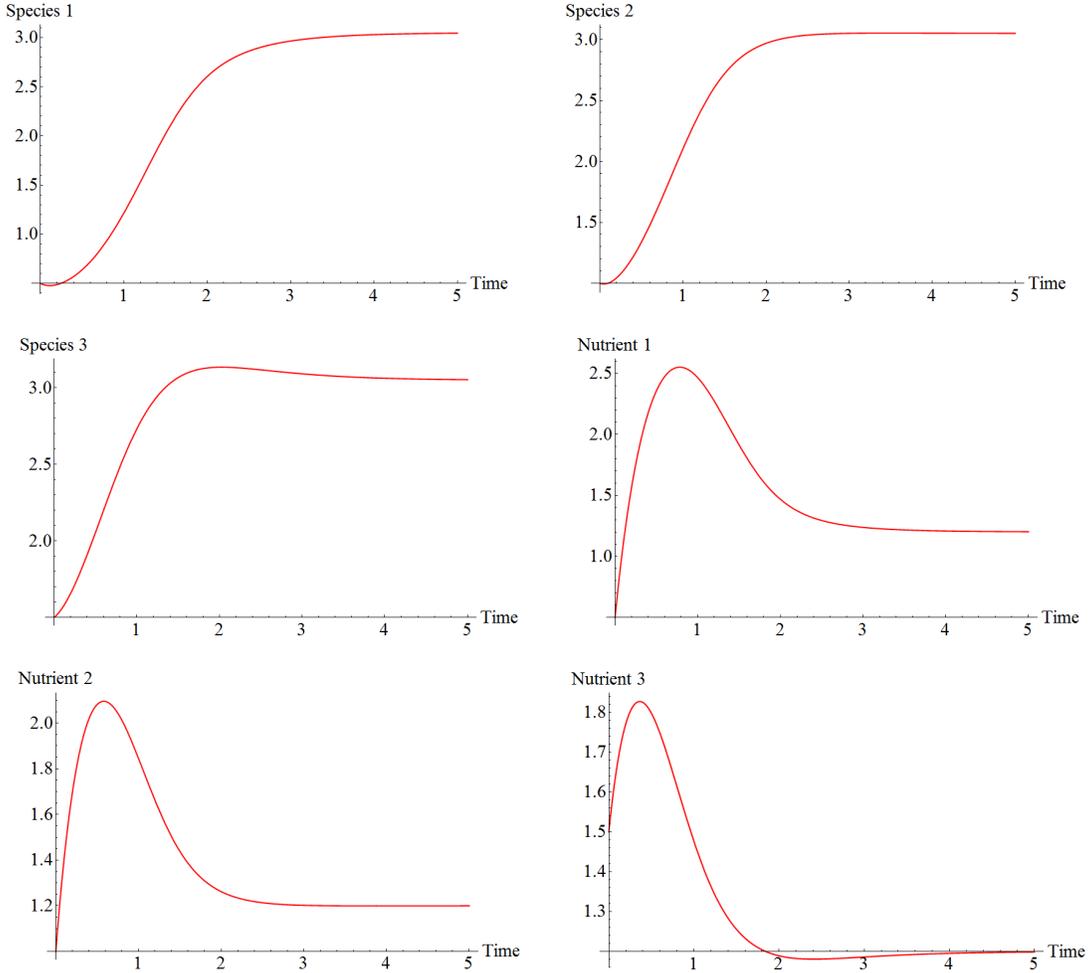


Figure 1: Simulation of (22) with $N = M = 3$ and (42)-(43).

6 Regulation of Species and Nutrient Levels

6.1 Statement of Result

In the previous sections, we took the dilution rate and input nutrient concentrations as given positive constants and showed asymptotic stability properties for certain positive equilibrium points. On the other hand, if D and each s_j^{in} can be chosen as controls, then there are many different possible positive equilibrium points that can be made globally asymptotically stable. In fact, we prove the following, where $\nu = (1, \dots, 1)^T \in \mathbb{R}^N$ as before:

Theorem 4 Assume that the system (22) with $M = N$ is associated with an invertible matrix $C = [c_{i,j}]$, and define $k_1, \dots, k_N \in \mathbb{R}$ by $C^{-1}\nu = (k_1, k_2, \dots, k_N)^\top$. Assume that $k_i > 0$ for all $i \in \{1, 2, \dots, N\}$. Let $\Xi_d = (\xi_1, \dots, \xi_N) \in (0, +\infty)^N$ be given and choose any constant

$$D \in \left(0, \min_{j \in \{1, 2, \dots, N\}} \frac{1}{k_j g_j}\right) \quad (44)$$

and

$$\varpi_j = \frac{Dk_j}{1 - Dk_j g_j} \quad \forall j \in \{1, 2, \dots, N\}. \quad (45)$$

Then (22) with the dilution rate $D_j^s \equiv D_i^x \equiv D$ and the constants

$$s_j^{in} = \varpi_j + k_j \sum_{i=1}^N c_{i,j} \xi_i, \quad j = 1, 2, \dots, N \quad (46)$$

admits $(\varpi_1, \dots, \varpi_N, \xi_1, \dots, \xi_N)$ as a globally asymptotically stable positive equilibrium relative to $(0, \infty)^{2N}$. \square

6.2 Proof of Theorem 4

Our choice of D implies that the constants in (45) are well-defined and positive, and that

$$\frac{\varpi_l}{1 + g_l \varpi_l} = Dk_l \quad \forall l \in \{1, 2, \dots, N\}. \quad (47)$$

Therefore,

$$-D + \sum_{l=1}^N c_{i,l} \frac{\varpi_l}{1 + g_l \varpi_l} = -D + \sum_{l=1}^N c_{i,l} Dk_l = -D + D(c_{i,1} \dots c_{i,N}) C^{-1} \nu = 0 \quad (48)$$

for all $i \in \{1, 2, \dots, N\}$, and our choice (46) gives

$$Ds_j^{in} - D\varpi_j - D \sum_{i=1}^N c_{i,j} \xi_i \frac{\varpi_j}{D(1 + g_j \varpi_j)} = 0 \quad (49)$$

for all $j \in \{1, 2, \dots, N\}$. The equalities (48)-(49) imply that $(\varpi_1, \dots, \varpi_N, \xi_1, \dots, \xi_N)$ is a positive equilibrium point of (22). Since C is invertible, Theorem 2 implies that $(\varpi_1, \dots, \varpi_N, \xi_1, \dots, \xi_N)$ is a globally asymptotically stable equilibrium point of (22) relative to $(0, \infty)^{2N}$.

6.3 Simulation for Theorem 4

To illustrate Theorem 4, we again simulated (22) using the parameters (43), but instead of using the values (42) for the dilution rate and input nutrient concentration, we took $D = 4.333$ and $s_j^{in} = 5$ for $j = 1, 2, 3$. These controller values satisfy the requirements from Theorem 4 for stabilizing the species levels to $\xi_1 = \xi_2 = \xi_3 = 1$. We took the same initial states as in our first simulation. We obtained the curves in Figure 2 below. This illustrates the convergence of the species levels to the desired equilibrium states.

7 Conclusion

We used Brouwer degree and Lyapunov methods to prove results on the existence and asymptotic stability and stabilization of componentwise nonnegative equilibrium points for chemostats with two or more competing species and two or more limiting nutrients. They can inspire many other results for chemostats with multiple nutrients, such as extensions to chemostats with time delays and unknown perturbations [9, 43, 49]; see for example [17, 32] for results on stabilization of equilibrium points under time delays for two species chemostats with one limiting substrate based on small gain theory and Lyapunov-Krasovskii functionals, respectively. These extensions will be the subjects of further works.

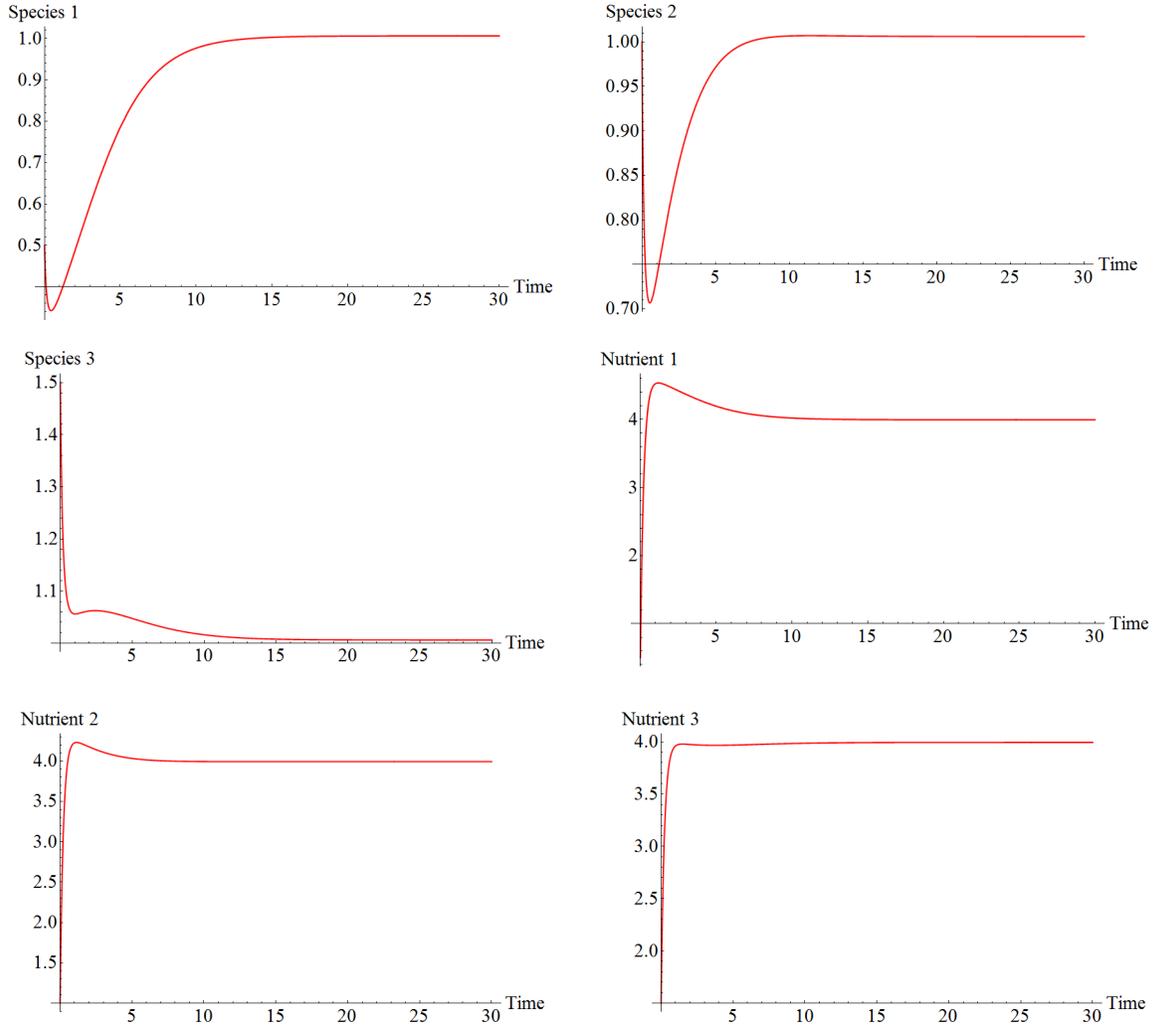


Figure 2: Simulation of (22) with $N = M = 3$ using the controllers $D = 4.333$ and $s_j^{in} = 5$ for $j = 1, 2, 3$ and the parameters (43).

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