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Stability and Robustness Analysis for a Multi-Species Chemostat Model with Uncertainties

Frédéric Mazenc Michael Malisoff Gonzalo Robledo

***Abstract*— We prove stability and robustness results for chemostat models with one substrate, an arbitrary number of species, a constant dilution rate, and constant inputs of the species. Unlike all previous works, we prove input-to-state stability under uncertainties in important cases where the controls are the input nutrient concentration and the species inputs. Our assumptions ensure global asymptotic stability for an equilibrium, which can allow persistence of multiple species, when the uncertainties are zero. We allow arbitrarily large bounds on the uncertainties in the species dynamics, and equilibria that can be in the boundary of the state space.**

***Index Terms*— Bioreactors, nonlinear, stability, robustness**

I. Introduction

The chemostat is a mathematical model and a laboratory device that is used for the continuous culture of microorganisms. Since its introduction in [14] and [16], it has been studied extensively, because of its vital role in ecology and microbiology as an ideal representation of microorganism growth, natural environments such as lakes, and wastewater treatment processes [1]. It is used in industrial applications that are of compelling engineering interest. See [18].

This has motivated our ongoing work (begun in [2], [3], [8], [9], [10], [11], [12], [13], and [17]) on methods to ensure desired asymptotic behaviors in chemostats, including the coexistence of multiple competing species, convergence to equilibria, or delay compensation. As noted in [18], the classical model of competition in the chemostat is

$$\begin{cases} \dot{s}(t) &= D[s_{\rm in} - s(t)] - \sum\limits_{i=1}^{n} Y_i^{-1}\mu_i(s(t))x_i(t) \\ \dot{x}_i(t) &= x_i(t)\mu_i(s(t)) - Dx_i(t),\ i = 1,\ldots,n \end{cases} \tag{1}$$

where $n \geq 2$ microbial species (with concentrations $x_1,\ldots,x_n$) compete for a nutrient with concentration s. The positive constants D and $s_{\rm in}$ are the dilution rate and input nutrient concentration, respectively, and Y_i is a positive yield constant related to the conversion of the substrate into biomass for each i. The μ_i's for $i = 1,\ldots,n$ are strictly increasing, satisfy $\mu_i(0) = 0$, and are assumed to be continuously differentiable; they describe the consumption of the nutrient by species i. The model assumes that the growth of species i is proportional to the nutrient consumption.

Well known results (e.g., [4] and [18]) imply that if the preceding conditions hold and $0 < \mu_n^{-1}(D) < \mu_{n-1}^{-1}(D) < \ldots < \mu_2^{-1}(D) < \mu_1^{-1}(D) < s_{\rm in}$, then the following competitive exclusion principle holds: $\lim_{t\to+\infty} s(t) = \mu_n^{-1}(D)$, $\lim_{t\to+\infty} x_n(t) = Y_n[s_{\rm in} - \mu_n^{-1}(D)]$, and $\lim_{t\to+\infty} x_i(t) = 0$ if $1 \leq i \leq n-1$. The preceding conditions imply that only the nth species persists, because it only needs the lowest nutrient concentration.

However, multiple species are often observed to persist in chemostats with one substrate, which motivated many works on ways to explain coexistence in chemostats. There are several approaches to explaining coexistence in bioreactor models, including models whose qualitative behavior and analytical treatment are considerably more complex than (1) and we refer to [2], [5], [7], [8], [11], [13], [15], and [19] without claiming completeness. Nevertheless, we will focus our attention on the approach from [17], which introduces a model with constant inputs $x_i^0 \geq 0$ of the ith competing species (for $i = 1,\ldots,n$) described by the system

$$\begin{cases} \dot{s}(t) = D[s_{\rm in} - s(t)] - \sum\limits_{i=1}^{n} Y_i^{-1}\mu_i(s(t))x_i(t) \\ \dot{x}_i(t) = x_i(t)\mu_i(s(t)) + D[x_i^0 - x_i(t)],\ 1 \leq i \leq n. \end{cases} \tag{2}$$

In [17], the authors obtained sufficient conditions ensuring the coexistence of multiple species. The work [17] used polytopic Lyapunov functions, which were also used in [3].

However, it is well known that chemostats can contain uncertainties (e.g., unmodeled features, or uncertainties in the input concentrations, which are common in applications). Therefore, an even more accurate model than (2) is

$$\begin{cases} \dot{s}(t) &= D[s_{\rm in} - s(t)] - \sum\limits_{i=1}^{n} \mu_i(s(t))x_i(t) + \delta_0(t) \\ \dot{x}_i(t) &= x_i(t)\mu_i(s(t)) \\ & \quad + D[x_i^0 - x_i(t)] + \delta_i(t),\ 1 \leq i \leq n, \end{cases} \tag{3}$$

where the μ_i's are as before, and the unknown measurable essentially bounded functions $\delta_i : [0,+\infty) \to [\underline{d}_i, \bar{d}_i]$ for $i = 0,1,\ldots,n$ represent uncertainties and have known upper and lower bounds $\bar{d}_i$ and $\underline{d}_i$, respectively, and where we used a change of coordinates (based on a scaling of the x_i's and x_i^0's) to remove the Y_i's. Two of our assumptions will be that $\underline{d}_0 > -Ds_{\rm in}$ and $\underline{d}_i \geq -Dx_i^0$ for $i = 1,2,\ldots,n$; see Section II for our assumptions. Therefore, all solutions of (3) with initial states $(s(0), x(0))$ in $\mathcal{X} = (0,+\infty)^{n+1}$ remain in $\mathcal{X}$ for all $t \geq 0$, so (3) has the state space $\mathcal{X}$, and (3) will be the subject of this paper.

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In the next section, we provide our theorem for (3), which uses $s_{\rm in}$ and the x_i^0's as controls. Our work is novel in its use of the model (3), which we believe has not been studied in the presence of nonzero uncertainties. Our new Lyapunov construction is the key ingredient for proving valuable input-to-state stability (ISS) robustness properties, which cannot be deduced from the polytopic Lyapunov functions from [17]. Also, the equilibria that we stabilize are in the boundary of $\mathcal{X}$ when at least one x_i^0 is 0, so the present paper covers a broad class of equilibria. Hence, this work provides a new theoretical result with valuable implications for future real time applications to bioprocess engineering.

II. Assumptions, Definitions, and Main Result

We will prove ISS properties for the dynamics for the error $\mathcal{E}(t) = (s(t) - s_*, x(t) - x_*)$ with respect to the disturbance vector $\delta = (\delta_0, \delta_1, \ldots, \delta_n)$, for a large class of possible equilibrium points $\mathcal{E}_* = (s_*, x_*)$, where (s, x) is the state of (3), $x_* = (x_{1*}, \ldots, x_{n*})$, and $x = (x_1, \ldots, x_n)$. The ISS framework is used extensively in engineering; see [6] for ISS for systems without state constraints. To allow state constraints, we use a variant of the usual ISS property.

To explain this variant, we first need two definitions. Let $\mathcal{K}_\infty$ be the set of all continuous strictly increasing unbounded functions $\gamma : [0, +\infty) \to [0, +\infty)$ such that $\gamma(0) = 0$; and let $\mathcal{KL}$ be the set of all continuous functions $\bar{\beta} : [0, +\infty) \times [0, +\infty) \to [0, +\infty)$ such that (i) for each $t \geq 0$, the function $f(s) = \bar{\beta}(s, t)$ is of class $\mathcal{K}_\infty$ and (ii) for each $s \geq 0$, the function $g(t) = \bar{\beta}(s, t)$ is nonincreasing and satisfies $\lim_{t\to+\infty} g(t) = 0$. By ISS of a system of the form $\dot{\mathcal{E}}(t) = \mathcal{F}(\mathcal{E}(t), \delta(t))$ with respect to a pair $(\mathcal{D}, \mathcal{S})$, we mean that there exist $\beta \in \mathcal{KL}$ and $\gamma \in \mathcal{K}_\infty$ such that $|\mathcal{E}(t)| \leq \beta(|\mathcal{E}(0)|, t) + \gamma(|\delta|_{[0,t]})$ holds for all $t \geq 0$, all solutions $\mathcal{E}(t)$ of this system that have initial states $\mathcal{E}(0) \in \mathcal{S}$, and all measurable essentially bounded functions $\delta : [0, +\infty) \to \mathcal{D}$. Here and in the sequel, $|\cdot|$ is the Euclidean norm, and $|\cdot|_{[0,t]}$ (resp., $|\cdot|_\infty$) is the essential supremum over $[0, t]$ for all $t \geq 0$ (resp., over $[0, +\infty)$). Assume:

Assumption 1: The μ_i's in (3) have the Monod form

$$\mu_i(s) = \tfrac{m_i s}{a_i + s} \text{ for } i = 1, 2, \ldots, n, \tag{4}$$

where the m_i's and a_i's are known positive constants. □

Assumption 2: The constants $s_* > 0$ and $s_{\rm in}$ are such that

$$\begin{aligned} &\mu_i(s_*) < D \text{ for } i = 1, 2, \ldots, n \\ &\text{and } s_{\rm in} = s_* + \sum_{i=1}^{n} \tfrac{\mu_i(s_*) x_i^0}{D - \mu_i(s_*)}, \end{aligned} \tag{5}$$

the x_i^0's are nonnegative constants, and $0 < D < \mu_n(s_{\rm in})$.□

From Assumption 2, we obtain $\mu_n(s_*) < \mu_n(s_{\rm in})$, so since μ_n is strictly increasing, it follows that $s_* \in (0, s_{\rm in})$. We can always satisfy Assumption 2 for all constants $D \in (0, m_n)$, by first fixing $s_* > 0$ such that $\mu_i(s_*) < D$ for all i, and then picking the x_i^0's to be large enough so that $D < \mu_n(s_{\rm in})$ and $s_{\rm in} > 0$, i.e., we view $s_{\rm in}$ as a constant control. By the symmetry of the system (3) in its components x_i, we can replace the condition $D < \mu_n(s_{\rm in})$ by the condition that $D < \mu_i(s_{\rm in})$ for any i, by renumbering the species. By Assumption 2, it follows that when the δ_i's in (3) are 0, the system (3) has the equilibrium $\mathcal{E}_* = (s_*, x_*)$, where

$$x_{i*} = \tfrac{D x_i^0}{D - \mu_i(s_*)} \text{ for } i = 1, ..., n. \tag{6}$$

We can allow many x_{i*}'s through different choices of x_i^0's, i.e., we also use the x_i^0's as controls. Since the x_i^0's are nonnegative, we have $\mathcal{E}_* \in [0, +\infty)^{n+1}$; and $\mathcal{E}_* \in (0, +\infty)^{n+1}$ when the x_i^0's are all positive. Our assumptions on the unknown measurable essentially bounded functions δ_i in (3) are as follows, where $\mathcal{P} = \{i \in \{1, 2, \ldots, n\} : x_i^0 > 0\}$:

Assumption 3: We have $\delta(t) \in [\underline{d}_0, \bar{d}_0] \times \ldots \times [\underline{d}_n, \bar{d}_n]$ for almost all $t \geq 0$, where the known constants $\underline{d}_i$ and $\bar{d}_i \geq 0$ are such that $D s_{\rm in} + \underline{d}_0 > 0$, $\bar{d}_0 < 0.5 D s_*$, and $D x_i^0 + \underline{d}_i > 0$ for all $i \in \mathcal{P}$, and $\underline{d}_i = 0$ for all $i \in \{1, 2, \ldots, n\} \setminus \mathcal{P}$. □

We can prove the following result, where $(s(t), x(t))$ is the state of (3):

Theorem 1: If Assumptions 1-3 hold, then for all constants $\underline{x} > 0$ and $\bar{s} \geq s_{\rm in}$, the dynamics for the error vector $\mathcal{E} = (s, x) - \mathcal{E}_*$ have the ISS property with respect to $(\mathcal{D}, \mathcal{S})$ with the disturbance set $\mathcal{D} = [\underline{d}_0, \bar{d}_0] \times \ldots \times [\underline{d}_n, \bar{d}_n]$ and $\mathcal{S} = \{\mathcal{E} : \mathcal{E} + \mathcal{E}_* \in (0, \bar{s}] \times (0, +\infty)^{n-1} \times (\underline{x}, +\infty)\}$. □

Before discussing our proof, we make several remarks about the novelty and value of our theorem.

Remark 1: Our choice of $\mathcal{S}$ in Theorem 1 corresponds to the requirement that $(s(0), x(0)) \in (0, \bar{s}] \times (0, +\infty)^{n-1} \times (\underline{x}, +\infty)$. However, since $\bar{s} \geq s_{\rm in}$ and $\bar{x} > 0$ are arbitrary, we conclude that when the δ_i's are zero, all solutions $(s(t), x(t))$ of (3) starting in $\mathcal{X} = (0, +\infty)^{n+1}$ remain in $\mathcal{X}$ at all positive times and satisfy $\lim_{t\to+\infty}(s(t), x(t)) = (s_*, x_*)$. This ensures persistence of the ith species for all $i \in \mathcal{P}$ (and $\lim_{t\to+\infty} x_i(t) = 0$ for all $i \in \{1, \ldots, n\} \setminus \mathcal{P}$). □

Remark 2: We do not restrict the values of $\bar{d}_i \geq 0$ for $i \geq 1$, so Theorem 1 ensures ISS under arbitrarily large sup norms on the δ_i's for $i \geq 1$. A key ingredient in our proof is a Lyapunov-like function V and a function $T_3 \in \mathcal{K}_\infty$ such that V satisfies the usual Lyapunov positive definiteness and decay conditions along all solutions $\mathcal{E}(t)$ of the error dynamics for all $t \geq T_3(|\mathcal{E}(0)|)$. Using V instead of the polytopic Lyapunov functions from [17] allows us to prove key ISS results that were beyond the scope of [17]. □

III. Sketch of Proof of Theorem 1

A. Preliminary State Bounds

Since (3) is forward complete on $\mathcal{X} = (0, +\infty)^{n+1}$, we can first fix any solution $(s(t), x(t))$ of (3) all of whose components are positive for all $t \geq 0$ for which $\mathcal{E}(0) \in \mathcal{S}$. Set $\bar{s}^\sharp = \bar{s} + (\bar{d}_0/D)$ and

$$(\tilde{s}, \tilde{x}) = (s - s_*, x - x_*). \tag{7}$$

Then Assumption 3 implies that $s(t) \leq \bar{s}^\sharp$ for all $t \geq 0$. We next produce functions $T_i \in \mathcal{K}_\infty$ for $i = 1, 2, 3$, whose class $\mathcal{K}_\infty$ properties will be used later to build an ISS estimate that is valid for all times $t \geq 0$, using three lemmas. Our first lemma is:

Lemma 1: If Assumptions 1-3 hold, then there is a $T_1 \in \mathcal{K}_\infty$ such that $s(t) \leq s_{\rm in} + (\bar{d}_0/D)$ for all $t \geq T_1(|\tilde{s}(0)|)$.□

Proof: (*Sketch.*) If there is a $t_l \geq 0$ such that $s(t_l) \leq s_{\rm in} + (\bar{d}_0/D)$, then for all $t > t_l$, we have $s(t) \leq s_{\rm in} + (\bar{d}_0/D)$. Next, consider the case where $s(0) > s_{\rm in} + (\bar{d}_0/D)$. Consider any $t \geq 0$ such that $\min_{\ell \in [0,t]} s(\ell) > s_{\rm in} + (\bar{d}_0/D)$. For any such t, we also have $\max_{\ell \in [0,t]} \dot{s}(\ell) < 0$. Then since $D < \mu_n(s_{\rm in})$, and since μ_n is nondecreasing and $Dx_n^0 + \underline{d}_n \geq 0$ and $s_* < s_{\rm in} \leq s(\ell)$ for all $\ell \in [0,t]$, we deduce from (3) that $\dot{x}_n(\ell) \geq 0$ and so also $x_n(\ell) \geq x_n(0) \geq \underline{x}$ for all $\ell \in [0,t]$, and $\dot{s}(\ell) \leq -\mu_n(s(\ell))x_n(\ell)$ for all $\ell \in [0,t]$, so

$$\begin{array}{rcl} t\mu_n(s_{\rm in})\underline{x} & \leq & \int_0^t \mu_n(s_{\rm in})x_n(\ell)\,{\rm d}\ell \\ & \leq & s(0) - s(t) \;\leq\; s(0) - s_* \;\leq\; |\tilde{s}(0)|. \end{array} \tag{8}$$

Hence, $t \leq |\tilde{s}(0)|/(\mu_n(s_{\rm in})\underline{x})$, so there is a $t_* \in [0, 2|\tilde{s}(0)|/(\mu_n(s_{\rm in})\underline{x})]$ such that $s(t_*) \leq s_{\rm in} + (\bar{d}_0/D)$. Hence, we can choose $T_1(r) = 2r/(\mu_n(s_{\rm in})\underline{x})$. ■

Set $\sigma(t) = s(t) + x_1(t) + \ldots + x_n(t)$ for all $t \geq 0$ and

$$C = 2\left(s_{\rm in} + \sum_{i=1}^n x_i^0 + \tfrac{1}{D}\sum_{i=0}^n \bar{d}_i\right) \tag{9}$$

and fix any constant $\lambda_1 > 1$. We prove:

Lemma 2: If Assumptions 1-3 hold, then there is a $T_2 \in \mathcal{K}_\infty$ such that $\sigma(t) \leq \lambda_1 C$ holds for all $t \geq T_2(|\mathcal{E}(0)|)$. □

Proof: (*Sketch.*) By (3), we have $\dot{\sigma}(t) \leq 0.5CD - D\sigma(t)$ for all $t \geq 0$. It follows that $\sigma(t) \leq u(t)$ for all $t \geq 0$, where u is the solution of the initial value problem

$$\dot{u}(t) = \tfrac{CD}{2} - \tfrac{1}{2}Du(t), \;\; u(0) = \sigma(0). \tag{10}$$

Since $\lambda_1 > 1$, we deduce that $\sigma(t) \leq u(t) \leq \lambda_1 C$ for all $t \geq 0$ if $\sigma(0) \in (0, \lambda_1 C]$. Hence, there exists a function $T_2^\flat \in \mathcal{K}_\infty$ such that $\sigma(t) \leq \lambda_1 C$ for all $t \geq T_2^\flat(\sigma(0))$ when $\sigma(0) > \lambda_1 C$. Therefore, the lemma will follow once we choose a function $T_2 \in \mathcal{K}_\infty$ such that $T_2(|\mathcal{E}(0)|) \geq T_2^\flat(\sigma(0))$ holds for all solutions of (3) such that $\sigma(0) > \lambda_1 C$.

To find T_2, first note that our formulas for σ and $s_{\rm in}$ give

$$\begin{array}{rcl} \sigma(0) & = & \tilde{s}(0) + \sum_{i=1}^n \tilde{x}_i(0) + s_* + \sum_{i=1}^n \frac{Dx_i^0}{D - \mu_i(s_*)} \\ & \leq & |\tilde{s}(0)| + \sum_{i=1}^n |\tilde{x}_i(0)| + s_{\rm in} + \sum_{i=1}^n x_i^0. \end{array} \tag{11}$$

We next consider two cases. Case 1: If $|\mathcal{E}(0)| \leq (s_{\rm in} + x_1^0 + \ldots + x_n^0)/(n+1)$, then the inequality in (11) gives $\sigma(0) \leq \lambda_1 C$, so this case does not produce any restriction on the allowable values of T_2. Case 2: If $|\mathcal{E}(0)| > (s_{\rm in} + x_1^0 + \ldots + x_n^0)/(n+1)$, then we use the fact that (11) gives $T_2^\flat((n+1)|\mathcal{E}(0)| + s_{\rm in} + x_1^0 + \ldots + x_n^0) \geq T_2^\flat(\sigma(0))$. Setting $a_* = (s_{\rm in} + x_1^0 + \ldots + x_n^0)/(n+1)$, we can then take

$$T_2(\ell) = T_1(\ell) + \left\{ \begin{array}{ll} (\ell/a_*)T_2^\flat\big(2(n+1)a_*\big), & 0 \leq \ell \leq a_* \\ T_2^\flat\big((n+1)(\ell + a_*)\big), & \ell > a_* \end{array} \right.$$

to satisfy our requirements. ■

We next fix any constant $\lambda_2 \in (0,1)$ and set

$$\underline{s}_\lambda = \lambda_2 \min\left\{ s_*, \frac{Ds_{\rm in} + \underline{d}_0}{D + \lambda_1 C \sum_{i=1}^n \frac{m_i}{a_i}} \right\} \tag{12}$$

and $\underline{x}_{i\lambda} = \lambda_2 \min\left\{x_{i*}, x_i^0 + (\underline{d}_i/D)\right\}$ for all i and prove:

Lemma 3: If Assumptions 1-3 hold, then there is a function $T_3 \in \mathcal{K}_\infty$ such that $s(t) \geq \underline{s}_\lambda$ and $x_i \geq \underline{x}_{i\lambda}$ hold for all $t \geq T_3(|\mathcal{E}(0)|)$ and all $i \in \mathcal{P}$. □

Proof: (*Sketch.*) For all $t \geq T_2(|\mathcal{E}(0)|)$, Lemma 2 gives $x_i(t) \leq \lambda_1 C$ for all $i \in \{1, 2, \ldots, n\}$. Hence, for all $t \geq T_2(|\mathcal{E}(0)|)$, (3) and our formula (4) for the μ_i's give

$$\dot{s}(t) \;\geq\; D(s_{\rm in} - s(t)) - \lambda_1 C \sum_{i=1}^n \tfrac{m_i s(t)}{a_i} + \underline{d}_0 \tag{13}$$

and

$$\dot{x}_i(t) \;\geq\; -Dx_i(t) + Dx_i^0 + \underline{d}_i \;\text{ for all } i \in \mathcal{P}. \tag{14}$$

The right side of (13) is bounded below by $(Ds_{\rm in} + \underline{d}_0)(1 - \lambda_2) > 0$ if t is such that $s(t) \leq \underline{s}_\lambda$. Also, for each $i \in \mathcal{P}$, the right side of (14) is bounded below by $(1 - \lambda_2)(Dx_i^0 + \underline{d}_i) > 0$ if t is such that $x_i(t) \leq \underline{x}_{i\lambda}$. Hence, for each $t_0 \geq 0$ such that $s(t_0) \geq \underline{s}_\lambda$, we have $s(t) \geq \underline{s}_\lambda$ for all $t \geq t_0$; and for each $i \in \mathcal{P}$, and for each $t_0 \geq 0$ such that $x_i(t_0) \geq \underline{x}_{i\lambda}$, we have $x_i(t) \geq \underline{x}_{i\lambda}$ for all $t \geq t_0$. Therefore', it suffices to choose $T_3 \in \mathcal{K}_\infty$ such that: (i) If $s(0) < \underline{s}_\lambda$, then $s(t) \geq \underline{s}_\lambda$ for some $t \in [0, T_3(|\mathcal{E}(0)|)]$ (which implies that $s(t) \geq \underline{s}_\lambda$ for all $t \geq T_3(|\mathcal{E}(0)|)$, by the preceding argument) and (ii) for each $i \in \mathcal{P}$ such that $x_i(0) < \underline{x}_{i\lambda}$, we have $x_i(t) \geq \underline{x}_{i\lambda}$ for some $t \in [0, T_3(|\mathcal{E}(0)|)]$ (which implies that $x_i(t) \geq \underline{x}_{i\lambda}$ for all $t \geq T_3(|\mathcal{E}(0)|)$, also by the preceding argument).

To find $T_3 \in \mathcal{K}_\infty$, first note that if we pick any constant

$$T_L > \tfrac{1}{1-\lambda_2} \max\left\{ \tfrac{\underline{s}_\lambda}{Ds_{\rm in} + \underline{d}_0}, \max\left\{ \tfrac{\underline{x}_{i\lambda}}{Dx_i^0 + \underline{d}_i} : i \in \mathcal{P} \right\} \right\}$$

then the Fundamental Theorem of Calculus and the positiveness of $s(t)$ and the $x_i(t)$'s imply that: (A) If $s(0) < \underline{s}_\lambda$, then $s(\ell) \geq \underline{s}_\lambda$ for some $\ell \in [0, T_L]$, hence for all $\ell \geq T_L$ and (B) if $i \in \mathcal{P}$ is such that $x_i(0) < \underline{x}_{i\lambda}$, then $x_i(\ell) \geq \underline{x}_{i\lambda}$ for some $\ell \in [0, T_L]$, hence for all $\ell \geq T_L$. Conditions (A)-(B) follow because $s(\ell) \geq s(0) + \ell(Ds_{\rm in} + \underline{d}_0)(1 - \lambda_2)$ for all ℓ such that $\max_{r \in [0,\ell]} s(r) < \underline{s}_\lambda$, and $x_i(\ell) \geq x_i(0) + \ell(1 - \lambda_2)(Dx_i^0 + \underline{d}_i)$ for all ℓ such that $\max_{r \in [0,\ell]} x_i(r) < \underline{x}_{i\lambda}$, so $\ell \leq T_L$. On the other hand, if $|\mathcal{E}(0)| \leq T_M$ where $T_M = (1 - \lambda_2)\min\{s_*, \min\{x_{i*} : i \in \mathcal{P}\}\}$, then $s(0) - s_* \geq -|\mathcal{E}(0)| \geq (\lambda_2 - 1)s_*$; and for all $i \in \mathcal{P}$, we have $x_i(0) - x_{i*} \geq -|\mathcal{E}(0)| \geq (\lambda_2 - 1)x_{i*}$; so $s(0) \geq \lambda_2 s_* \geq \underline{s}_\lambda$ and $x_i(0) \geq \lambda_2 x_{i*} \geq \underline{x}_{i\lambda}$ for all $i \in \mathcal{P}$, which imply that $s(t) \geq \underline{s}_\lambda$ and $x_i(t) \geq \underline{x}_{i\lambda}$ hold for all $t \geq 0$ and $i \in \mathcal{P}$, by the previous paragraph. Hence,

$$T_3(r) = T_2(r) + \left\{ \begin{array}{ll} (T_L + T_M)\frac{r}{T_M}, & 0 \leq r \leq T_M \\ T_L + r, & r > T_M \end{array} \right. \tag{15}$$

satisfies our requirements. ■

B. Representing the Error Dynamics

Let us introduce the functions and the constant

$$\begin{array}{l} \Gamma(s) = D + \sum_{i=1}^n \frac{a_i m_i x_{i*}}{(a_i + s_*)(a_i + s)}, \;\; \tilde{s}(t) = s(t) - s_*, \\ \tilde{x}_i(t) = x_i(t) - x_{i*} \text{ for } i = 1, 2, \ldots, n, \\ \text{and } \;\Gamma_0 = D + \sum_{i=1}^n \frac{a_i m_i x_{i*}}{(a_i + s_*)(a_i + \bar{s}^\sharp)}. \end{array} \tag{16}$$

Then $\Gamma(s(t)) \geq \Gamma_0$ for all $t \geq 0$. By our formulas for $s_{\rm in}$ and the x_{i*}'s from (5) and (6), we have $Ds_{\rm in} = Ds_* + \mu_1(s_*)x_{1*} + \ldots + \mu_n(s_*)x_{n*}$ and $Dx_i^0 = Dx_{i*} - \mu_i(s_*)x_{i*}$ for all $i \in \{1, 2, \ldots, n\}$. Hence, using (3) and the formulas for x_{i*} from (6), and reorganizing terms gives:

$$\left\{\begin{array}{rcl} \dot{\tilde{s}}(t) & = & -D\tilde{s}(t) + \sum\limits_{i=1}^{n}[\mu_i(s_*) - \mu_i(s(t))]x_{i*} \\ & & -\sum\limits_{i=1}^{n}\mu_i(s(t))\tilde{x}_i(t) + \delta_0(t) \\ \dot{\tilde{x}}_i(t) & = & [\mu_i(s(t)) - \mu_i(s_*)]x_i(t) + \tilde{x}_i(t)\mu_i(s_*) \\ & & -D\tilde{x}_i(t) + \delta_i(t),\ i = 1, ..., n. \end{array}\right. \tag{17}$$

For all $s > 0$, we can use our formulas (4) for the μ_i's to check that Γ can be rewritten as

$$\Gamma(s) = D + \sum_{i=1}^{n} \tfrac{\mu_i(s) - \mu_i(s_*)}{s - s_*} x_{i*} \tag{18}$$

for all $s \neq s_*$. Using the constants $p_i = D - \mu_i(s_*)$ (which are positive, by (5) in Assumption 2), we obtain

$$\left\{\begin{array}{rcl} \dot{\tilde{s}}(t) & = & -\Gamma(s(t))\tilde{s}(t) - \sum\limits_{i=1}^{n}\mu_i(s(t))\tilde{x}_i(t) + \delta_0(t) \\ \dot{\tilde{x}}_i(t) & = & -p_i\tilde{x}_i(t) + c_i x_i(t)\mu_i(s(t))\frac{\tilde{s}(t)}{s(t)} \\ & & +\delta_i(t),\ i = 1, ..., n\ , \end{array}\right. \tag{19}$$

where $c_i = \frac{a_i}{a_i + s_*}$ for all $i \in \{1, ..., n\}$.

C. Construction of a Lyapunov-Like Functional

Let us define the C^1 function V by

$$\begin{array}{l} V(\mathcal{E}) = \nu(\tilde{s}) + \sum\limits_{i=1}^{n}\frac{1}{c_i}\Psi_i(\tilde{x}_i), \text{ where} \\ \nu(\tilde{s}) = \tilde{s} - s_* \ln\left(\frac{\tilde{s} + s_*}{s_*}\right) \\ \text{and } \Psi_i(\tilde{x}_i) = \tilde{x}_i - x_{i*}\ln\left(\frac{\tilde{x}_i + x_{i*}}{x_{i*}}\right) \end{array}$$

for all $i \in \mathcal{P}$, and $\Psi_i(\tilde{x}_i) = x_i$ for all $i \in \{1, \ldots, n\} \setminus \mathcal{P}$. By the chain rule, it follows that for all $t \geq T_3(|\mathcal{E}(0)|)$, the time derivative of V along the solutions of (19) satisfies

$$\begin{array}{rcl} \dot{V}(t) & \leq & -\mathcal{N}(\mathcal{E}(t)) + \bar{N}|\delta|_{[0,t]}, \text{ where} \\ \mathcal{N}(\mathcal{E}(t)) & = & \Gamma_0\frac{\tilde{s}^2(t)}{s(t)} + \sum\limits_{i=1}^{n} q_i\frac{\tilde{x}_i^2(t)}{x_i(t)} \end{array} \tag{20}$$

and where $q_i = p_i/c_i = (D - \mu_i(s_*))/c_i$ and the formula

$$\bar{N} = (n+1)\max\left\{\frac{\bar{s}^\sharp + s_*}{\underline{s}_\lambda}, \max_{i \notin \mathcal{P}}\frac{1}{c_i}, \max_{i \in \mathcal{P}}\frac{\lambda_1 C + x_{i*}}{c_i \underline{x}_\lambda}\right\}$$

follows from Lemmas 2-3. Although (20) only holds for times $t \geq T_3(|\mathcal{E}(0)|)$, we can combine (20) with Gronwall's inequality to produce the final ISS estimate; see the appendix.

IV. Illustration

Consider the system (3) with $n = 2$, $D = 0.4$, $s_* = 0.5$, $x_1^0 = 1$, and $x_2^0 = 0.55$ and the growth functions

$$\mu_1(s) = \tfrac{s}{5+s} \quad \text{and} \quad \mu_2(s) = \tfrac{s}{2+s}. \tag{21}$$

Then Assumption 2 is satisfied with $s_{\rm in} = 1.34412$, and our formulas (6) for the x_{i*}'s give

$$x_{1*} = 1.29412 \ \text{ and } \ x_{2*} = 1.1. \tag{22}$$

In this illustration, we will only use the uncertainty vectors $\delta(t)$ to model uncertainties in applying the constant input concentrations x_1^0 and x_2^0 (which may occur in applications, because it may be difficult to maintain the inputs x_i^0 at constant levels), so we set $\delta_0(t) = 0$ and therefore can choose $\underline{d}_0 = \bar{d}_0 = 0$, $\underline{d}_1 = -0.39$, $\underline{d}_2 = -0.21$, and any constants $\bar{d}_1 \geq 0$ and $\bar{d}_2 \geq 0$ to satisfy all of our assumptions.

We simulated (3) using the command `NDSolve` in Mathematica, with the preceding choices of the parameters, and the disturbance vector $\delta(t) = (\delta_0(t), \delta_1(t), \delta_2(t)) = (0, -0.1\sin(t), 0.1\cos(t))$. We report our results in Fig. 1, with the initial state $(s(0), x_1(0), x_2(0)) = (0.2, 0.1, 1)$, and then with the initial state $(s(0), x_1(0), x_2(0)) = (1.3, 0.2, 0.1)$. The figure shows rapid convergence towards an oscillatory steady state, with a deviation from the equilibrium $(s_*, x_{1*}, x_{2*}) = (0.5, 1.29412, 1.1)$ that can be explained by the presence of the uncertainties δ_1 and δ_2, and therefore helps illustrate our theory.

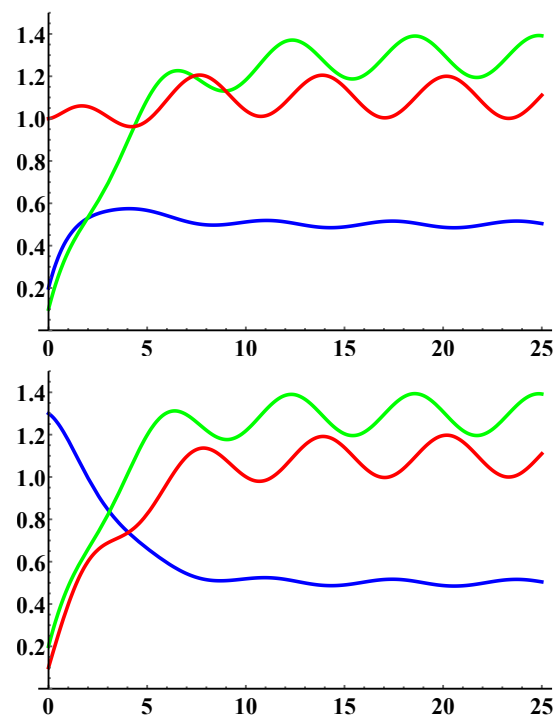

Fig. 1. Solution Components of (3) on Time Interval $[0, 25]$. Species $x_1(t)$ and $x_2(t)$ are Green and Red Curves, Respectively. Substrate $s(t)$ is Blue Curve. Top Panel: Using Initial State $(s(0), x_1(0), x_2(0)) = (0.2, 0.1, 1)$. Bottom Panel: Using Initial State $(s(0), x_1(0), x_2(0)) = (1.3, 0.2, 0.1)$.

V. Conclusions

We solved a key input-to-state stabilization problem for a chemostat model with one limiting substrate, an arbitrary number of competing species, a constant dilution rate, and uncertainties, using constant inputs of the species. In the special case where the uncertainties are zero, this implies that all solutions with initial states in $(0, \infty)^{n+1}$ remain in $(0, \infty)^{n+1}$ at all future times and asymptotically converge to an equilibrium, which corresponds to persistence of all species whose constant inputs are positive. This contrasts with the competitive exclusion principle, which does not consider

the possibility of introducing positive constant inputs of the species. The uncertainties can represent unmodeled features that commonly occur in biotechnological applications, so our work has the potential to benefit the study of some robustness issues.

APPENDIX: LAST PART OF PROOF OF THEOREM 1

To convert (20) into an ISS estimate for all $t \geq 0$, first note that we can use our lemmas to find a $\underline{\gamma} \in \mathcal{K}_\infty$ such that

$$\Gamma_0 \frac{\tilde{s}^2(t)}{s(t)} + \sum_{i=1}^{n} q_i \frac{\tilde{x}_i^2(t)}{x_i(t)} \;\geq\; \underline{\gamma}\left(V\left(\mathcal{E}(t)\right)\right) \tag{A.1}$$

and therefore also

$$\tfrac{d}{dt} V(\mathcal{E}(t)) \leq -\underline{\gamma}(V(\mathcal{E}(t))) + \bar{N}|\delta|_{[0,t]} \tag{A.2}$$

along all trajectories of the $\mathcal{E}$ dynamics starting in our set $\mathcal{S}$ of initial states from the statement of our theorem, and for all $t \geq T_3(|\mathcal{E}(0)|)$. One method for finding $\underline{\gamma}$ is as follows. First, let $\mathcal{O}$ be the set of all points $(\tilde{s}, \tilde{x}_1, \ldots \tilde{x}_n) \in \mathbb{R}^{n+1}$ such that (i) $\tilde{s} \in [\underline{s}_\lambda - s_*, \lambda_1 C - s_*]$, (ii) $\tilde{x}_i \in [\underline{x}_{i\lambda} - x_{i*}, \lambda_1 C - x_{i*}]$ for all $i \in \mathcal{P}$, and (iii) $\tilde{x} \in (0, \lambda_1 C]$ for all $i \in \{1, \ldots, n\} \setminus \mathcal{P}$. Next, pick a function $\underline{\gamma}_0 \in \mathcal{K}_\infty$ such that

$$(n+1)\nu(\tilde{s}) \leq \underline{\gamma}_0(|\tilde{s}|) \text{ and } (n+1)\tfrac{\Psi_i(\tilde{x}_i)}{c_i} \leq \underline{\gamma}_0(|\tilde{x}_i|)$$

for all values $\mathcal{E} \in \mathcal{O}$. Then

$$V_1(\mathcal{E}(t)) \leq \underline{\gamma}_0(|\mathcal{E}(t)|) \tag{A.3}$$

for all $t \geq T_3(|\mathcal{E}(0)|)$. Hence, we can use Lemma 2 to obtain

$$\left(\underline{\gamma}_0^{-1}(V_1(\mathcal{E}(t)))\right)^2 \leq |\mathcal{E}(t)|^2 \leq \lambda_1 C \left(\tfrac{\tilde{s}^2(t)}{s(t)} + \sum_{i=1}^{n} \tfrac{\tilde{x}_i^2(t)}{x_i(t)}\right)$$

for all $t \geq T_3(|\mathcal{E}(0)|)$. Therefore, we can choose

$$\underline{\gamma}(r) = \frac{1}{\lambda_1 C}(\underline{\gamma}_0^{-1}(r))^2 \min\{\Gamma_0, q_1, \ldots, q_n\}. \tag{A.4}$$

Hence, combining (20) and (A.1) gives (A.2), so standard ISS arguments [6] provide $\beta_0 \in \mathcal{KL}$ and $\gamma_0 \in \mathcal{K}_\infty$ such that

$$V\left(\mathcal{E}(t)\right) \leq \beta_0\left(V\left(\mathcal{E}(T_3(|\mathcal{E}(0)|))\right), t\right) + \gamma_0(|\delta|_{[0,t]}) \tag{A.5}$$

holds for all $t \geq T_3(|\mathcal{E}(0)|)$. Then the structure of V provides functions $\beta_1 \in \mathcal{KL}$ and $\gamma_1 \in \mathcal{K}_\infty$ such that

$$|\mathcal{E}(t)| \leq \beta_1(|\mathcal{E}(T_3(|\mathcal{E}(0)|))|, t) + \gamma_1(|\delta|_\infty) \tag{A.6}$$

for all $t \geq T_3(|\mathcal{E}(0)|)$.

To extend (A.6) to obtain an ISS estimate on $[0, +\infty)$, first note that the structure of the $\mathcal{E}$ dynamics (17), combined with our bounds on the μ_i's and Γ and the Lipschitzness of the μ_i's, provide a constant $\bar{L}$ (that is independent of the choice of the solution) such that

$$|\mathcal{E}'(\ell)| \leq \bar{L}\left(|\mathcal{E}(\ell)| + |\delta|_\infty\right) \tag{A.7}$$

holds for all $\ell \in [0, T_3(|\mathcal{E}(0)|)]$; this can be done by rewriting $x_i(t)$ in (17) in the form $\tilde{x}_i(t) + x_{i*}$. Integrating (A.7) over $[0, t]$ for any $t \in [0, T_3(|\mathcal{E}(0)|)]$ and applying the Fundamental Theorem of Calculus to $\mathcal{E}$ gives

$$|\mathcal{E}(t)| \leq |\mathcal{E}(0)| + \bar{L}\int_0^t |\mathcal{E}(\ell)| \mathrm{d}\ell + \bar{L}T_3(|\mathcal{E}(0)|)|\delta|_\infty. \tag{A.8}$$

We now apply Gronwall's inequality [6] to $|\mathcal{E}|$ to get

$$\begin{aligned} |\mathcal{E}(t)| \;&\leq\; |\mathcal{E}(0)| e^{\bar{L}T_3(|\mathcal{E}(0)|)} \\ &\quad + \left\{\bar{L}T_3(|\mathcal{E}(0)|)e^{\bar{L}T_3(|\mathcal{E}(0)|)}\right\}\{|\delta|_\infty\} \\ &\leq\; e^{T_3(|\mathcal{E}(0)|)-t}\Big[|\mathcal{E}(0)|\, e^{\bar{L}T_3(|\mathcal{E}(0)|)} \\ &\quad + \tfrac{1}{2}\bar{L}^2 T_3^2(|\mathcal{E}(0)|)e^{2\bar{L}T_3(|\mathcal{E}(0)|)}\Big] + \tfrac{1}{2}|\delta|_\infty^2 \end{aligned} \tag{A.9}$$

for all $t \in [0, T_3(|\mathcal{E}(0)|)]$, by applying the triangle inequality to the terms in curly braces in (A.9). The ISS estimate now follows from adding the bounds (A.6) and (A.9), and using (A.9) with the choice $t = T_3(|\mathcal{E}(0)|)$ to upper bound the $|\mathcal{E}(T_3(|\mathcal{E}(0)|))|$ that occurs in the right side of (A.6), because $|\mathcal{E}(t)|$ is independent of values of $\delta(r)$ for times $r > t$.

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