Recent Results on Control Problems for Chemostats

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Published in *Automatica* in 2010
Sponsored by NSF/DMS Grant 0708084

SIAM Minisymposium on Applications of Difference and Differential Equations in Ecology and Epidemiology
2011 Joint Meetings, New Orleans
Chemostat Apparatus
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Bioreactor.
Chemostat Apparatus

Bioreactor. Fresh medium continuously added.
Chemostat Apparatus

Bioreactor. Fresh medium continuously added. Culture liquid continuously removed.
Chemostat Apparatus

Two-Species Chemostat Model
Two-Species Chemostat Model

\[ \begin{align*}
\dot{S} &= (s_{in} - S) D(Y) - \mu_1(S) \frac{X_1}{G_1} - \mu_2(S) \frac{X_2}{G_2} \\
\dot{X}_i &= [\mu_i(S) - D(Y)] X_i, \quad i = 1, 2 \\
Y &= X_1 + X_2, \quad (S, X_1, X_2) \in (0, \infty)^3.
\end{align*} \] (CM)
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\[ S = \text{level of the substrate}. \]
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$S$ = level of the substrate. $X_i$ = concentration of species $i$.
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$S =$ level of the substrate. $X_i =$ concentration of species $i$. $s_{\text{in}} =$ positive constants.
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► Main Goal:
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- **Main Goal**: Design \( D \) to render an appropriate equilibrium \((s_*, x_{1*}, x_{2*}) \in (0, \infty)^3\) GAS.
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  De Leenheer, Gouzé
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► \( D \) cannot be constant if the \( \mu_i \)'s are monotone.
Case 1: $G_1 > G_2$

Since the assumptions on the $\mu_j$'s will be asymmetric, we must treat the cases $G_1 > G_2$ and $G_1 < G_2$ separately.
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$$y = x_1(t - \tau) + ax_2(t - \tau), \quad a = G_2/G_1 \in (0, 1)$$

(NV1)
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**Goal**: Global asymptotic stabilization of a suitable equilibrium $(s_*, x_1*, x_2*) \in (0, \infty)^3$
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\end{align*} \]  

Goal: Global asymptotic stabilization of a suitable equilibrium $(s_*, x_{1*}, x_{2*}) \in (0, \infty)^3$ under Haldane uptake functions

\[ \mu_i(s) = \frac{K_i s}{L_i + s + g_i s^2} \]  

(HG)
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\mu_i(s) = \frac{K_i s}{L_i + s + g_i s^2}
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and uncertain constant delays $\tau$.
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\hspace{1cm} (NV1)

Goal: Global asymptotic stabilization of a suitable equilibrium $(s_*, x_{1*}, x_{2*}) \in (0, \infty)^3$ under Haldane uptake functions

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\mu_i(s) = \frac{K_is}{L_i + s + g_is^2}
\]  
\hspace{1cm} (HG)

and uncertain constant delays $\tau$. $g_i \geq 0$ and $L_i, K_i > 0$ constants.
Assumptions for Case where $G_1 > G_2$
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- There is a constant $s_\ast \in (0, s_{in})$ such that $\mu_1(s_\ast) = \mu_2(s_\ast)$. 
Assumptions for Case where $G_1 > G_2$

- There is a constant $s_* \in (0, s_{in})$ such that $\mu_1(s_*) = \mu_2(s_*)$.
- The constants $\delta_i = L_i - g_i s_* s_{in}$ for $i = 1, 2$ are positive.
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\kappa = \delta_1 \mu_1(s_*) \left[ 1 + \frac{1}{s_*} \sum_{i=1}^{2} \frac{\delta_i}{L_i + s_{in} + g_i s_{in}^2} x_{i*} \right] + K_2 s_* x_{2*} \frac{L_2 g_1 - L_1 g_2}{\delta_2} > 0
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\]
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+ K_2 s_* x_2^* \frac{L_2 g_1 - L_1 g_2}{\delta_2} > 0
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\[
\mathcal{U} = \frac{s_*}{(1-a)\mu_1(s_*)} \left[ -K_1 + \frac{L_1 - g_1 s_*^2}{L_2 - g_1 s_*^2} K_2 \right] \neq 0 \quad (SC)
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\[ \mathcal{N} = \delta_1 \mu_1(s_*) \left[ 1 + \frac{1}{s_*} \sum_{i=1}^{2} \frac{\delta_i}{L_i + s_{in} + g_i s_{in}^2} x_{i*} \right] \]  

\[ + K_2 s_* x_{2*} \frac{L_2 g_1 - L_1 g_2}{\delta_2} > 0 \]  

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- $\min\{\mu_1(s_{in}), \mu_2(s_{in})\} > \mu_1(s_*)$, and $L_2 g_1 - L_1 g_2 \leq 0$. 
Assumptions for Case where $G_1 > G_2$

- There is a constant $s_* \in (0, s_{in})$ such that $\mu_1(s_*) = \mu_2(s_*)$.
- The constants $\delta_i = L_i - g_i s_* s_{in}$ for $i = 1, 2$ are positive.

$$
\Upsilon = \delta_1 \mu_1(s_*) \left[ 1 + \frac{1}{s_*} \sum_{i=1}^{2} \frac{\delta_i}{L_i + s_{in} + g_i s_{in}^2} x_i^* \right] \quad \text{(SG)}
$$

$$
+ K_2 s_* x_2^* \frac{L_2 g_1 - L_1 g_2}{\delta_2} > 0
$$

$$
\Upsilon = \frac{s_*}{(1-a) \mu_1(s_*)} \left[ -K_1 + \frac{L_1 - g_1 s_*^2}{L_2 - g_2 s_*^2} K_2 \right] \neq 0 \quad \text{(SC)}
$$

- $\min \{ \mu_1(s_{in}), \mu_2(s_{in}) \} > \mu_1(s_*)$, and $L_2 g_1 - L_1 g_2 \leq 0$.
- There is a known constant $\tau_M > 0$ so that $0 \leq \tau \leq \tau_M$. 
Assumptions for Case where $G_1 > G_2$

- There is a constant $s_* \in (0, s_{in})$ such that $\mu_1(s_*) = \mu_2(s_*)$.
- The constants $\delta_i = L_i - g_is_*s_{in}$ for $i = 1, 2$ are positive.

$$\nabla = \delta_1 \mu_1(s_*) \left[ 1 + \frac{1}{s_*} \sum_{i=1}^{2} \frac{\delta_i}{L_i s_{in} + g_i s^2_{in}} x_{i*} \right]$$  \hfill (SG)

$$+ K_2 s_* x_{2*} \frac{L_2 g_1 - L_1 g_2}{\delta_2} > 0$$

$$\bar{\omega} = \frac{s_*}{(1-a)\mu_1(s_*)} \left[ -K_1 + \frac{L_1 - g_1 s^2_*}{L_2 - g_2 s^2_*} K_2 \right] \neq 0$$ \hfill (SC)

- $\min\{\mu_1(s_{in}), \mu_2(s_{in})\} > \mu_1(s_*)$, and $L_2 g_1 - L_1 g_2 \leq 0$.
- There is a known constant $\tau_M > 0$ so that $0 \leq \tau \leq \tau_M$. $x_{1*}, x_{2*} > 0$ are any constants such that $s_* + x_{1*} + x_{2*} = s_{in}$.
Haldane Growth Functions

Uptake

Substrate
Haldane Growth Functions

\[ (K_1, L_1, g_1) = (6, 8, 0.12) \text{ and } (K_2, L_2, g_2) = (2, 1, 0.04) \]
Main Result for Case where $G_1 > G_2$
Main Result for Case where $G_1 > G_2$

We can compute constants $\bar{\epsilon}_i$ depending on $\tau_M$ so that for any constants $\epsilon_i \in (0, \bar{\epsilon}_i)$ for $i = 1, 2$ such that $\epsilon_1 \epsilon_2 \leq \bar{\epsilon}_3$, the control

$$D = \mu_1(s_*) - \text{sign}(\mathcal{U}) \epsilon_1 \sigma(\epsilon_2\{x_1(t-\tau) + ax_2(t-\tau) - x_1^* - ax_2^*\})$$

globally asymptotically stabilizes $(s^*, x_1^*, x_2^*)$ for all initializations $(\phi_s, \phi_{x_1}, \phi_{x_2}) \in C([-2\tau_M, 0], (0, \infty)^3)$. 
Main Result for Case where $G_1 > G_2$

We can compute constants $\bar{\varepsilon}_i$ depending on $\tau_M$ so that for any constants $\varepsilon_i \in (0, \bar{\varepsilon}_i)$ for $i = 1, 2$ such that $\varepsilon_1 \varepsilon_2 \leq \bar{\varepsilon}_3$, the control

$$D = \mu_1(s_*) - \text{sign}(U) \varepsilon_1 \sigma(\varepsilon_2 \{ x_1(t-\tau) + ax_2(t-\tau) - x_1* - ax_2* \})$$

globally asymptotically stabilizes $(s_*, x_1*, x_2*)$ for all initializations $(\phi_s, \phi_{x_1}, \phi_{x_2}) \in C([-2\tau_M, 0], (0, \infty)^3)$. $\sigma = \text{standard saturation}$. 
Main Result for Case where $G_1 > G_2$

We can compute constants $\bar{\varepsilon}_i$ depending on $\tau_M$ so that for any constants $\varepsilon_i \in (0, \bar{\varepsilon}_i)$ for $i = 1, 2$ such that $\varepsilon_1 \varepsilon_2 \leq \bar{\varepsilon}_3$, the control

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- Standard Poincaré-Bendixson and Lyapunov function methods do not apply under delays.
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- Standard Poincaré-Bendixson and Lyapunov function methods do not apply under delays. Instead, the proof constructs a Lyapunov-Krasovskii functional $U_1$. 
**Main Result for Case where** $G_1 > G_2$

We can compute constants $\bar{\varepsilon}_i$ depending on $\tau_M$ so that for any constants $\varepsilon_i \in (0, \bar{\varepsilon}_i)$ for $i = 1, 2$ such that $\varepsilon_1 \varepsilon_2 \leq \bar{\varepsilon}_3$, the control

$$D = \mu_1(s_*) - \text{sign}(\bar{U}) \varepsilon_1 \sigma \{ \varepsilon_2 \{ x_1(t-\tau) + ax_2(t-\tau) - x_1* - ax_2* \} \}$$

globally asymptotically stabilizes $(s_*, x_1*, x_2*)$ for all initializations $(\phi_s, \phi_{x_1}, \phi_{x_2}) \in C([-2\tau_M, 0], (0, \infty)^3)$. $\sigma = \text{standard saturation}$.

- Standard Poincaré-Bendixson and Lyapunov function methods do not apply under delays. Instead, the proof constructs a Lyapunov-Krasovskii functional $U_1$.

- At each time $t$, $U_1$ depends on the history of the error variable $(\tilde{s}, \tilde{x}) = (s - s_*, x - x_*)$ over $[t - 2\tau_M, t]$.
Main Result for Case where $G_1 > G_2$

We can compute constants $\bar{\varepsilon}_i$ depending on $\tau_M$ so that for any constants $\varepsilon_i \in (0, \bar{\varepsilon}_i)$ for $i = 1, 2$ such that $\varepsilon_1 \varepsilon_2 \leq \bar{\varepsilon}_3$, the control

$$D = \mu_1(s_\star) - \text{sign}(\tilde{U})\varepsilon_1 \sigma(\varepsilon_2 \{x_1(t-\tau) + ax_2(t-\tau) - x_1^* - ax_2^*\})$$

globally asymptotically stabilizes $(s_\star, x_1^*, x_2^*)$ for all initializations $(\phi_s, \phi_{x_1}, \phi_{x_2}) \in C([-2\tau_M, 0], (0, \infty)^3)$. $\sigma = \text{standard saturation}$.

- Standard Poincaré-Bendixson and Lyapunov function methods do not apply under delays. Instead, the proof constructs a Lyapunov-Krasovskii functional $U_1$.
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- Along the error dynamics, $\dot{U}_1$ is negative definite:
Main Result for Case where $G_1 > G_2$

We can compute constants $\bar{\varepsilon}_i$ depending on $\tau_M$ so that for any constants $\varepsilon_i \in (0, \bar{\varepsilon}_i)$ for $i = 1, 2$ such that $\varepsilon_1 \varepsilon_2 \leq \bar{\varepsilon}_3$, the control

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globally asymptotically stabilizes $(s_*, x_1*, x_2*)$ for all initializations $(\phi_s, \phi_{x_1}, \phi_{x_2}) \in C([-2\tau_M, 0], (0, \infty)^3)$. $\sigma = \text{standard saturation}$.

- Standard Poincaré-Bendixson and Lyapunov function methods do not apply under delays. Instead, the proof constructs a Lyapunov-Krasovskii functional $U_1$.

- At each time $t$, $U_1$ depends on the history of the error variable $(\tilde{s}, \tilde{x}) = (s - s_*, x - x_*)$ over $[t - 2\tau_M, t]$.

- Along the error dynamics, $\dot{U}_1$ is negative definite:

$$\dot{U}_1 \leq -(\tilde{s} + \tilde{x}_1 + \tilde{x}_2)^2 - \frac{5}{6} \frac{\tilde{s}^2}{s} - \frac{\varepsilon_1 \varepsilon_2 |\mathcal{U}|}{8} (\tilde{x}_1 + a\tilde{x}_2)^2, \quad t \geq \tau .$$
Case 2: $G_1 < G_2$

The analysis from Case 1 does not apply in this situation.
Case 2: $G_1 < G_2$

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\begin{align*}
\dot{s} &= (s_{in} - s)D(y) - \mu_1(s)x_1 - \mu_2(s)x_2 \\
\dot{x}_i &= [\mu_i(s) - D(y)]x_i, \quad i = 1, 2 \\
y &= x_1 + ax_2, \quad a = \frac{G_2}{G_1} > 1
\end{align*}
\]  

(NV2)
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New Assumption:
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New Assumption: The $\mu_i$’s are asymmetric, as follows:
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\end{align*}
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(NewV2)

New Assumption: The $\mu_i$'s are asymmetric, as follows: The $\mu_i$'s are zero at $s = 0$ and $C^1$, and $\mu_i'(s) > 0$ for $i = 1, 2$ and all $s \geq 0$. 
Case 2: $G_1 < G_2$

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\dot{s} = (s_{\text{in}} - s)D(y) - \mu_1(s)x_1 - \mu_2(s)x_2 \\
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y = x_1 + ax_2, \ a = \frac{G_2}{G_1} > 1 \tag{NV2}
\]

**New Assumption:** The $\mu_i$'s are asymmetric, as follows: The $\mu_i$'s are zero at $s = 0$ and $C^1$, and $\mu_i'(s) > 0$ for $i = 1, 2$ and all $s \geq 0$. There is a constant $s_* \in (0, s_{\text{in}})$ so that $\mu_1(s) > \mu_2(s)$ on $(0, s_*)$ and $\mu_1(s) < \mu_2(s)$ on $(s_*, s_{\text{in}})$. 
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The $\mu_i$’s are zero at $s = 0$ and $C^1$, and $\mu_i'(s) > 0$ for $i = 1, 2$ and all $s \geq 0$. There is a constant $s_* \in (0, s_{in})$ so that $\mu_1(s) > \mu_2(s)$ on $(0, s_*)$ and $\mu_1(s) < \mu_2(s)$ on $(s_*, s_{in})$. Also, $\mu_1'(s_*) < \mu_2'(s_*)$. 


Main Result for Case where $G_1 < G_2$
Main Result for Case where $G_1 < G_2$

Fix any constants $x_{i*} > 0$ such that $x_{1*} + x_{2*} = s_{in} - s_*$. 
Main Result for Case where $G_1 < G_2$

Fix any constants $x_{i^*} > 0$ such that $x_{1^*} + x_{2^*} = s_{\text{in}} - s_*$. 

$$K_0 = \min \left\{ \frac{\mu_1(s_{\text{in}}) - \mu_1(s_*)}{(a+1)x_{1^*} + 2ax_{2^*}}, \frac{\mu_1(s_*)}{4(a+1)s_{\text{in}}}, \frac{1}{a} \min \left\{ \mu_i'(s) : s \in [0, s_{\text{in}}], i = 1, 2 \right\} \right\}$$
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Let $\sigma : \mathbb{R} \to [-1, 1]$ denote the usual saturation.
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**Theorem:** For each constant $K \in (0, K_0)$ and each constant $a > 1$, 

Main Result for Case where $G_1 < G_2$

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Let $\sigma : \mathbb{R} \to [-1, 1]$ denote the usual saturation.

**Theorem:** For each constant $K \in (0, K_0)$ and each constant $a > 1$, (NV2) in closed loop with the bounded positive controller

$$D(y) = \mu_1(s_*) - 2(1 + a)s_{in}K\sigma \left( \frac{1}{2(1+a)s_{in}} [y - x_{1*} - ax_{2*}] \right)$$

is GAS to the equilibrium $(s_*, x_{1*}, x_{2*})$ on $(0, \infty)^3$. 
Main Result for Case where $G_1 < G_2$

Fix any constants $x_{i*} > 0$ such that $x_{1*} + x_{2*} = s_{in} - s_*$. 

$$K_0 = \min \left\{ \frac{\mu_1(s_{in}) - \mu_1(s_*)}{(a+1)x_{1*} + 2ax_{2*}}, \frac{\mu_1(s_*)}{4(a+1)s_{in}}, \frac{1}{a} \min \{ \mu_i'(s) : s \in [0, s_{in}], i = 1, 2 \} \right\}$$

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(C) is GAS to the equilibrium $(s_*, x_{1*}, x_{2*})$ on $(0, \infty)^3$.

**Proof:**
Main Result for Case where $G_1 < G_2$

Fix any constants $x_{i*} > 0$ such that $x_{1*} + x_{2*} = s_{in} - s_*$.  

$$K_0 = \min \left\{ \frac{\mu_1(s_{in})-\mu_1(s_*)}{(a+1)x_{1*}+2ax_{2*}}, \frac{\mu_1(s_*)}{4(a+1)s_{in}}, \frac{1}{a} \min \{ \mu_i'(s) : s \in [0, s_{in}], i = 1, 2 \} \right\}$$

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is GAS to the equilibrium $(s_*, x_{1*}, x_{2*})$ on $(0, \infty)^3$.

**Proof:** Use Poincaré-Bendixson Theorem and dimension reduction to a manifold where $s + x_1 + x_2 = s_{in}$. 
Main Result for Case where $G_1 < G_2$

Fix any constants $x_{i*} > 0$ such that $x_{1*} + x_{2*} = s_{in} - s_*$. 

$$K_0 = \min \left\{ \frac{\mu_1(s_{in}) - \mu_1(s_*)}{(a+1)x_{1*} + 2ax_{2*}}, \frac{\mu_1(s_*)}{4(a+1)s_{in}}, \frac{1}{a} \min \{ \mu_i'(s) : s \in [0, s_{in}], i = 1, 2 \} \right\}$$

Let $\sigma : \mathbb{R} \to [-1, 1]$ denote the usual saturation.

**Theorem**: For each constant $K \in (0, K_0)$ and each constant $a > 1$, (NV2) in closed loop with the bounded positive controller

$$D(y) = \mu_1(s_*) - 2(1 + a)s_{in}K\sigma \left( \frac{1}{2(1+a)s_{in}}[y - x_{1*} - ax_{2*}] \right)$$

is GAS to the equilibrium $(s_*, x_{1*}, x_{2*})$ on $(0, \infty)^3$.

**Proof**: Use Poincaré-Bendixson Theorem and dimension reduction to a manifold where $s + x_1 + x_2 = s_{in}$.

The case $a = 1$ would give a nonisolated equilibrium.
Robustness Corollary for Case where $G_1 \prec G_2$
Robustness Corollary for Case where $G_1 < G_2$

Suppose we compute $D(y)$ from (C) using a pair of $\mu_i$’s, but the actual uptake functions are some other functions $\nu_j$ that satisfy:
Robustness Corollary for Case where $G_1 < G_2$

Suppose we compute $D(y)$ from (C) using a pair of $\mu_i$’s, but the actual uptake functions are some other functions $\nu_i$ that satisfy:

Assumption:
Robustness Corollary for Case where $G_1 < G_2$

Suppose we compute $D(y)$ from (C) using a pair of $\mu_i$’s, but the actual uptake functions are some other functions $\nu_i$ that satisfy:

Assumption: (a) The $\nu_i$’s are 0 at 0 and $C^1$, 

Robustness Corollary for Case where $G_1 < G_2$

Suppose we compute $D(y)$ from (C) using a pair of $\mu_i$'s, but the actual uptake functions are some other functions $\nu_i$ that satisfy:

Assumption: (a) The $\nu_i$'s are 0 at 0 and $C^1$, (b) $\nu_i'(s) > 0$ for $i = 1, 2$ and all $s \geq 0$, 
Robustness Corollary for Case where $G_1 < G_2$

Suppose we compute $D(y)$ from (C) using a pair of $\mu_i$'s, but the actual uptake functions are some other functions $\nu_i$ that satisfy:

**Assumption:** (a) The $\nu_i$'s are 0 at 0 and $C^1$, (b) $\nu_i'(s) > 0$ for $i = 1, 2$ and all $s \geq 0$, (c) there is a constant $s_v \in (0, s_{in})$ so that $\nu_1(s) > \nu_2(s)$ on $(0, s_v)$ and $\nu_1(s) < \nu_2(s)$ on $(s_v, s_{in})$
Robustness Corollary for Case where $G_1 < G_2$

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Robustness Corollary for Case where $G_1 < G_2$

Suppose we compute $D(y)$ from (C) using a pair of $\mu_i$’s, but the actual uptake functions are some other functions $\nu_i$ that satisfy:

Assumption: (a) The $\nu_i$’s are 0 at 0 and $C^1$, (b) $\nu_i'(s) > 0$ for $i = 1, 2$ and all $s \geq 0$, (c) there is a constant $s_v \in (0, s_{in})$ so that $\nu_1(s) > \nu_2(s)$ on $(0, s_v)$ and $\nu_1(s) < \nu_2(s)$ on $(s_v, s_{in})$, and (d) $\nu_1'(s_v) < \nu_2'(s_v)$.

Corollary: We can choose $K$ and a constant $\varepsilon > 0$ such that if $T(\mu, \nu) = \max\{|\mu_i'(s) - \nu_i'(s)| : i = 1, 2; s \in [0, s_{in}]\} < \varepsilon$, then

$$\begin{cases} \dot{s} &= D(y)[s_{in} - s] - \nu_1(s)x_1 - \nu_2(s)x_2 \\ \dot{x}_i &= [\nu_i(s) - D(y)]x_i, \ i = 1, 2 \end{cases} \quad (RC)$$

is GAS to some point $(s_v, x_{1v}, x_{2v}) \in (0, \infty)^3$. 
Conclusions
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- We achieved output feedback GAS of componentwise positive equilibria using only the sum of the species levels.
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Conclusions

- We achieved output feedback GAS of componentwise positive equilibria using only the sum of the species levels.
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- When $G_1 < G_2$, we can allow uncertain monotone uptake functions $\mu_i$ that are not necessary concave.
Conclusions

- We achieved output feedback GAS of componentwise positive equilibria using only the sum of the species levels.

- Competitive exclusion required us to use a nonconstant controller to get permanence of both species.

- We dropped the usual assumption on the relative sizes of the growth yields $G_i$.

- When $G_1 < G_2$, we can allow uncertain monotone uptake functions $\mu_i$ that are not necessary concave.

- When $G_1 > G_2$, we can cover time delays, nonmonotone uptake functions, and robustness to actuator errors.
Conclusions

- We achieved output feedback GAS of componentwise positive equilibria using only the sum of the species levels.
- Competitive exclusion required us to use a nonconstant controller to get permanence of both species.
- We dropped the usual assumption on the relative sizes of the growth yields $G_i$.
- When $G_1 < G_2$, we can allow uncertain monotone uptake functions $\mu_i$ that are not necessary concave.
- When $G_1 > G_2$, we can cover time delays, nonmonotone uptake functions, and robustness to actuator errors.
- Desirable extensions would allow more than two species, or multiple limiting substrates.