

On the Stability of Periodic Solutions in the Perturbed Chemostat



MICHAEL MALISOFF

Department of Mathematics
Louisiana State University



Joint work with **Frédéric Mazenc** (INRIA-INRA)
and **Patrick De Leenheer** (University of FL)

SIAM Minisymposium on Mathematical Modeling
of Complex Systems in Biology I

AMS Joint Meetings, New Orleans, LA, January 6, 2007

GENERAL n SPECIES CHEMOSTAT MODEL

$$\dot{S} = D(S_0 - S) - \sum_{i=1}^n \mu_i(S)x_i/\gamma_i; \quad \dot{x}_i = x_i(\mu_i(S) - D) \quad (\Sigma_n)$$

x_i = concentration of i th species, S = concentration of limiting nutrient,

μ_i = i th per-capita growth rate, $\gamma_i \in (0, 1)$ = constant i th yield factor.

Controls: dilution rate D and input nutrient concentration S_0 .

GENERAL n SPECIES CHEMOSTAT MODEL

$$\dot{S} = D(S_0 - S) - \sum_{i=1}^n \mu_i(S)x_i/\gamma_i; \quad \dot{x}_i = x_i(\mu_i(S) - D) \quad (\Sigma_n)$$

x_i = concentration of i th species, S = concentration of limiting nutrient,
 μ_i = i th per-capita growth rate, $\gamma_i \in (0, 1)$ = constant i th yield factor.

Controls: dilution rate D and input nutrient concentration S_0 .

Derivation: Use mass-balance equations for total amounts of nutrient and each of the species, assuming the reactor content is well-mixed.

GENERAL n SPECIES CHEMOSTAT MODEL

$$\dot{S} = D(S_0 - S) - \sum_{i=1}^n \mu_i(S)x_i/\gamma_i; \quad \dot{x}_i = x_i(\mu_i(S) - D) \quad (\Sigma_n)$$

x_i = concentration of i th species, S = concentration of limiting nutrient,
 μ_i = i th per-capita growth rate, $\gamma_i \in (0, 1)$ = constant i th yield factor.

Controls: dilution rate D and input nutrient concentration S_0 .

Derivation: Use mass-balance equations for total amounts of nutrient and each of the species, assuming the reactor content is well-mixed.

Importance: Chemostat models provide the foundation for much of current research in **bioengineering**, **ecology**, and **population biology**.

GENERAL n SPECIES CHEMOSTAT MODEL

$$\dot{S} = D(S_0 - S) - \sum_{i=1}^n \mu_i(S)x_i/\gamma_i; \quad \dot{x}_i = x_i(\mu_i(S) - D) \quad (\Sigma_n)$$

x_i = concentration of i th species, S = concentration of limiting nutrient,
 μ_i = i th per-capita growth rate, $\gamma_i \in (0, 1)$ = constant i th yield factor.

Controls: dilution rate D and input nutrient concentration S_0 .

Derivation: Use mass-balance equations for total amounts of nutrient and each of the species, assuming the reactor content is well-mixed.

Importance: Chemostat models provide the foundation for much of current research in **bioengineering**, **ecology**, and **population biology**.

Competitive Exclusion: When S_0 and D are constant and the μ_i 's are increasing, **at most one species survives**. (There is a steady state with at most one nonzero species concentration, which attracts a.a. solutions.)

OVERVIEW of LITERATURE

Coexistence: In real ecological systems, **many species can coexist**, so much of the literature aims at choosing S_0 and/or D to force coexistence. “**The Paradox of the plankton**,” Hutchinson, *American Naturalist*, 1961.

OVERVIEW of LITERATURE

Coexistence: In real ecological systems, **many species can coexist**, so much of the literature aims at choosing S_0 and/or D to force coexistence. “**The Paradox of the plankton**,” Hutchinson, *American Naturalist*, 1961.

Time-Varying Controls: Have competitive exclusion if $n = 2$ and one of the controls is fixed and the other is periodic. See Hal Smith (*SIAP*'81), Hale-Somolinos (*JMB*'83), Butler-Hsu-Waltman (*SIAP*'85).

OVERVIEW of LITERATURE

Coexistence: In real ecological systems, **many species can coexist**, so much of the literature aims at choosing S_0 and/or D to force coexistence. “**The Paradox of the plankton**,” Hutchinson, *American Naturalist*, 1961.

Time-Varying Controls: Have competitive exclusion if $n = 2$ and one of the controls is fixed and the other is periodic. See Hal Smith (*SIAP*'81), Hale-Somolinos (*JMB*'83), Butler-Hsu-Waltman (*SIAP*'85).

State-Dependent Controls: A feedback control perspective based on **mathematical control theory** was pursued e.g. in De Leenheer-Smith (*JMB*'03) to generate a coexistence equilibrium for $n = 2, 3$.

OVERVIEW of LITERATURE

Coexistence: In real ecological systems, **many species can coexist**, so much of the literature aims at choosing S_0 and/or D to force coexistence. “**The Paradox of the plankton**,” Hutchinson, *American Naturalist*, 1961.

Time-Varying Controls: Have competitive exclusion if $n = 2$ and one of the controls is fixed and the other is periodic. See Hal Smith (*SIAP*'81), Hale-Somolinos (*JMB*'83), Butler-Hsu-Waltman (*SIAP*'85).

State-Dependent Controls: A feedback control perspective based on **mathematical control theory** was pursued e.g. in De Leenheer-Smith (*JMB*'03) to generate a coexistence equilibrium for $n = 2, 3$.

Intra-Specific Competition: This can be modeled with growth rates $\mu_i(S, x_i)$ that decrease in x_i . See Mazenc-Lobry-Rapaport (*EJDE*'07), Grognard-Mazenc-Rapaport (*DCDS*'07).

OUR WORK for ONE SPECIES CASE

Taking S_0 to be constant and rescaling gives

$$\dot{S} = D(1 - S) - \mu(S)x, \quad \dot{x} = x(\mu(S) - D) \quad (\Sigma_1)$$

evolving on $\mathcal{X} = (0, \infty)^2$. We assume a Monod growth rate

$$\mu(S) = \frac{mS}{a + S}, \quad m > 4a + 1. \quad (\text{G})$$

OUR WORK for ONE SPECIES CASE

Taking S_0 to be constant and rescaling gives

$$\dot{S} = D(1 - S) - \mu(S)x, \quad \dot{x} = x(\mu(S) - D) \quad (\Sigma_1)$$

evolving on $\mathcal{X} = (0, \infty)^2$. We assume a Monod growth rate

$$\mu(S) = \frac{mS}{a + S}, \quad m > 4a + 1. \quad (\text{G})$$

Summary of Our Work:

- Instead of studying coexistence, we prove the **stability** of a **prescribed periodic solution** using a Lyapunov-type analysis; i.e., **tracking**.

OUR WORK for ONE SPECIES CASE

Taking S_0 to be constant and rescaling gives

$$\dot{S} = D(1 - S) - \mu(S)x, \quad \dot{x} = x(\mu(S) - D) \quad (\Sigma_1)$$

evolving on $\mathcal{X} = (0, \infty)^2$. We assume a Monod growth rate

$$\mu(S) = \frac{mS}{a + S}, \quad m > 4a + 1. \quad (\text{G})$$

Summary of Our Work:

- Instead of studying coexistence, we prove the **stability** of a **prescribed periodic solution** using a Lyapunov-type analysis; i.e., **tracking**.
- Lyapunov functions are useful for robustness analysis but have infrequently been used in chemostat research.

OUR WORK for ONE SPECIES CASE

Taking S_0 to be constant and rescaling gives

$$\dot{S} = D(1 - S) - \mu(S)x, \quad \dot{x} = x(\mu(S) - D) \quad (\Sigma_1)$$

evolving on $\mathcal{X} = (0, \infty)^2$. We assume a Monod growth rate

$$\mu(S) = \frac{mS}{a + S}, \quad m > 4a + 1. \quad (\text{G})$$

Summary of Our Work:

- Instead of studying coexistence, we prove the **stability** of a **prescribed periodic solution** using a Lyapunov-type analysis; i.e., **tracking**.
- Lyapunov functions are useful for robustness analysis but have infrequently been used in chemostat research.
- Most chemostat/Lyapunov results use *nonstrict* Lyapunov functions and LaSalle invariance which are not suited to robustness analysis.

MAIN TRACKING RESULT for Σ_1

Statement of Main Tracking Result: Given any componentwise positive trajectory $(S, x) : [0, \infty) \rightarrow \mathcal{X}$ for (Σ_1) and the dilution rate

$$D(t) = \frac{\sin(t)}{2 + \cos(t)} + \frac{m(2 - \cos(t))}{4a + 2 - \cos(t)} \quad (\text{D})$$

and μ as in (G) with $m > 4a + 1$, the corresponding deviation

$$(\tilde{S}(t), \tilde{x}(t)) := (S(t) - S_r(t), x(t) - x_r(t)) \quad (\text{E})$$

of (S, x) from the reference trajectory

$$(S_r(t), x_r(t)) := \left(\frac{1}{2} - \frac{1}{4} \cos(t), \frac{1}{2} + \frac{1}{4} \cos(t) \right) \quad (\text{R})$$

for (Σ_1) asymptotically approaches $(0, 0)$ as $t \rightarrow +\infty$.

MAIN TRACKING RESULT for Σ_1

Statement of Main Tracking Result: Given any componentwise positive trajectory $(S, x) : [0, \infty) \rightarrow \mathcal{X}$ for (Σ_1) and the dilution rate

$$D(t) = \frac{\sin(t)}{2 + \cos(t)} + \frac{m(2 - \cos(t))}{4a + 2 - \cos(t)} \quad (\text{D})$$

and μ as in (G) with $m > 4a + 1$, the corresponding deviation

$$(\tilde{S}(t), \tilde{x}(t)) := (S(t) - S_r(t), x(t) - x_r(t)) \quad (\text{E})$$

of (S, x) from the reference trajectory

$$(S_r(t), x_r(t)) := \left(\frac{1}{2} - \frac{1}{4} \cos(t), \frac{1}{2} + \frac{1}{4} \cos(t) \right) \quad (\text{R})$$

for (Σ_1) asymptotically approaches $(0, 0)$ as $t \rightarrow +\infty$.

(Similar results hold if we instead pick any $x_r(t)$ s.t. $\exists \ell > 0$ s.t. $\forall t \geq 0$, $\max\{\ell, |\dot{x}_r(t)|\} \leq x_r(t) \leq \frac{3}{4}$ and $S_r = 1 - x_r$, for suitable D .)

OUTLINE of PROOF of MAIN TRACKING RESULT for Σ_1

First transform the error dynamics for (E) into

$$\begin{cases} \dot{\tilde{z}} &= -D(t)\tilde{z}, \\ \dot{\tilde{\xi}} &= \mu(z - e^\xi) - \mu(1 - e^{\xi_r(t)}), \end{cases} \quad (\text{TE})$$

where $\tilde{z} := z - 1$, $z = S + x$, $\tilde{\xi} := \xi - \xi_r$, $\xi := \ln(x)$, and $\xi_r := \ln(x_r)$.

OUTLINE of PROOF of MAIN TRACKING RESULT for Σ_1

First transform the error dynamics for (E) into

$$\begin{cases} \dot{\tilde{z}} &= -D(t)\tilde{z}, \\ \dot{\tilde{\xi}} &= \mu(z - e^{\tilde{\xi}}) - \mu(1 - e^{\xi_r(t)}), \end{cases} \quad (\text{TE})$$

where $\tilde{z} := z - 1$, $z = S + x$, $\tilde{\xi} := \xi - \xi_r$, $\xi := \ln(x)$, and $\xi_r := \ln(x_r)$.

Next show that (TE) admits the Lyapunov-like function

$$L_3(\tilde{z}, \tilde{\xi}) := e^{\tilde{\xi}} - 1 - \tilde{\xi} + \frac{4m}{a\underline{D}} \tilde{z}^2 \quad (\text{L})$$

where $D(t) \geq \underline{D} > 0 \forall t$. Along the trajectories of (TE), we get

$$\dot{L}_3 \leq -\frac{ma(e^{\tilde{\xi}} - 1)^2}{16(a + 2 + \tilde{z}^2)(a + 1)} - \frac{4m}{a} \tilde{z}^2. \quad (\text{DK})$$

Using a Barbalat's Lemma argument, $(\tilde{z}, \tilde{\xi}) \rightarrow 0$ exponentially.

ROBUSTNESS with respect to n ADDITIONAL SPECIES

$$\left\{ \begin{array}{l} \dot{S} = D(t)(1 - S) - \mu(S)x - \sum_{i=1}^n \nu_i(S)y_i, \\ \dot{x} = x(\mu(S) - D(t)), \quad \dot{y}_i = y_i(\nu_i(S) - D(t)) \end{array} \right. \quad (\text{AS})$$

D is from (D), y_i = concentration of the i th additional species, each ν_i is continuous and increasing and satisfies $\nu_i(0) = 0$ and $\nu_i(1) < \underline{D}$.

ROBUSTNESS with respect to n ADDITIONAL SPECIES

$$\begin{cases} \dot{S} &= D(t)(1 - S) - \mu(S)x - \sum_{i=1}^n \nu_i(S)y_i, \\ \dot{x} &= x(\mu(S) - D(t)), \quad \dot{y}_i &= y_i(\nu_i(S) - D(t)) \end{cases} \quad (\text{AS})$$

D is from (D), y_i = concentration of the i th additional species, each ν_i is continuous and increasing and satisfies $\nu_i(0) = 0$ and $\nu_i(1) < \underline{D}$.

Multi-Species Result: The error between any componentwise positive solution $(S, x, y_1, y_2, \dots, y_n)$ of (AS) and

$$(S_r, x_r, 0, \dots, 0) = \left(\frac{1}{2} - \frac{1}{4} \cos(t), \frac{1}{2} + \frac{1}{4} \cos(t), 0, \dots, 0 \right)$$

converges exponentially to the zero vector as $t \rightarrow +\infty$.

ROBUSTNESS with respect to n ADDITIONAL SPECIES

$$\begin{cases} \dot{S} &= D(t)(1 - S) - \mu(S)x - \sum_{i=1}^n \nu_i(S)y_i, \\ \dot{x} &= x(\mu(S) - D(t)), \quad \dot{y}_i &= y_i(\nu_i(S) - D(t)) \end{cases} \quad (\text{AS})$$

D is from (D), $y_i =$ concentration of the i th additional species, each ν_i is continuous and increasing and satisfies $\nu_i(0) = 0$ and $\nu_i(1) < \underline{D}$.

Multi-Species Result: The error between any componentwise positive solution $(S, x, y_1, y_2, \dots, y_n)$ of (AS) and

$$(S_r, x_r, 0, \dots, 0) = \left(\frac{1}{2} - \frac{1}{4} \cos(t), \frac{1}{2} + \frac{1}{4} \cos(t), 0, \dots, 0 \right)$$

converges exponentially to the zero vector as $t \rightarrow +\infty$.

Significance: The stability of the reference trajectory (R) is robust with respect to additional species that are exponentially decaying to extinction.

OUTLINE of PROOF of MULTI-SPECIES RESULT

Since $\nu_i(1) < \underline{D}$ for each i , the form of the dynamics for S along our componentwise positive trajectories implies that there exist $\varepsilon > 0$ and $T \geq 0$ such that (i) $S(t) \leq 1 + \varepsilon$ for all $t \geq T$ and (ii) $\nu_i(1 + \varepsilon) < \underline{D}$ for all $i = 1, 2, \dots, n$. We next choose

$$\delta := \underline{D} - \max_{i=1, \dots, n} \nu_i(1 + \varepsilon) > 0.$$

OUTLINE of PROOF of MULTI-SPECIES RESULT

Since $\nu_i(1) < \underline{D}$ for each i , the form of the dynamics for S along our componentwise positive trajectories implies that there exist $\varepsilon > 0$ and $T \geq 0$ such that (i) $S(t) \leq 1 + \varepsilon$ for all $t \geq T$ and (ii) $\nu_i(1 + \varepsilon) < \underline{D}$ for all $i = 1, 2, \dots, n$. We next choose

$$\delta := \underline{D} - \max_{i=1, \dots, n} \nu_i(1 + \varepsilon) > 0.$$

The result now follows using the Lyapunov-like function

$$L_4(\tilde{z}, \tilde{\xi}, y_1, \dots, y_n) = L_3(\tilde{z}, \tilde{\xi}) + A \sum_{i=1}^n y_i^2, \quad \text{where } A := \frac{16mn^2}{a\delta}.$$

in conjunction with Barbalat's Lemma. Along the relevant trajectories,

$$\dot{L}_4 \leq -\frac{ma(e^{\tilde{\xi}} - 1)^2}{16(a+1)(a+2+\tilde{z}^2)} - \frac{3m}{a}\tilde{z}^2 - \frac{16mn^2}{a} \sum_{i=1}^n y_i^2.$$

ROBUSTNESS with respect to ACTUATOR ERRORS

$$\begin{cases} \dot{S}(t) &= [D(t) + u_1(t)](1 + u_2(t) - S(t)) - \mu(S(t))x(t), \\ \dot{x}(t) &= x(t)[\mu(S(t)) - D(t) - u_1(t)]. \end{cases} \quad (\Sigma_p)$$

ROBUSTNESS with respect to ACTUATOR ERRORS

$$\begin{cases} \dot{S}(t) &= [D(t) + u_1(t)](1 + u_2(t) - S(t)) - \mu(S(t))x(t), \\ \dot{x}(t) &= x(t)[\mu(S(t)) - D(t) - u_1(t)]. \end{cases} \quad (\Sigma_p)$$

If $|u|$ stays below a computable prescribed bound, then there are functions $\beta \in \mathcal{KL}$ and $\gamma \in \mathcal{K}_\infty$ such that the transformed error vector

$$y(t; t_o, y_o, \alpha) := (S(t; t_o, (S, x)(0), \alpha) - S_r(t), \ln(x(t; t_o, (S, x)(0), \alpha)) - \ln(x_r(t)))$$

for all disturbances $u = (u_1, u_2) = \alpha$ and initial conditions satisfies

$$|y(t; t_o, y_o, \alpha)| \leq \beta(|y_o|, t - t_o) + \gamma(|\alpha|_\infty). \quad (\text{ISS})$$

ROBUSTNESS with respect to ACTUATOR ERRORS

$$\begin{cases} \dot{S}(t) &= [D(t) + u_1(t)](1 + u_2(t) - S(t)) - \mu(S(t))x(t), \\ \dot{x}(t) &= x(t)[\mu(S(t)) - D(t) - u_1(t)]. \end{cases} \quad (\Sigma_p)$$

If $|u|$ stays below a computable prescribed bound, then there are functions $\beta \in \mathcal{KL}$ and $\gamma \in \mathcal{K}_\infty$ such that the transformed error vector

$$y(t; t_o, y_o, \alpha) := (S(t; t_o, (S, x)(0), \alpha) - S_r(t), \ln(x(t; t_o, (S, x)(0), \alpha)) - \ln(x_r(t)))$$

for all disturbances $u = (u_1, u_2) = \alpha$ and initial conditions satisfies

$$|y(t; t_o, y_o, \alpha)| \leq \beta(|y_o|, t - t_o) + \gamma(|\alpha|_\infty). \quad (\text{ISS})$$

Under the less stringent condition $|u| < \frac{1}{2} \min\{1, \underline{D}\}$, there are functions $\delta_i \in \mathcal{K}_\infty$ and $\beta \in \mathcal{KL}$ so that the trajectories everywhere satisfy

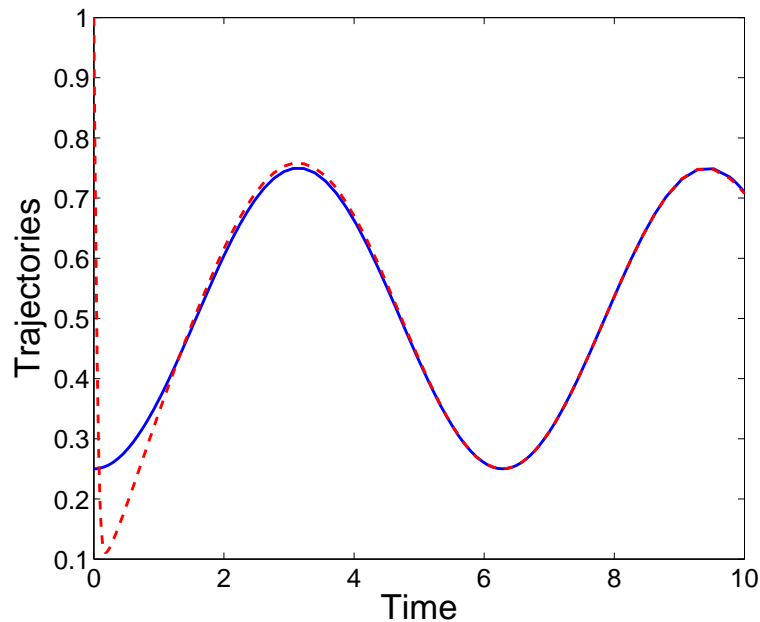
$$\delta_1(|y(t; t_o, y_o, \alpha)|) \leq \beta(|y_o|, t - t_o) + \int_{t_o}^{t+t_o} \delta_2(|\alpha(r)|) dr. \quad (\text{iISS})$$

SIMULATIONS

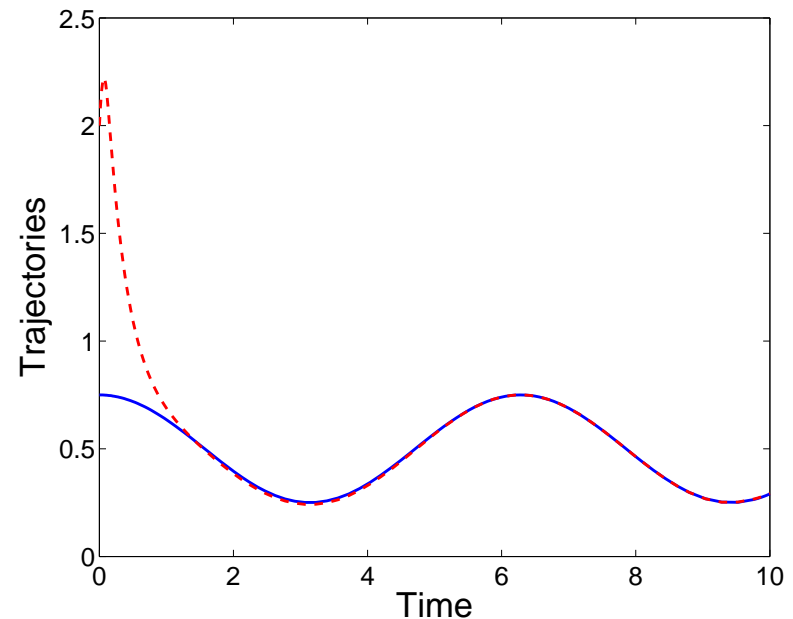
We simulated (Σ_p) with $m = 10$, $a = \frac{1}{2}$, $u_1(t) = 0.5e^{-t}$, $u_2(t) \equiv 0$, $t_o = 0$, $x(0) = 2$, and $S(0) = 1$. Our theory implies that the convergence of $(S(t), x(t))$ to $(S_r(t), x_r(t))$ satisfies iISS for disturbances u that are valued in $[-\bar{u}, \bar{u}]^2$ for any positive constant $\bar{u} < \min\{1, \underline{D}\} = 1$.

SIMULATIONS

We simulated (Σ_p) with $m = 10$, $a = \frac{1}{2}$, $u_1(t) = 0.5e^{-t}$, $u_2(t) \equiv 0$, $t_o = 0$, $x(0) = 2$, and $S(0) = 1$. Our theory implies that the convergence of $(S(t), x(t))$ to $(S_r(t), x_r(t))$ satisfies iISS for disturbances u that are valued in $[-\bar{u}, \bar{u}]^2$ for any positive constant $\bar{u} < \min\{1, \underline{D}\} = 1$.



(a) $S(t)$ Tracking $S_r(t)$



(b) $x(t)$ Tracking $x_r(t)$

CONCLUSIONS

- Chemostats provide an important framework for modeling **species competing** for nutrients. They provide the foundation for much current research in **bioengineering**, **ecology**, and **population biology**.

CONCLUSIONS

- Chemostats provide an important framework for modeling **species competing** for nutrients. They provide the foundation for much current research in **bioengineering**, **ecology**, and **population biology**.
- For the case of one species competing for one nutrient and a suitable time-varying dilution rate, we proved the stability of an appropriate **reference trajectory** using **Lyapunov function methods**.

CONCLUSIONS

- Chemostats provide an important framework for modeling **species competing** for nutrients. They provide the foundation for much current research in **bioengineering**, **ecology**, and **population biology**.
- For the case of one species competing for one nutrient and a suitable time-varying dilution rate, we proved the stability of an appropriate **reference trajectory** using **Lyapunov function methods**.
- The stability is maintained when there are additional species that are being driven to extinction, or **disturbances of small magnitude** on the dilution rate and input nutrient concentration.

CONCLUSIONS

- Chemostats provide an important framework for modeling **species competing** for nutrients. They provide the foundation for much current research in **bioengineering**, **ecology**, and **population biology**.
- For the case of one species competing for one nutrient and a suitable time-varying dilution rate, we proved the stability of an appropriate **reference trajectory** using **Lyapunov function methods**.
- The stability is maintained when there are additional species that are being driven to extinction, or **disturbances of small magnitude** on the dilution rate and input nutrient concentration.
- Extensions to chemostats with **multiple competing species**, time **delays**, **limited information** about the current state, and **measurement uncertainty** would be desirable and are being studied.

ACKNOWLEDGEMENTS

- Malisoff was supported by NSF/DMS Grant 0424011. De Leenheer was supported by NSF/DMS Grant 0500861. The authors thank Jeff Sheldon and Hairui Tu for assisting with the graphics.

ACKNOWLEDGEMENTS

- Malisoff was supported by NSF/DMS Grant 0424011. De Leenheer was supported by NSF/DMS Grant 0500861. The authors thank Jeff Sheldon and Hairui Tu for assisting with the graphics.
- A journal version will appear in *Mathematical Biosciences and Engineering*. The authors thank Yang Kuang for the opportunity to publish their work in his esteemed journal.

ACKNOWLEDGEMENTS

- Malisoff was supported by NSF/DMS Grant 0424011. De Leenheer was supported by NSF/DMS Grant 0500861. The authors thank Jeff Sheldon and Hairui Tu for assisting with the graphics.
- A journal version will appear in *Mathematical Biosciences and Engineering*. The authors thank Yang Kuang for the opportunity to publish their work in his esteemed journal.
- Part of this work was done while Mazenc and De Leenheer visited the Louisiana State University (LSU) Department of Mathematics. They thank LSU for the kind hospitality they enjoyed.

ACKNOWLEDGEMENTS

- Malisoff was supported by NSF/DMS Grant 0424011. De Leenheer was supported by NSF/DMS Grant 0500861. The authors thank Jeff Sheldon and Hairui Tu for assisting with the graphics.
- A journal version will appear in *Mathematical Biosciences and Engineering*. The authors thank Yang Kuang for the opportunity to publish their work in his esteemed journal.
- Part of this work was done while Mazenc and De Leenheer visited the Louisiana State University (LSU) Department of Mathematics. They thank LSU for the kind hospitality they enjoyed.
- The authors thank the referees, Madalena Chaves, and Eduardo Sontag for illuminating comments and discussions at the 45th IEEE Conference on Decision and Control in San Diego, CA.