

Stability and Robustness Analysis for a Multispecies Chemostat Model with Delays in the Growth Rates and Uncertainties

Frederic Mazenc

Michael Malisoff

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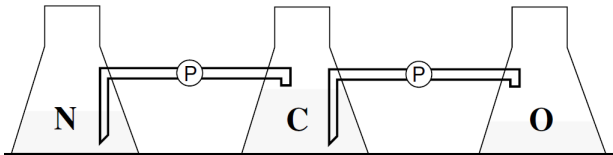
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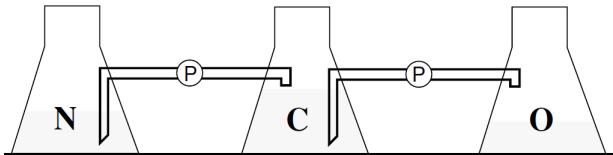
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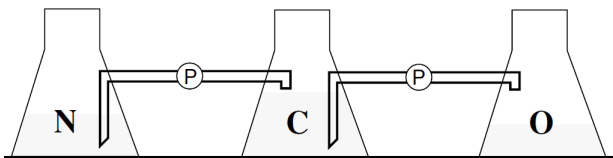
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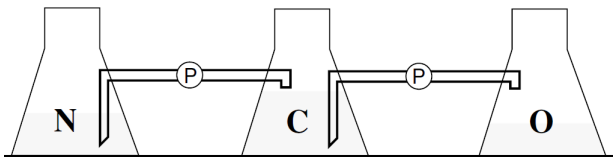


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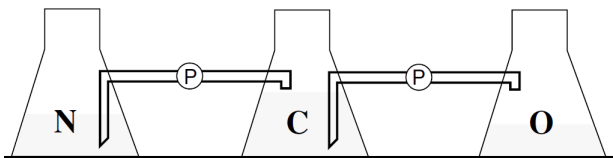
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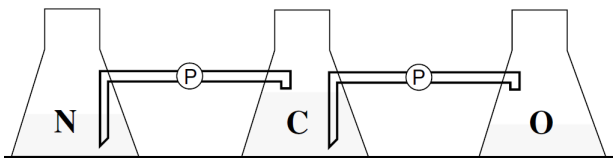
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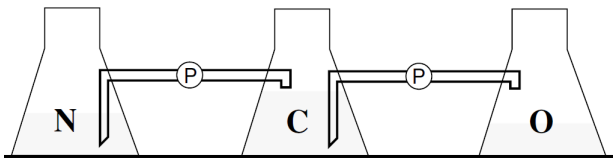
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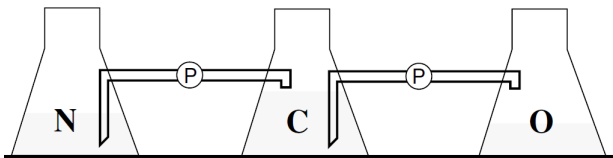
rate of change of organism = growth - washout.

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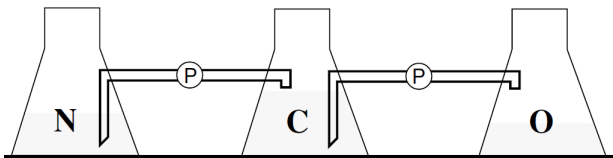
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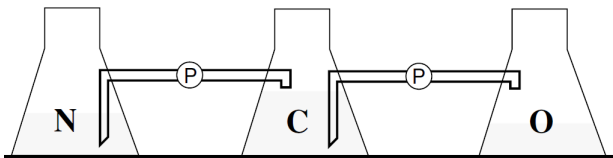


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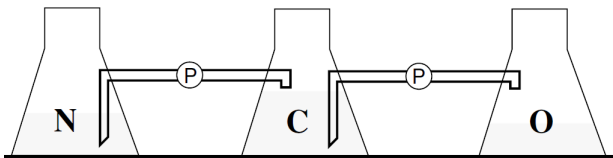
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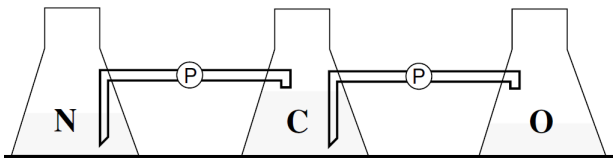
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Our Models and Theorem

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$$\begin{cases} \dot{s}(t) = D[s_{\text{in}} - s(t)] - \sum_{i=1}^n \mu_i(s(t))x_i(t) + \delta_0(t) \\ \dot{x}_i(t) = x_i(t)\mu_i(s(t-\tau_i)) + D[x_i^0 - x_i(t)] + \delta_i(t), \quad 1 \leq i \leq n \end{cases} \quad (\text{M})$$

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Assumptions. The equilibria and disturbance bounds satisfy:

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- 2) $\delta_i(t) \in [\underline{d}_i, \bar{d}_i]$ for all i where $Ds_{\text{in}} + \underline{d}_0 > 0$, $\bar{d}_0 < 0.5Ds_*$, $Dx_i^0 + \underline{d}_i > 0$ for all indices $i \in \mathcal{P}$, and $\underline{d}_i = 0$ for all indices $i \in \{1, 2, \dots, n\} \setminus \mathcal{P}$, where $\mathcal{P} = \{i \in \{1, 2, \dots, n\} : x_i^0 > 0\}$.

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Assumption 2) maintains forward invariance of $(0, \infty)^{n+1}$ for (M).

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Constant Controls: x_i^0 and s_{in} . x_i^0 : inputs from other chemostats.

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We also have an Assumption 3) with a bound $\bar{\tau}$ on the delays τ_i .

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Theorem: Under our assumptions, for all constants $\underline{x} > 0$ and $\bar{s} \geq s_{\text{in}}$, the dynamics for the error vector $\mathcal{E} = (s, x) - \mathcal{E}_*$ satisfy ISS on the set $\mathcal{S}_{\bar{s}, \underline{x}} = \{\mathcal{E} : \mathcal{E} + \mathcal{E}_* \in (0, \bar{s}] \times (0, \infty)^{n-1} \times (\underline{x}, \infty)\}$. \square

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Significance: Uniform persistence of all species for which $x_i^0 > 0$. ISS for arbitrarily large upper bounds \bar{d}_i on $\delta_i(t)$ for $i \geq 1$.

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Significance: Since $\underline{x} > 0$ and $\bar{s} \geq s_{\text{in}}$ are arbitrary, we get ISS properties on all of $(0, \infty)^{n+1}$ under our disturbance bounds.

Main Idea of Proof: Undelayed Case

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Construct a function $T \in \mathcal{K}_\infty$ and constants $c_i > 0$ and $k_i > 0$ such that the time derivative of

$$V(\mathcal{E}) = \tilde{s} - s_* \ln \left(\frac{\tilde{s} + s_*}{s_*} \right) + \sum_{i=1}^n \frac{1}{c_i} \Psi_i(\tilde{x}_i), \text{ where}$$

$$\Psi_i(\tilde{x}_i) = \tilde{x}_i - x_{i*} \ln \left(\frac{\tilde{x}_i + x_{i*}}{x_{i*}} \right) \text{ for all } i \in \mathcal{P}$$

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along all solutions of (M) starting in any $\mathcal{S}_{\tilde{s}, \underline{x}}$ with $\tau_i = 0$ satisfies

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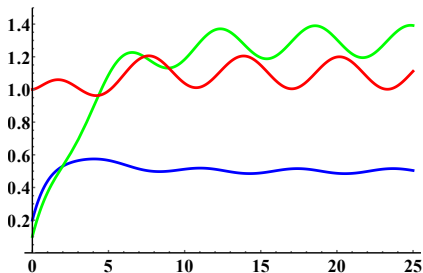
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Simulations

$$\begin{aligned} n = 2, \quad D = 0.4, \quad s_* = 0.5, \quad x_1^0 = 1, \quad x_2^0 = 0.55, \quad s_{\text{in}} = 1.34412, \\ \mu_1(s) = \frac{s}{5+s}, \quad \mu_2(s) = \frac{s}{2+s}, \quad x_{1*} = 1.29412, \quad x_{2*} = 1.1, \quad \tau = (0.14, 0) \\ \delta(t) = (\delta_0(t), \delta_1(t), \delta_2(t)) = (0, -0.1 \sin(t), 0.1 \cos(t)). \end{aligned}$$

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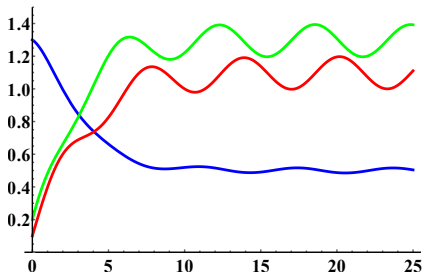
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$x_1(t)$ and $x_2(t)$ are Green and Red Curves, Respectively. $s(t)$ is Blue Curve. Initial State $(s(0), x_1(0), x_2(0)) = (0.2, 0.1, 1)$.

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$x_1(t)$ and $x_2(t)$ are Green and Red Curves, Respectively. $s(t)$ is Blue Curve. Initial State $(s(0), x_1(0), x_2(0)) = (1.3, 0.2, 0.1)$.

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Backup Slides to Use if
Time Allows or Questions Warrant

Our Models and Theorem

$$\begin{cases} \dot{s}(t) = D[s_{\text{in}} - s(t)] - \sum_{i=1}^n \mu_i(s(t))x_i(t) + \delta_0(t) \\ \dot{x}_i(t) = x_i(t)\mu_i(s(t-\tau_i)) + D[x_i^0 - x_i(t)] + \delta_i(t), \quad 1 \leq i \leq n \end{cases} \quad (\text{M})$$

$\mu_i(s) = \frac{m_i s}{a_i + s}$. Equilibria: $\mathcal{E}_* = (s_*, x_{1*}, \dots, x_{n*}) \in (0, \infty) \times [0, \infty)^n$.

Reduces to Gouze-Robledo model when uncertainties δ_i and delays τ_i are 0 and usual model when the inputs $x_i^0 \geq 0$ are zero.

Theorem: Under our assumptions, for all constants $\underline{x} > 0$ and $\bar{s} \geq s_{\text{in}}$, the dynamics for the error vector $\mathcal{E} = (s, x) - \mathcal{E}_*$ satisfy ISS on the set $\mathcal{S}_{\bar{s}, \underline{x}} = \{\mathcal{E} : \mathcal{E} + \mathcal{E}_* \in (0, \bar{s}] \times (0, \infty)^{n-1} \times (\underline{x}, \infty)\}$. \square

Significance: Since $\underline{x} > 0$ and $\bar{s} \geq s_{\text{in}}$ are arbitrary, we get ISS properties on all of $(0, \infty)^{n+1}$ under our disturbance bounds.

Main Idea of Proof: Undelayed Case

Construct a function $T \in \mathcal{K}_\infty$ and constants $c_i > 0$ and $k_i > 0$ such that the time derivative of

$$V(\mathcal{E}) = \tilde{s} - s_* \ln \left(\frac{\tilde{s} + s_*}{s_*} \right) + \sum_{i=1}^n \frac{1}{c_i} \Psi_i(\tilde{x}_i), \text{ where}$$

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along all solutions of (M) starting in any $\mathcal{S}_{\tilde{s}, X}$ with $\tau_i = 0$ satisfies

$$\frac{d}{dt} V(\mathcal{E}(t)) \leq -k_1 \left(\frac{\tilde{s}^2(t)}{s(t)} + \sum_{i=1}^n \frac{\tilde{x}_i^2(t)}{x_i(t)} \right) + k_2 |\delta|_{[0,t]} \quad (1)$$

for all $t \geq T(|\mathcal{E}(0)|)$, where $\tilde{x}_i = x_i - x_{i*}$ for all i and $\tilde{s} = s - s_*$.
Extend this to ISS estimate on $[0, \infty)$ by a trajectory analysis.

Main Idea of Proof: Delayed Case

Build $T \in \mathcal{K}_\infty$ and positive constants \mathcal{M}_* , v_0 , and \bar{N} such that

$$V^\#(\tilde{s}_t, \tilde{\alpha}(t)) = V(\tilde{s}(t), \tilde{\alpha}(t)) + \mathcal{M}_* \int_{t-\bar{\tau}}^t \int_{\ell}^t \frac{\tilde{s}^2(r)}{s(r)} dr d\ell \quad (2)$$

satisfies

$$\overbrace{V^\#(\tilde{s}_t, \tilde{\alpha}(t))}^{\cdot} \leq -v_0 \left(\frac{\tilde{s}^2(t)}{s(t)} + \sum_{i=1}^n \frac{\tilde{\alpha}_i^2(t)}{\alpha_i(t)} + \int_{t-\bar{\tau}}^t \int_{\ell}^t \frac{\tilde{s}^2(r)}{s(r)} dr d\ell \right) + \bar{N} |\delta|_{[0,t]}$$

along all solutions of the $(\tilde{s}, \tilde{\alpha})$ system for all $t \geq T(|\mathcal{E}(0)|)$ where

$$\alpha_i(t) = x_i(t) e^{\int_{t-\tau_i}^t [\mu_i(s(\ell)) - \mu_i(s_*)] d\ell} \quad (3)$$

for all i , V is the Lyapunov construction from the undelayed case, $\tilde{s} = s - s_*$ is as before, and $\tilde{\alpha}_i = \alpha_i - x_{i*}$ and $\tau_i \leq \bar{\tau}$ for all i .

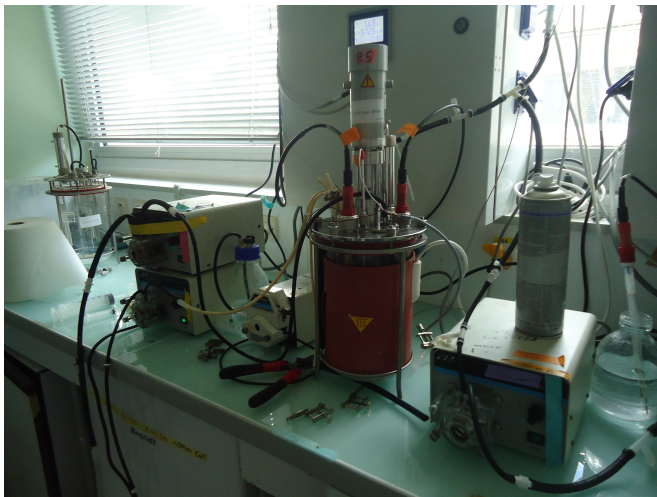
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References with Hyperlinked Paper Titles

Mazenc, F., G. Robledo, and M. Malisoff, "Stability and robustness analysis for a multispecies chemostat model with delays in the growth rates and uncertainties," *Discrete and Continuous Dynamical Systems Series B*, to appear.

Mazenc, F., J. Harmand, and M. Malisoff, "Stabilization in a chemostat with sampled and delayed measurements and uncertain growth functions," *Automatica*, Volume 78, April 2017, pp. 241-249.

Karafyllis, I., M. Malisoff, and M. Krstic, "Sampled-data feedback stabilization of age-structured chemostat models," in *Proceedings of the 2015 American Control Conference (Chicago, IL, 1-3 July 2015)*, pp. 4549-4554.

References with Hyperlinked Paper Titles

Mazenc, F., and M. Malisoff, "Stability and stabilization for models of chemostats with multiple limiting substrates," *Journal of Biological Dynamics*, Volume 6, Issue 2, 2012, pp. 612-627.

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