

Stabilization in a Chemostat with Sampled and Delayed Measurements

Michael Malisoff

Joint with Jerome Harmand and Frederic Mazenc

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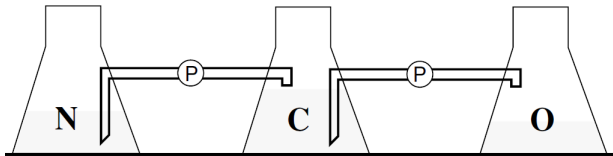
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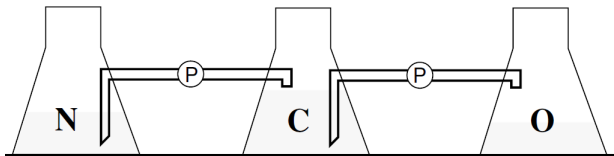
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Review of Simple Chemostat



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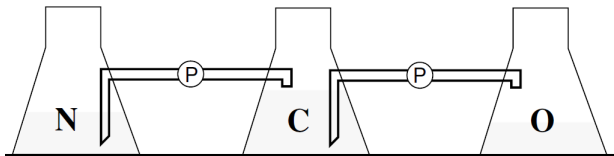
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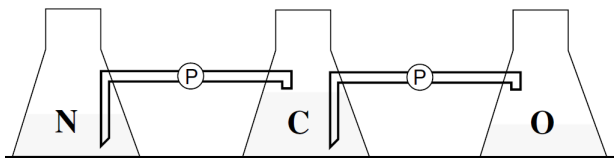


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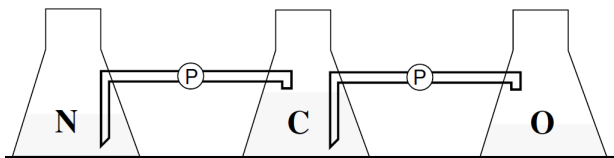
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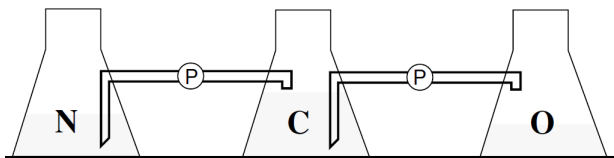
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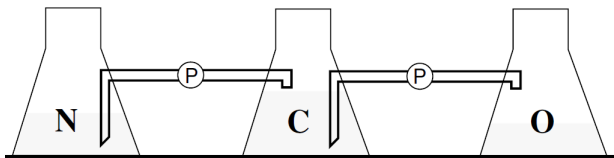
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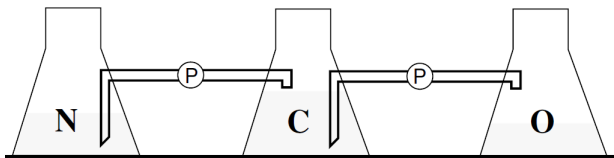
rate of change of organism = growth - washout.

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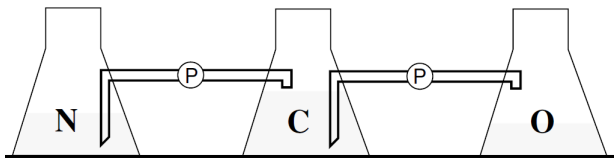
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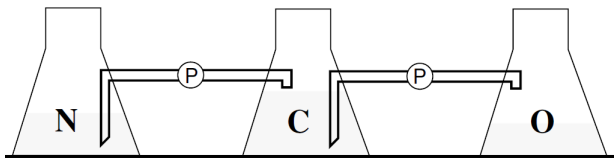


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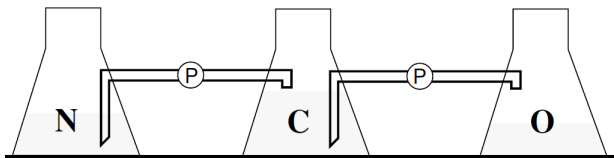
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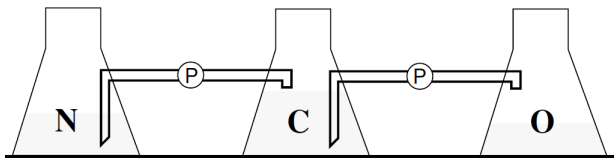
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$\gamma_i \in \mathcal{K}_\infty$: 0 at 0, strictly increasing, unbounded. $\sup_{t \geq 0} \tau(t) \leq \bar{\tau}$.

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Equivalent to \mathcal{KL} formulation; see Sontag 1998 SCL paper.

Uncertain Controlled Chemostat with Sampling

$$\begin{cases} \dot{s}(t) = D(s(t - \tau(t)))[s_{\text{in}} - s(t)] - (1 + \delta(t))\mu(s(t))x(t) \\ \dot{x}(t) = [(1 + \delta(t))\mu(s(t)) - D(s(t - \tau(t)))]x(t) \end{cases} \quad (\text{C})$$

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Assumption 1: The function μ is C^1 and $\mu(0) = 0$. Also, there is a constant $s_M \in (0, s_{\text{in}}]$ such that $\mu'(s) > 0$ for all $s \in [0, s_M)$ and $\mu'(s) \leq 0$ for all $s \in [s_M, \infty)$. Finally, $\mu(s) > 0$ for all $s > 0$.

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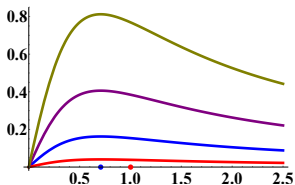
$\mu(s) \stackrel{(*)}{=} \frac{\mu_1(s)}{1 + \gamma(s)}$, with a unique maximizer $s_M \in (0, s_{\text{in}}]$

Lemma: Under Assumption 1, there are $\mu_1 \in C^1 \cap \mathcal{K}_\infty$ and a nondecreasing C^1 function $\gamma : \mathbb{R} \rightarrow [0, \infty)$ such that $(*)$ holds for all $s \geq 0$, $\mu'_1(s) > 0$ on $[0, \infty)$, and $\gamma'(s) > 0$ on $[s_M, \infty)$.

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$(1 + \delta)\mu(s)$ for Different Constant δ Choices, $s_M = 1/\sqrt{2}$ and $s_{\text{in}} = 1$

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Goal: Under suitable conditions on an upper bound τ_M for the delay $\tau(t)$, and for constants $s_* \in (0, s_{\text{in}})$, design the control D to render the dynamics for $X(t) = (s(t), x(t)) - (s_*, s_{\text{in}} - s_*)$ ISS.

Main Result for Unperturbed Case

$$\omega_s = \inf_{s \in [0, s_{in}]} \mu'_1(s), \quad \omega_l = \sup_{s \in [0, s_{in}]} \mu'_1(s), \quad \rho_l = \sup_{s \in [0, s_{in}]} \gamma'(s),$$

$$\rho_m = \frac{\rho_l^2}{2\omega_s} \max_{l \in [0, s_{in}]} \frac{\mu_1^2(l + 1.1\mu_1(s_*)s_{in}\tau_M)}{1 + \gamma(l)}, \quad \text{where } \mu(s) = \frac{\mu_1(s)}{1 + \gamma(s)}$$

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$$\text{and } \tau_M \stackrel{(b)}{<} \max \left\{ \frac{1}{2s_{in}\sqrt{2\rho_m\omega_l}}, \frac{1}{2\rho_l s_{in}\mu_1(s_{in})} \right\}, \quad \text{with } s_* < s_{in}.$$

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Theorem 1: For all componentwise positive initial conditions, all solutions of the chemostat system (C) with $\delta(t) = 0$ and

$$D(s(t - \tau(t))) = \frac{\mu_1(s_*)}{1 + \gamma(s(t - \tau(t)))} \quad (1)$$

remain in $(0, \infty)^2$ and converge to $(s_*, s_{\text{in}} - s_*)$. \square

Proof Outline for $\delta = 0$ Unperturbed Case

Step 1: For any fixed $\bar{s} \geq s_{\text{in}}$, show that $z = s_{\text{in}} - s - x$ satisfies

$$|z(t)| \leq |z(0)| e^{\frac{-t\mu_1(s_*)}{1+\gamma(\bar{s})}} \text{ for all } t \geq 0. \quad (\text{ES})$$

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$z = -(x - s_{\text{in}} + s_*) - (s - s_*) = -X_2 - X_1$. X = error variable.

Proof Outline for $\delta = 0$ Unperturbed Case

Step 1: For any fixed $\bar{s} \geq s_{\text{in}}$, show that $z = s_{\text{in}} - s - x$ satisfies

$$|z(t)| \leq |z(0)| e^{\frac{-t\mu_1(s_*)}{1+\gamma(\bar{s})}} \text{ for all } t \geq 0. \quad (\text{ES})$$

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Step 2: Build $\mathcal{T} \in \mathcal{K}_\infty$ and a constant $\bar{c} > 0$ such that

$$\mathcal{U}_1(s) = \int_0^{s-s_*} \frac{m}{s_{\text{in}} - s_* - m} dm, \quad (2)$$

satisfies

$$\begin{aligned} \dot{\mathcal{U}}_1(t) \leq & \frac{(s(t) - s_*)(\mu_1(s_*) - \mu_1(s(t)))}{2[1 + \gamma(s(t - \tau(t)))]} \\ & + \rho m \tau_M \int_{t-\tau(t)}^t (\dot{s}(m))^2 dm + \bar{c} |s(t) - s_*| |z(t)| \end{aligned} \quad (3)$$

for all $t \geq \mathcal{T}(|X(0)|)$ where $X(t) = (s(t), x(t)) - (s_*, s_{\text{in}} - s_*)$.

Proof Outline for $\delta = 0$ Unperturbed Case

Step 3: Find constants $c_i > 0$ such that

$$\mathcal{U}_2(\mathbf{s}_t) = \int_0^{s^{(t)}-s_*} \frac{m}{s_{\text{in}}-s_*-m} dm + 2\rho_m \tau_M \int_{t-\tau_M}^t \int_{\ell}^t (\dot{s}(m))^2 dm d\ell. \quad (4)$$

satisfies

$$\dot{\mathcal{U}}_2(t) \leq -c_1 \mathcal{U}_2(\mathbf{s}_t) + c_2 z^2(t) + \bar{c} |s(t) - s_*| |z(t)| \quad (5)$$

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Step 4: The sum \mathcal{U}_3 of a quadratic Lyapunov function for the z variable and \mathcal{U}_2 admits a constant $c_3 > 0$ such that

$$\dot{\mathcal{U}}_3(t) \leq -c_3 \mathcal{U}_3(\mathbf{s}_t, z(t)) \quad (6)$$

for all $t \geq \mathcal{T}(|X(0)|)$.

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ISS with respect to $\delta(t)$ without upper bounds on $|\delta|_\infty \dots$

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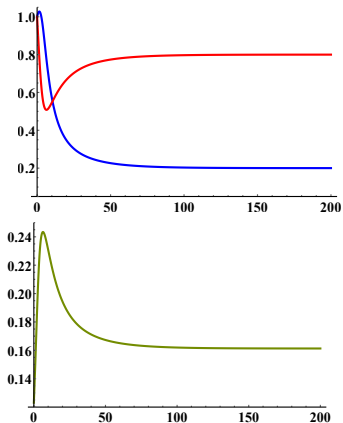
$$\frac{(1+d)\mu_1(s_{in})}{1+\gamma(s_{in})} - \frac{\mu_1(s_*)}{1+\gamma(s_{in}-\mu_1(s_*)s_{in}\tau_M)} \stackrel{(a)}{>} 0 \quad \dots(1 + \delta(t))\mu(s(t))\dots$$

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Mazenc, F., J. Harmand, and M. Malisoff, "Stabilization in a chemostat with sampled and delayed measurements and uncertain growth functions," *Automatica*, 2017.

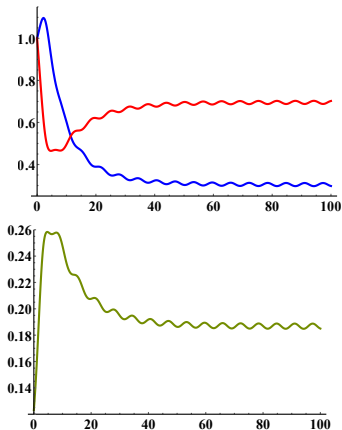
Mathematica Simulations of (C)



$$s_{\text{in}} = 1, \mu(s) = \frac{0.5s}{1+0.25s+2s^2}, t_j = 0.24j, \delta(t) = 0.$$

$s(t)$ in Red, $x(t)$ in Blue, $D(t)$ in Green.

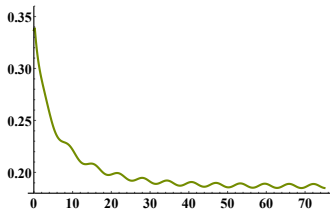
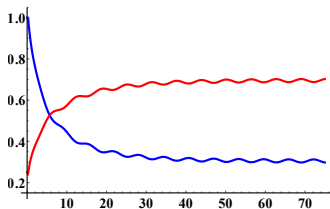
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Thank you for your attention!

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.

Mazenc, F., and M. Malisoff, "Strict Lyapunov function constructions under LaSalle conditions with an application to Lotka-Volterra systems," *IEEE Transactions on Automatic Control*, Volume 55, Issue 4, April 2010, pp. 841-854.

Mazenc, F., M. Malisoff, and J. Harmand, "Further results on stabilization of periodic trajectories for a chemostat with two species," *IEEE Transactions on Automatic Control*, Volume 53, Special Issue on Systems Biology, January 2008, pp. 66-74.