


Stabilization of age-structured chemostat hyperbolic PDE with actuator dynamics

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Abstract

For population systems modeled by age-structured hyperbolic partial differential equations (PDEs), we redesign the existing feedback laws, designed under the assumption that the dilution input is directly actuated, to the more realistic case where dilution is governed by actuation dynamics (modeled simply by an integrator). In addition to the standard constraint that the population density must remain positive, the dilution dynamics introduce constraints of not only positivity of dilution, but possibly of given positive lower and upper bounds on dilution. We present several designs, of varying complexity, and with various measurement requirements, which not only ensure global asymptotic (and local exponential) stabilization of a desired positive population density profile from all positive initial conditions, but do so without violating the constraints on the dilution state. To develop the results, we exploit the relation between first-order hyperbolic PDEs and an equivalent representation in which a scalar input-driven mode is decoupled from input-free infinite-dimensional internal dynamics represented by an integral delay system.

KEYWORDS

chemostat, first-order hyperbolic PDE, state constraints, time-delay systems

1 | INTRODUCTION

1.1 | Motivation: Chemostat as a benchmark for nonlinear control and for control in epidemiology

Many industrial biotechnology processes can be described by a nonlinear PDE (partial differential equation) of population dynamics that are structured around age. Reflecting the maturation of enzymes, microbial organisms, animal or plant cells and tissues,^{1–3} these models of biological and biochemical systems are often exploited to favor the desired functionalities and achieve cost-effective bioreactors' production rate.^{4–6} The word “chemostat” denotes a biological process in which is fed a nutrient at a certain rate and from which a bioproduct-nutrient mix is being extracted/removed at the same rate.⁴ This rate is referred to as the “dilution rate.” The relevance of chemostats in control engineering extends beyond their own application in biotechnology (such as the manufacturing of pharmaceuticals). First, a chemostat is a nonlinear control problem—even when the limiting substrate(s) nonlinear dynamics are neglected—due to the fact that its dynamic model

Abbreviations: BC, boundary condition; IDE, integral delay equation; ODE, ordinary differential equation; OE, output equation; PDE, partial differential equation.

contains a product of the population density and the dilution rate. Second, the relevance of the chemostat is also in the fact that it is an example of a “positive system,” namely, a control system whose state is subject to an inequality constraint.^{7,8}

Third, and perhaps most important at present, chemostat is a special case of more complex population dynamics such as those that arise in epidemiology.^{9,10} In fact, Reference 11 makes the connection between chemostat and SIR models explicit. Before one takes on control design of SIR-type (susceptible-infected-recovered) models in epidemiology, in which control is being applied to more than one population (e.g., to the susceptible and the infected populations), it is necessary to understand how to control single-population chemostats. Just as there is a parallel between the biomass in a chemostat and the infected population in epidemiology, as well as between the substrate in a chemostat and the susceptible population in epidemiology,^{9,12} there is likewise a parallel between the treatment/therapy being administered as an input in epidemiology and the dilution input of a chemostat.

Hence, the study of control of an age-structured chemostat that we undertake here is an important first step towards designing controllers for *age-structured* models in epidemiology.

1.2 | Age-structured population dynamics

Age-structured chemostat models are described by a particular first order hyperbolic partial differential equation (PDE) with a non-local boundary condition: the McKendrick-von Foerster equation (see References 13–18 and the references therein). Age-structured models are extensions of the chemostat models described by ordinary differential equations (ODEs; see Reference 19). A particular and deep mathematical tool has been developed for the study of age-structured models: the ergodic theorem, also known as the asymptotic behavior (see References 18,20,21 for similar results on asymptotic similarity and Reference 4 for the proof of the ergodic theorem by means of Lyapunov arguments).

Control studies for age-structured models are rare. Optimal control problems have been studied (see References 16,22,23 and the references therein). On the other hand, feedback control of infinite-dimensional population dynamics was introduced in Reference 4 and further considered in References 6,24. More specifically, the use of the ergodic theorem and the corresponding study of linear integral delay equations in Reference 4 led to a special nonlinear infinite-dimensional change of variables, from the age-structured population density (a population density that is a function of the continuum age) into

1. a scalar variable that represents the controllable mode of the bilinear non-local hyperbolic PDE system which is directly actuated by the dilution rate input, and
2. an infinite-dimensional uncontrollable but exponentially stable dynamical system described by linear integral delay equations,

and has subsequently been the cornerstone of the control design and stability analysis of age-structured population dynamics.

The control studies in References 4,6,24 used the dilution rate as the control input as in many other control studies of chemostat models described by ODEs (see References 25–29). Actuation by dilution rate is both physical and plausible and it amounts to harvesting the population. In simplistic terms, a steady level of harvesting is needed to maintain the population at a sustained level (equilibrium) and, when the population exceeds such an equilibrium, it is over-harvested by (over) dilution, whereas when the population drops below such an equilibrium, it is under-harvested by (under) dilution. How this over- and under-harvesting is to be done exactly is highly non-trivial because the population is age-structured, meaning that its state is functional/infinite-dimensional, due to which one cannot really speak of overpopulation and under population in a bulk sense. One has, instead, to take into account that the population can vary from the equilibrium in infinitely many ways (overpopulated old with underpopulated young, vice-versa, and so on). This infinite variety in the state profiles, in addition to the infinite number of states (age-specific densities), along with the nonlinearity of the problem, is one of the theoretical attractions to this control design problem.

1.3 | Chemostat with dynamic actuation of dilution

While dilution is a plausible form of actuation, it is not possible to actuate it instantaneously. As with any other actuation, it is governed by its own dynamics. In the case of dilution, it is affected by the dynamics of pipes and valves that

are used to run the nutrients into a chemostat and the population-nutrient mix out of the chemostat. In biochemical engineering, the dilution rate is defined as the ratio of the inlet volumetric flow rate to the reactor volume. Since the volume of the reactor is not necessarily constant, it follows that the dynamics of the dilution rate can play an important role.

In this paper we design stabilizing feedback laws for the age-structured chemostat with dilution dynamics governed by a single, scalar integrator. In the most advanced versions of our designs, we ensure that not only the population density, but also the dilution rate, remains in a specific interval (and positive). Dilution rate being positive means that we are not feeding population back into the chemostat but are only harvesting/removing population.

While the age-structured chemostat with a constant dilution rate is a PDE system with one eigenvalue at the origin and all other eigenvalues in the left half plane, meaning that it is not open-loop unstable, and meaning that it can, at worst, settle at an undesirable age profile for the population (provided the constant dilution is at a population-sustaining level), the system with dilution dynamics modeled by an integrator has two eigenvalues at the origin, meaning that it is open-loop unstable. This is one more way of noting the need for a more sophisticated control design for this PDE system once the dynamics of the dilution actuation are introduced.

In this paper we tackle three design challenges:

1. we overcome the dynamics of the integrator modeling the dilution actuation,
2. we perform the design and the analysis using feedback of only a sensor of bulk population, which has an unknown profile in sensing populations of different ages,
3. we ensure that the dilution rate that drives the population to the desired age-structured equilibrium from all initial positive population density age profiles remains itself in a specific interval (and positive).

While in the initial work on control of the age-structured chemostat⁴ the state space of the systems was, so to speak, the “positive orthant” of infinite dimension (the age-structured population density), in this work the state space increases by one positive-valued state when the dilution dynamics are modeled by an integrator and becomes, so to speak, a “positive orthant” of dimension $\infty + 1$. From a mathematical point of view, the paper deals with a global feedback stabilization problem for a constrained nonlinear infinite-dimensional control system which is defined on a specific open set. Finite-dimensional control systems defined on open sets were recently studied in Reference 30.

In comparing the results of the present paper with those in the landmark and incredibly complex Reference 4, by the time the reader has made it through Sections 3,4,5, the reader will note that even a single integrator takes the demands in control design and stability analysis to a whole next level in complexity. Furthermore, by the time the reader has completed the study of Sections 6 and 7, s/he will note that maintaining the positivity of that extra scalar state, the dilution, requires another two or three levels of complexity, in both control design and Lyapunov construction.

Organization: The structure of the paper is as follows. Section 2 introduces the mathematical model as well as the stabilization problem. Sections 3 and 4 study the backstepping design of the problem with unrestricted dilution rate assuming that the state is available, while Section 5 provides globally stabilizing output feedback laws. Sections 6 and 7 are devoted to the feedback stabilization problem of the more demanding case where the dilution rate is restricted to take values in a specific interval.

Notation:

1. \mathbb{R}_+ denotes the interval $[0, +\infty)$.
2. Let U be an open subset of a metric space and $\Omega \subseteq \mathbb{R}^m$ be a set. By $C^0(U; \Omega)$, we denote the class of continuous mappings on U , which take values in Ω . When $U \subseteq \mathbb{R}^n$, by $C^1(U; \Omega)$, we denote the class of continuously differentiable functions on U , which take values in Ω . When $U = [a, b] \subseteq \mathbb{R}$ (or $U = [a, b] \subseteq \mathbb{R}$) with $a < b$, $C^0([a, b]; \Omega)$ (or $C^0([a, b]; \Omega)$) denotes all functions $f : [a, b] \rightarrow \Omega$ (or $f : [a, b] \rightarrow \Omega$), which are continuous on (a, b) and satisfy $\lim_{s \rightarrow a^+} f(s) = f(a)$ (or $\lim_{s \rightarrow a^+} f(s) = f(a)$ and $\lim_{s \rightarrow b^-} f(s) = f(b)$). When $U = [a, b] \subseteq \mathbb{R}$, $C^1([a, b]; \Omega)$ denotes all functions $f : [a, b] \rightarrow \Omega$ which are continuously differentiable on (a, b) and satisfy $\lim_{s \rightarrow a^+} (f(s)) = f(a)$ and $\lim_{h \rightarrow 0^+} h^{-1}(f(a+h) - f(a)) = \lim_{s \rightarrow a^+} f'(s)$.
3. \mathcal{K}_∞ is the class of all strictly increasing, unbounded functions $a \in C^0(\mathbb{R}_+; \mathbb{R}_+)$, with $a(0) = 0$ (see References 31,32).
4. \mathcal{KL} is the class of functions $\beta : \mathbb{R}_+ \times \mathbb{R}_+ \rightarrow \mathbb{R}_+$ which satisfy the following: For each $t \geq 0$, the mapping $\beta(\cdot, t)$ is of class \mathcal{K} , and, for each $s \geq 0$, the mapping $\beta(s, \cdot)$ is nonincreasing with $\lim_{t \rightarrow \infty} \beta(s, t) = 0$ (see References 31,32).
5. For any subset $S \subseteq \mathbb{R}$ and for any $A > 0$, $PC^1([0, A]; S)$ denotes the class of all functions $f \in C^0([0, A]; S)$ for which there exists a finite (or empty) set $B \subset (0, A)$ such that: (i) the derivative $f'(a)$ exists at every $a \in (0, A) \setminus B$ and is a continuous

function on $(0, A) \setminus B$, (ii) all meaningful right and left limits of $f'(a)$ when a tends to a point in $B \cup \{0, A\}$ exist and are finite.

6. Let a function $f \in C^0(\mathbb{R}_+ \times [0, A])$ be given, where $A > 0$ is a constant. We use the notation $f[t]$ to denote the profile at certain $t \geq 0$, that is, $(f[t])(a) = f(a, t)$ for all $a \in [0, A]$.
7. Let a function $x \in C^0([-A, +\infty); \mathbb{R})$ be given, where $A > 0$ is a constant. We use the notation $x_t \in C^0([-A, 0]; \mathbb{R})$ to denote the “ A -history” of x at certain $t \geq 0$, that is, $(x_t)(-a) = x(t - a)$ for all $a \in [0, A]$.
8. Let a function $f \in C^0(\mathbb{R}_+; \mathbb{R})$ be given. By $D^+f : \mathbb{R}_+ \rightarrow \mathbb{R}$, $t \mapsto (D^+f)(t) = \limsup_{h \rightarrow 0^+} \{h^{-1}(f(t+h) - f(t))\}$, we denote the upper Dini derivative.
9. Let A, B be logical statements. Their logical conjunction is denoted by $A \wedge B$.

2 | POPULATION MODEL WITH ACTUATOR DYNAMICS

We consider the age distribution of the population of a microorganism in a bioreactor governed by the following equations

$$\text{PDE: } \frac{\partial f}{\partial t}(a, t) + \frac{\partial f}{\partial a}(a, t) = -(\mu(a) + D(t))f(a, t) \quad (1a)$$

$$\text{ODE: } \dot{D}(t) = u(t) \quad (1b)$$

$$\text{OE: } y(t) = \int_0^A p(a)f(a, t)da \quad (1c)$$

$$\text{BC: } f(0, t) = \int_0^A k(a)f(a, t)da \quad (1d)$$

where $a \in [0, A]$ is the age variable, A is the maximum reproductive age of the microorganism (a constant), $t \in \mathbb{R}_+$ is time, $f(a, t) > 0$ denotes the distribution of the microbial mass in the reactor at age $a \in [0, A]$ and time t , μ and k are the mortality rate profile and birth rate profile, respectively, and p is the sensor kernel. The functions $\mu : [0, A] \rightarrow \mathbb{R}_+$ and $k : [0, A] \rightarrow \mathbb{R}_+$ are assumed to be continuous in age a , and the function $p : [0, A] \rightarrow \mathbb{R}_+$ continuously differentiable in a with $\int_0^A p(a)da > 0$. The population of microorganisms grows at a rate regulated by the dilution rate $D(t)$, which is the control input of model (1a–d). Accounting for the inlet and outlet rate of the bioreactor, the PDE (1a) expresses the microbial mass balance as a variation of the *McKendrick-von Foerster* equation.^{13–15,17,18} The internal boundary feedback (1d), is the renewal condition, which expresses the reproduction of the microorganism as the current mass of the newborns $f(0, t)$. From a mathematical point of view, the boundary condition (1d) involves non-local terms. The measured output defined in (1c) is a weighted average of the mass of the microorganism with an age-specific kernel $p(a)$.

In chemostat reactors, the dilution rate is defined as the ratio of the inlet volumetric flow rate to the reactor volume. Although, the reactor’s inlet flow and outlet volumetric flow rates are readily adjustable, the volume of the reactor is not necessarily constant and its variations can be described by the dynamic actuation introduced as (1b). Indeed, the population balance (1a–d) is a realistic extension of the model studied in Reference 4, which does not account for a dynamic actuation and consequently assumes no possible variations of the reactor volume. Equation (1b) defines an appropriate control input $u(t) \in \mathbb{R}$ that depends on the reactor volume, the reactor inlet and outlet volumetric flow rates as well as on the time derivative of the reactor inlet volumetric flow rate.

It should also be noticed that model (1a–d) is derived by neglecting the dependence of the growth of the microorganism on the concentration of a limiting substrate. However, resource-based models that incorporate limiting substrates or uptake of nutrients are more suitable to describe the dynamics of continuous microbial culture and might exhibit limit cycles that are induced by the behavior of a limiting resource assuming constant dilution rates.^{12,33} Model (1a–d) presupposes that the growth or decay of a living population only depends on irreversible incidences of birth and death and is therefore suitable to predict the evolution of macro-populations in demography, epidemiology⁹ and ecology.³⁴

The state of model (1a–d) is $(f[t], D(t)) \in \mathcal{F} \times \mathbb{R}$, where \mathcal{F} is the function space defined by the following equation:

$$\mathcal{F} = \left\{ f \in PC^1([0, A]; (0, \infty)) : f(0) = \int_0^A k(a)f(a)da \right\}. \quad (2)$$

The results of this contribution encompass two different cases for the state space. For the first case, the state space is defined as $\mathcal{F} \times \mathbb{R}$, allowing for the dilution rate $D(t)$ to take arbitrary real values. However, as noted above, the dilution

rate is the ratio of the inlet volumetric flow rate to the reactor volume and consequently, it is physically meaningful to restrict its set of admissible values to the interval $I \subseteq \mathbb{R}_+$, which is much more demanding as the state is constrained and the state space defined as $\mathcal{F} \times I$.

Our main assumption for model (1a-d) is the existence of a constant $D^* > 0$ such that

$$1 = \int_0^A k(a) \exp\left(-D^*a - \int_0^a \mu(s)ds\right) da, \quad (3)$$

which is the analogue of the Lotka-Sharpe equation (see Reference 14) and equivalent to assuming population viability. When the above assumption holds, model (1a-d) admits a family of equilibrium points (f^*, D^*) (as the model without actuator dynamics⁴), given by the following equation for arbitrary $M > 0$:

$$f^*(a) = M \exp\left(-D^*a - \int_0^a \mu(s)ds\right). \quad (4)$$

The existence of a continuum of equilibria for model (1a-d) implies that none of the equilibrium points is asymptotically stable. Therefore, if we want the bioreactor to operate on a specific equilibrium point, then we need to stabilize such an equilibrium point by means of feedback control.

3 | BACKSTEPPING DESIGN WITH UNRESTRICTED DILUTION

Our objective is to stabilize a desired steady-state (2) for a chosen $M > 0$ or equivalently, thanks to detectability, regulate the output to an appropriate output setpoint

$$y^* = \int_0^A p(a)f^*(a) da > 0. \quad (5)$$

Our design is build upon the control law proposed in Reference 4 for the stabilization of system (1a-d) without actuator dynamics. We recall the output-feedback controller⁴

$$D_{\text{nom}}(t) = D^* + k_1 \ln \frac{y(t)}{y^*}, \quad k_1 > 0 \quad (6)$$

that stabilizes the equilibrium corresponding to y^* . To extend controller (6) to the case with actuator dynamics described by system (1a-d), a backstepping approach is adopted. Defining the dilution rate error as follows

$$\delta(t) := D(t) - D_{\text{nom}}(t) \quad (7)$$

and taking its time-derivative along the output $y(t)$ given by (1c), with the help of integration by parts, the following ODE is derived

$$\dot{\delta}(t) = u(t) - k_1 \frac{\dot{y}(t)}{y(t)} \quad (8)$$

$$= u(t) + k_1 D(t) + \frac{k_1}{y(t)} \left[p(A)f(A, t) - p(0)f(0, t) - \int_0^A \tilde{p}(a)f(a, t) da \right] \quad (9)$$

where

$$\tilde{p}(a) := p'(a) - p(a)\mu(a). \quad (10)$$

At this point, we aim at designing a control law $u(t)$ that achieves exponential convergence of the error $\delta(t)$. Selecting $k_2 > 0$ such that

$$\dot{\delta}(t) = -k_2 \delta(t), \quad (11)$$

the following controller is designed

$$u(t) = u_c(t) + u_s(t) \quad (12a)$$

$$u_c(t) = -k_1 D(t) - \frac{k_1}{y(t)} \left[p(A)f(A, t) - p(0)f(0, t) - \int_0^A \tilde{p}(a)f(a, t) da \right] \quad (12b)$$

$$u_s(t) = -k_2 \left(D(t) - D^* - k_1 \ln \frac{y(t)}{y^*} \right) = -k_2 \delta(t), \quad (12c)$$

which is a superposition of canceling and stabilizing terms $u_c(t)$ and $u_s(t)$. In the most general case, the controller (12a–c) requires full measurement of the plant and the actuator states $f(a, t)$ and $D(t)$, respectively. Furthermore, the feasibility of controller (12a–c) depends on the knowledge of the parameters p , p' , μ and D^* . However, assuming constant kernel p and mortality rate μ , the canceling terms (12b) of backstepping controller (12a–c) reduces to the following feedback law

$$u_c(t) = -k_1 \left\{ D(t) + \frac{p}{y(t)} [f(A, t) - f(0, t)] + \mu \right\}, \quad (13)$$

which removes the burden of full-state measurement of the plant's state.

To illustrate the stabilizing effect of the control law (12a–c), we first present simulation results before conducting a stability analysis. Following Galerkin's approach,^{35,36} the approximate population density, $\hat{f} : [0, A] \times \mathbb{R}_+ \rightarrow \mathbb{R}$ is defined as follows

$$\hat{f}(a, t) = \sum_{j=1}^N \phi_j(a) \xi_j(t) =: \phi(a)^\top \xi(t) \quad (14)$$

where $\phi_j : [0, A] \rightarrow \mathbb{R}$ are the trial functions satisfying the boundary condition (1d), chosen as in Reference 35 with $N = 6$, and the temporal weights $\xi_j : \mathbb{R}_+ \rightarrow \mathbb{R}$ are solutions to the initial value problem below

$$\dot{\xi}(t) = (A_\phi - D(t)I)\xi(t), \quad t \geq 0 \quad (15a)$$

$$\xi(0) = \xi_0 \quad (15b)$$

where $A_\phi \in \mathbb{R}^{N \times N}$ is determined by the choice of trial functions ϕ_j , and $\xi_0 \in \mathbb{R}^N$ is computed for a given initial population density $f_0 \in \mathcal{F}$ of system (1a–d). A parameter set of the initial condition $f_0(a)$, birth rate $k(a)$, death rate $\mu(a)$, steady-state input D^* and maximum age of reproduction A used throughout this work is given below

$$f_0(a) = 8 - 3a + \phi_2(a), \quad \mu(a) = \frac{1}{20 - 5a}, \quad k(a) = a, \quad p(a) = 1 + \frac{a^2}{10}, \quad (16a)$$

$$D^* \approx 0.48, \quad A = 2, \quad \phi_2(a) = \sin(\omega_1 a) \exp(\sigma_1 a) \frac{f^*(a)}{f^*(0)}, \quad \omega_1 \approx 3.82, \quad \sigma_1 \approx 0.91. \quad (16b)$$

As shown in a representative simulation example in Figure 1, controller (12a–c) achieves convergence to the desired output $y^* = y_{\text{des}}$. However, the controller stabilizes the equilibrium profile without restricting the dilution rate $D(t)$ to physically meaningful values.

4 | CLOSED-LOOP STABILITY FOR ALL POSITIVE INITIAL POPULATION DENSITIES

For the stability proof, we invoke the transformation $\Pi : \mathcal{F} \rightarrow \mathbb{R} \times C^0([-A, 0])$, $f[t] \mapsto (\eta(t), \psi_t)$ mapping the age-profile $f[t]$ to its unstable “malthusian” and “asymptotic” mode

$$\eta(t) = \ln \Pi(f[t]) \quad (17a)$$

$$\psi(t - a) = \frac{f(a, t)}{f^*(a)\Pi(f[t])} - 1 \quad (17b)$$

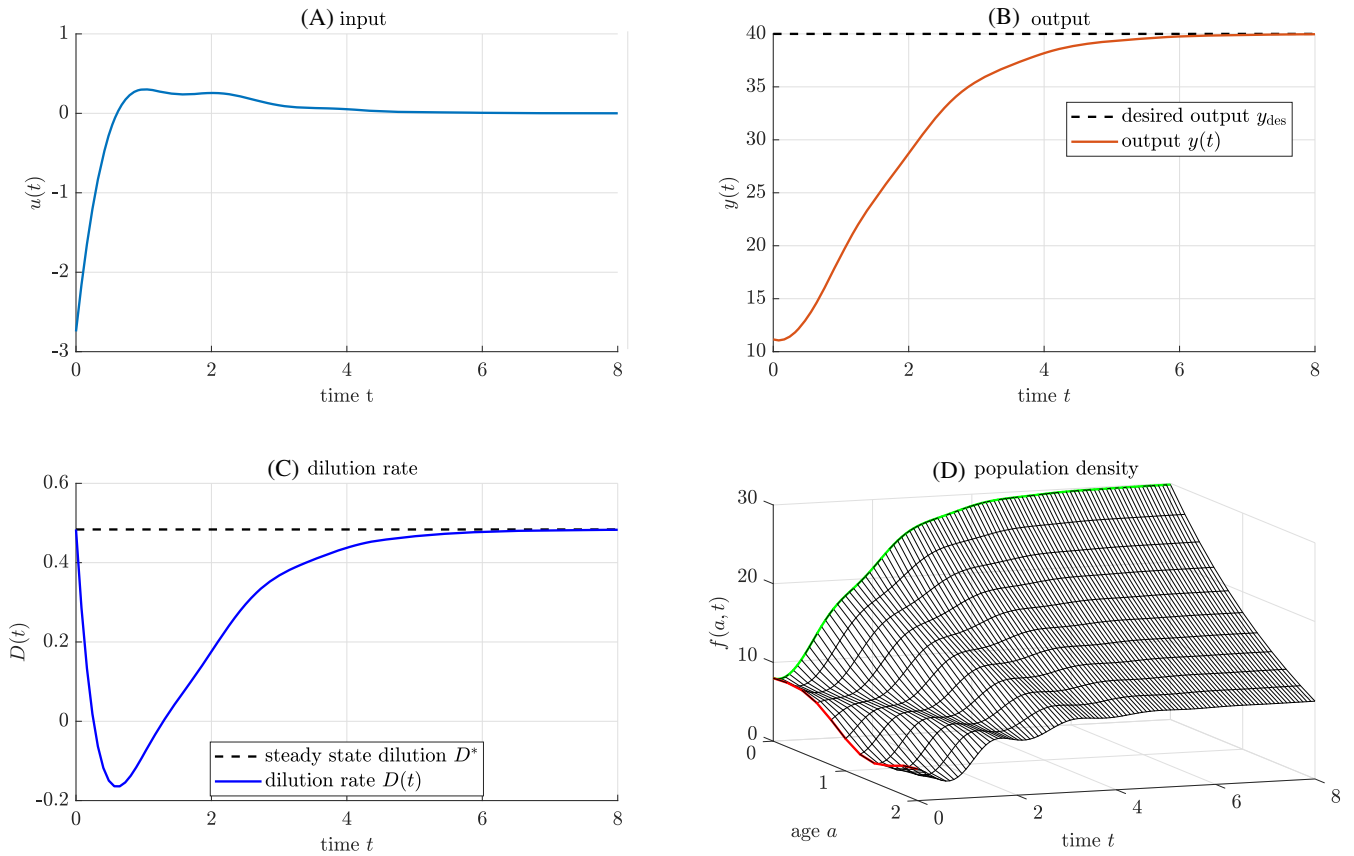


FIGURE 1 Simulation results of system (1a–d) under the control law (12a–c) and with the parameters and the initial condition given by (16a,b). The gains of the controller are chosen as $k_1 = 1$ and $k_2 = 2$. Convergence to the steady-state is achieved but with possibly negative dilution rate $D(t)$. (A) Input. (B) Output. (C) Dilution rate. (D) Population density.

where

$$\Pi(f) = \frac{\int_0^A \pi(a)f(a)da}{\int_0^A ak(a)f^*(a)da}, \quad \pi(a) = \int_a^A k(s) \exp\left(\int_s^a (\mu(\alpha) + D^*)d\alpha\right) ds, \quad a \in [0, A]. \quad (18)$$

Equation (17b) has been proven to be a valid transformation,⁴ that is, the right hand side is indeed a function of $(t - a)$. Transforming the open-loop system (1a–d) in light of (17a,b), one receives

$$\dot{\eta}(t) = D^* - D(t) \quad (19a)$$

$$\dot{D}(t) = u(t) \quad (19b)$$

$$\psi(t) = \int_0^A \tilde{k}(a)\psi(t - a) da. \quad (19c)$$

After transforming the closed-loop system consisting of (1a–d) and (12a–c), with the aid of the substitution of (12a–c) into (9), we arrive at the dynamics

$$\dot{\eta}(t) = -k_1\eta(t) - \delta(t) - k_1v(\psi_t) \quad (20a)$$

$$\dot{\delta}(t) = -k_2\delta(t) \quad (20b)$$

$$\psi(t) = \int_0^A \tilde{k}(a)\psi(t - a) da \quad (20c)$$

where (20c) is derived in Reference 4 and

$$\tilde{k}(a) := k(a) \frac{f^*(a)}{f^*(0)}, \quad g(a) := \frac{p(a)f^*(a)}{\int_0^A p(a)f^*(a)da}, \quad v(\psi_t) := \ln \left(1 + \int_0^A g(a)\psi(t-a)da \right), \quad (21)$$

and the equilibrium $(\eta, \delta, \psi) = 0$ is to be proven asymptotically stable. This can be achieved using a member of the family of Control Lyapunov Functionals provided in Reference 4. For this, we have to make a technical assumption:

Assumption 1 (Technical assumption on birth kernel). There exists a constant $\lambda > 0$ such that $\int_0^A |\tilde{k}(a) - r\lambda \int_a^A \tilde{k}(s)ds| da < 1$ where $r^{-1} = \int_0^A \tilde{k}(a)ada$. Let $\sigma > 0$ be a sufficiently small constant that satisfies the inequality

$$\int_0^A \left| \tilde{k}(a) - r\lambda \int_a^A \tilde{k}(s)ds \right| \exp(\sigma a) da < 1. \quad (22)$$

Assumption 1 is a mild technical assumption, since it is satisfied by arbitrary mortality rate μ for every birth kernel k that has a finite number of zeros on $[0, A]$. From a modeling standpoint, this means that individuals of ages zero to A are reproducing at *almost every* age (see Reference 4).

Remark 1. The state ψ of the internal dynamics (19c) is restricted (see Reference 4) to the set

$$S = \left\{ \psi \in C^0([-A, 0]; (-1, \infty)) : P(\psi) = 0 \wedge \psi(0) = \int_0^A \tilde{k}(a)\psi(-a)da \right\} \quad (23)$$

where

$$P(\psi) = \int_0^A \psi(-a) \int_a^A \tilde{k}(s)ds da \left(\int_0^A a\tilde{k}(a)da \right)^{-1}. \quad (24)$$

Theorem 1 (Lyapunov stability of backstepping controller with unrestricted dilution). *Let Assumption 1 hold. Then for every $k_1, k_2 > 0$, there exists a function $\alpha_1 \in \mathcal{K}_\infty$ such that for every $(f_0, D_0) \in \mathcal{F} \times \mathbb{R}$ the unique solution $(f[t], D(t)) \in \mathcal{F} \times \mathbb{R}$ of the closed-loop system (1a–d) with (12a–c) and initial condition $(f[0], D(0)) = (f_0, D_0)$ exists for all $t \geq 0$ and satisfies the following stability estimate for all $t \geq 0$*

$$R_1(f[t], D(t)) \leq \exp\left(-\frac{\sigma_1}{2}t\right) \alpha_1(R_1(f_0, D_0)) \quad (25)$$

where $\sigma_1 = \min\left(\frac{k_1}{2}, k_2, \sigma\right) > 0$ and

$$R_1(f, D) := \max_{a \in [0, A]} \left| \ln \frac{f(a)}{f^*(a)} \right| + |D - D^*| \quad (26)$$

for all $(f, D) \in \mathcal{F} \times \mathbb{R}$.

Proof of Theorem 1. Lemma 4.1 of Reference 4 provides existence and uniqueness of the solution $\psi_t \in S$ and also

$$\inf_{t \geq -A} \psi(t) \geq \min_{t \in [-A, 0]} \psi(t) > -1, \quad \forall t \geq 0. \quad (27)$$

Notice that the second inequality is given by $\psi_0 \in S$ and is guaranteed for all physical initial conditions $f_0 \in \mathcal{F}$. Indeed, the initial condition of (20c) is given by

$$\psi_0(a) = \psi(-a) = \frac{f_0(a)}{f^*(a)\Pi(f_0)} - 1 > -1, \quad \forall a \in [0, A] \quad (28)$$

where $f_0(a), f^*(a)$ and $\Pi(f_0)$ are positive on the domain $[0, A]$. Since $g(a) \geq 0$, $\int_0^A g(a)da = 1$ according to (21) and inequality (27) holds, the map

$$v(\psi_t) := \ln\left(1 + \int_0^A g(a)\psi(t-a)da\right), \quad \text{for } t \geq 0 \tag{29}$$

is continuous. Thus, the ODE subsystem of the closed-loop system (20a–c), namely, Equations (20a) and (20b) locally admits a unique solution. Consider first the Lyapunov function

$$U_1(\eta, \delta) = \frac{1}{2}(\eta^2 + b_1\delta^2), \quad \forall(\eta, \delta) \in \mathbb{R}^2 \tag{30}$$

where $b_1 > 0$ is a constant to be chosen. The time derivative of $U_1(\eta(t), \delta(t))$ along the solutions of (20a) and (20b) can be upper bounded for all times $t \geq 0$ for which the solution $(\eta(t), \delta(t))$ exists as follows:

$$\frac{d}{dt}U_1(\eta(t), \delta(t)) \leq -\frac{k_1}{4}\eta(t)^2 - \left(b_1k_2 - \frac{1}{k_1}\right)\delta(t)^2 + \frac{k_1}{2}v(\psi_t)^2. \tag{31}$$

Inequality (31) was derived using the inequalities $-\eta(t)\delta(t) \leq \frac{k_1}{4}\eta(t)^2 + \frac{1}{k_1}\delta(t)^2$ and $-\eta(t)v(\psi) \leq \frac{1}{2}v(\psi)^2 + \frac{1}{2}\eta(t)^2$, which follow from the general Young inequality $-\eta\delta \leq \frac{1}{2\epsilon}\eta^2 + \frac{\epsilon}{2}\delta^2$, for $\epsilon = \frac{2}{k_1}$ and $\epsilon = 1$, respectively. Next, as in the proof of Reference 4; [lemma 5.1], we use corollary 4.6 of the latter with $C(\psi_t) = (1 + \min(0, \min_{a \in [0,A]} \psi(a)))^{-2}$ and $b(s) = \frac{1}{2}s^2$ under Assumption 1 with sufficiently small parameter $\sigma > 0$ to obtain that the functional

$$G(\psi_t) := \frac{\max_{a \in [0,A]} |\psi(t-a)| \exp(-\sigma a)}{1 + \min(0, \min_{a \in [0,A]} \psi(t-a))} \tag{32}$$

satisfies

$$D^+G(\psi_t)^2 \leq -2\sigma G(\psi_t)^2, \quad \forall t \geq 0 \tag{33}$$

along solutions ψ_t of the IDE (20c). Now, Reference 4; (A.43) also provides that

$$|v(\psi_t)| \leq G(\psi_t) \exp(\sigma A), \quad \forall t \geq 0. \tag{34}$$

Given this fact, the bounds (31) and (33) and defining the Lyapunov functional

$$\begin{aligned} V_1(\eta, \delta, \psi) &= U_1(\eta, \delta) + \frac{1}{2}b_2G(\psi)^2, \\ &= \frac{1}{2}(\eta^2 + b_1\delta^2 + b_2G(\psi)^2), \quad \forall(\eta, \delta, \psi) \in \mathbb{R} \times \mathbb{R} \times \mathcal{S} \end{aligned} \tag{35}$$

with $b_1 = \frac{2}{k_2k_1}$, $b_2 = \frac{k_1}{\sigma} \exp(2\sigma A)$, we derive the differential inequality

$$D^+V_1(\eta(t), \delta(t), \psi_t) \leq -\sigma_1 V_1(\eta(t), \delta(t), \psi_t), \quad \forall t \geq 0 \tag{36}$$

where $\sigma_1 = \min\left(\frac{k_1}{2}, k_2, \sigma\right) > 0$. Since estimate (36) implies that all solutions stay bounded for all times for which they exist, we can conclude existence for all times. The differential inequality (36) in conjunction with lemma 2.12 on pp. 77–78 in Reference 32, or simply using the comparison lemma in Reference 31, implies the following estimate for all $t \geq 0$:

$$V_1(\eta(t), \delta(t), \psi_t) \leq \exp(-\sigma_1 t)V_1(\eta(0), \delta(0), \psi_0). \tag{37}$$

We next show that the estimate (25) holds. Recall from (7) that

$$\delta(t) = \tilde{D}(t) - k_1(\eta(t) + v(\psi_t)), \quad t \geq 0 \tag{38}$$

where

$$\tilde{D}(t) = D(t) - D^*, \quad t \geq 0. \tag{39}$$

Define the positive definite quadratic function $U_2 : \mathbb{R}^3 \rightarrow \mathbb{R}$

$$U_2(\eta, \tilde{D}, v) = \eta^2 + \frac{b_2}{2} \exp(-2\sigma A)v^2 + b_1(\tilde{D} - k_1\eta - k_1v)^2 \tag{40}$$

where v is given by (29). Clearly, there exist constants $\underline{c}, \bar{c} > 0$ such that for all $(\eta, \tilde{D}, v) \in \mathbb{R}^3$ the following inequalities hold:

$$\underline{c}(\eta^2 + \tilde{D}^2 + v^2) \leq U_2(\eta, \tilde{D}, v) \leq \bar{c}(\eta^2 + \tilde{D}^2 + v^2). \tag{41}$$

Consequently, (41) in conjunction with (35), (38), (41), (34) implies the following estimate:

$$V_1(\eta(t), \delta(t), \psi_t) = \frac{1}{2} \left(U_2(\eta(t), \tilde{D}(t), v(\psi_t)) + b_2 G(\psi_t)^2 - \frac{b_2}{2} \exp(-2\sigma A)v(\psi_t)^2 \right) \tag{42}$$

$$\geq \frac{1}{2} \left(\underline{c}(\eta(t)^2 + \tilde{D}(t)^2 + v(\psi_t)^2) + \frac{b_2}{2} G(\psi_t)^2 \right), \quad t \geq 0. \tag{43}$$

Using (43), we conclude that there exists an appropriate constant $\tilde{c} > 0$ (independent of the solution), for which the following estimate holds:

$$|\eta(t)| + \exp(\sigma A)G(\psi_t) + |\tilde{D}(t)| \leq \tilde{c} \sqrt{V_1(\eta(t), \delta(t), \psi_t)}, \quad t \geq 0. \tag{44}$$

From Reference 4; (5.24),

$$\max_{a \in [0, A]} \left| \ln \frac{f[t](a)}{f^*(a)} \right| \leq |\eta(t)| + \exp(\sigma A)G(\psi_t), \quad t \geq 0, \tag{45}$$

that is, we arrive at the left-hand side of (25) after combining (44) and (45). To complete the proof of (25), we need to show that there exists $\tilde{\alpha} \in \mathcal{K}_\infty$ such that

$$V_1(\eta(0), \delta(0), \psi_0) \leq \tilde{\alpha} \left(\max_{a \in [0, A]} \left| \ln \frac{f_0(a)}{f^*(a)} \right| + |\tilde{D}(0)| \right). \tag{46}$$

We first note that Reference 4; (5.27) provides the existence of $\tilde{\alpha}_1, \tilde{\alpha}_2 \in \mathcal{K}_\infty$

$$|\eta_0| \leq \tilde{\alpha}_1 \left(\max_{a \in [0, A]} \left| \ln \frac{f_0(a)}{f^*(a)} \right| \right), \quad G(\psi_0) \leq \tilde{\alpha}_2 \left(\max_{a \in [0, A]} \left| \ln \frac{f_0(a)}{f^*(a)} \right| \right), \tag{47}$$

and, using (41), we upper bound

$$V_1(\eta, \delta, \psi) \leq \frac{1}{2} (\bar{c}(\eta^2 + \tilde{D}(\eta, \delta, \psi)^2) + \tilde{b}G(\psi)^2), \quad (\eta, \delta, \psi) \in \mathbb{R} \times \mathbb{R} \times \mathcal{S} \tag{48}$$

for an appropriate constant $\tilde{b} > 0$. The inequalities (47) and (48) allow us to conclude that there exists appropriate $\tilde{\alpha}$ (independent of the solution) for which (46) holds. Combining (37), (44), (45) and (46), we obtain estimate (25). ■

Remark 2. Notice that the exponential convergence rate σ_1 of (36) is the minimum of three constants: the nominal control gain k_1 , the backstepping convergence rate k_2 and the convergence rate of the internal dynamics σ .

5 | EASIER-TO-IMPLEMENT BACKSTEPPING CONTROLLER: OUTPUT FEEDBACK WITHOUT SENSOR MODEL

Recall the canceling controller (12b)

$$u_c(t) = k_1(-D(t) + D^* + v_1(\psi_t)) \quad (49)$$

where, with a substitution of (5) and (19c) into (12b), the term $v_1(\psi_t)$, defined in the lengthy fashion

$$v_1(\psi_t) = -D^* + \frac{1}{\int_0^A p(a)f^*(a)(1 + \psi(t-a))da} \times \left[p(A)f^*(A)(1 + \psi(t-A)) - p(0)f^*(0)(1 + \psi(t)) - \int_0^A \tilde{p}(a)f^*(a)(1 + \psi(t-a))da \right], \quad (50)$$

is a functional of the internal state variable ψ and, in spite of its seeming complexity, has the fortunate and crucial property that it decays exponentially to $v_1(0) = 0$. We relax the canceling control from exact cancellation to now only canceling the steady-state value

$$u_c(t) = k_1(-D(t) + D^*) \quad (51)$$

drastically reducing the measurement requirements. This approach achieves convergence $y(t) \rightarrow y^*$ to the desired output, which is illustrated by means of a representative simulation example in Figure 2.

Finding the closed-loop dynamics of (1a-d), (12a-c) and (51)

$$\dot{\eta}(t) = -k_1\eta(t) - \delta(t) - k_1v_1(\psi_t) \quad (52a)$$

$$\dot{\delta}(t) = -k_2\delta(t) - k_1v_1(\psi_t) \quad (52b)$$

$$\dot{\psi}(t) = \int_0^A \tilde{k}(a)\psi(t-a) da, \quad (52c)$$

we notice that, as a result of simplifying the controller, the dynamics of δ have become more complex, and as a consequence the Lyapunov-like stability proof becomes harder to establish.

In our proof of stability, we make use of the following result, whose proof we state in the Appendix A.

Lemma 1. *There exists a constant $c_1 > 0$ such that every solution ψ_t of the IDE (52c) satisfies the following estimate for all $t \geq 0$:*

$$|v_1(\psi_t)| \leq \sqrt{c_1} \frac{\max_{a \in [0, A]} |\psi(t-a)|}{1 + \min_{a \in [0, A]} |\psi(t-a)|}. \quad (53)$$

Theorem 2 (Lyapunov stability of static output feedback backstepping controller with unrestricted dilution). *Let Assumption 1 hold. Then for every $k_1, k_2 > 0$, there exists a function $\alpha_2 \in \mathcal{K}_\infty$ such that for every $(f_0, D_0) \in \mathcal{F} \times \mathbb{R}$ the unique solution $(f[t], D(t)) \in \mathcal{F} \times \mathbb{R}$ of the closed-loop system (1a-d) with*

$$u(t) = -(k_1 + k_2)(D(t) - D^*) + k_1k_2 \ln \frac{y(t)}{y^*} \quad (54)$$

and initial condition $(f[0], D(0)) = (f_0, D_0)$ exists for all $t \geq 0$ and satisfies the following stability estimate for all $t \geq 0$

$$R_1(f[t], D(t)) \leq \exp\left(-\frac{\sigma_1}{2}t\right) \alpha_2(R_1(f_0, D_0)) \quad (55)$$

where $\sigma_1 = \min\left(\frac{k_1}{2}, \frac{k_2}{2}, \sigma\right) > 0$ and R_1 is defined in (26).

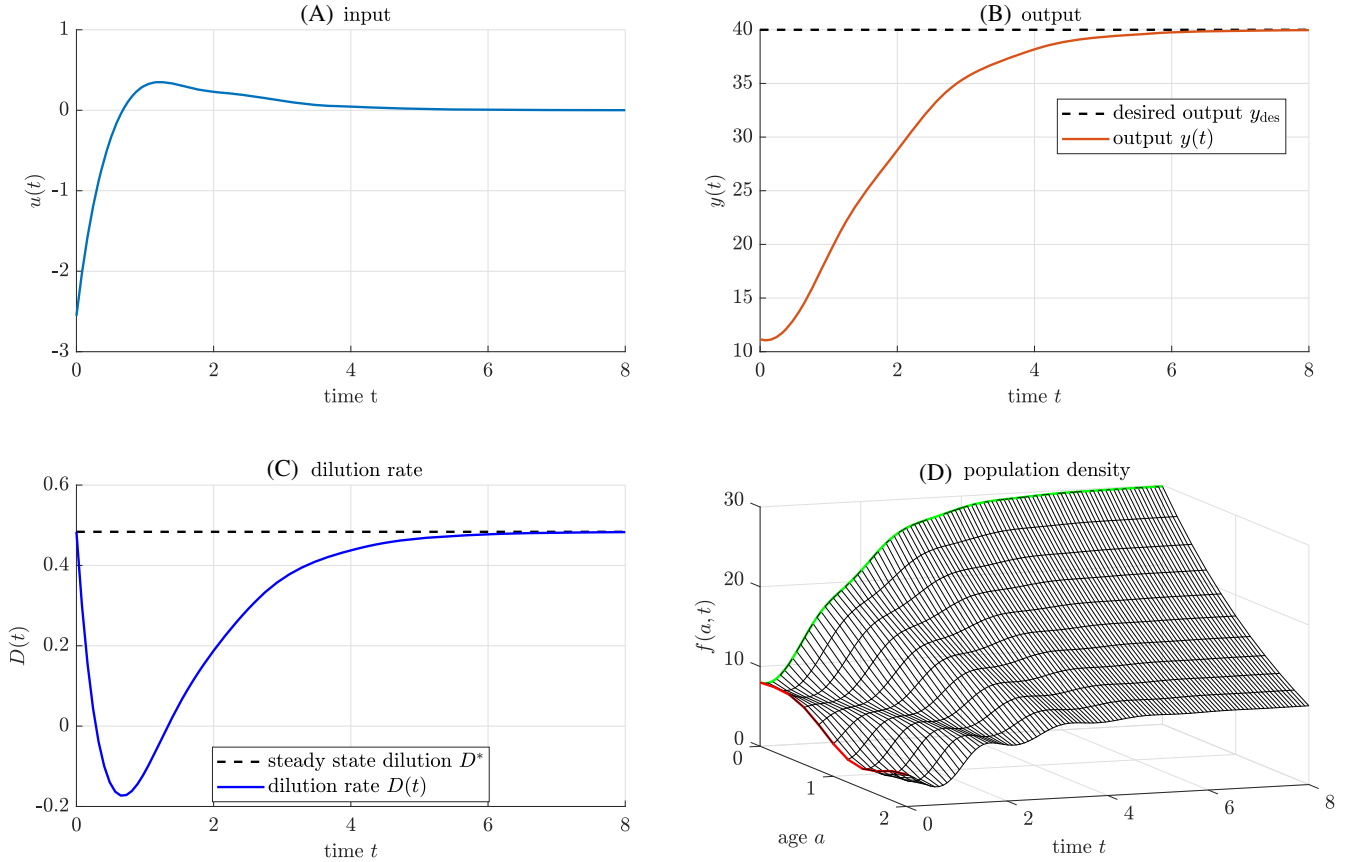


FIGURE 2 Simulation results of system (1a–d) with parameters and initial condition (16a,b) and controller (12a–c) but relaxed canceling terms (51) with gains $k_1 = 1, k_2 = 2$. Convergence to the desired output $y^* = y_{\text{des}}$ is achieved. The controller employs a non-physical negative dilution $D(t)$ in the transient to achieve stabilization globally (for all positive population densities). A more complicated backstepping re-design that employs global stabilization using only positive dilution is presented in Section 6. (A) Input. (B) Output. (C) Dilution rate. (D) Population density.

Proof of Theorem 2. Again, like in (28), we know that the map $t \mapsto v(\psi_t)$ is well-defined for all $t \geq 0$ and is continuous. Thus, the closed-loop system (52a–c) locally admits a solution. We first consider the function

$$U_1(\eta, \delta) = \frac{1}{2}(\eta^2 + b_1\delta^2), \quad (\eta, \delta) \in \mathbb{R}^2, \quad (56)$$

where $b_1 > 0$ is a constant to be chosen. The time derivative of $U_1(\eta(t), \delta(t))$ along solutions of (52a) and (52b) can be upper bounded for all times $t \geq 0$ for which the solution $(\eta(t), \delta(t))$ exists

$$\begin{aligned} \frac{d}{dt}U_1(\eta(t), \delta(t)) &\leq -\frac{k_1}{4}\eta(t)^2 - \left(\frac{1}{2}b_1k_2 - \frac{1}{k_1}\right)\delta(t)^2 \\ &\quad + \frac{k_1}{2}v(\psi_t)^2 + b_1\frac{k_1^2}{2k_2}v_1(\psi_t)^2. \end{aligned} \quad (57)$$

The bound (57) was achieved using the inequalities $-\eta(t)\delta(t) \leq \frac{k_1}{4}\eta(t)^2 + \frac{1}{k_1}\delta(t)^2$, $-\eta(t)v(\psi_t) \leq \frac{1}{2}\eta(t)^2 + \frac{1}{2}v(\psi_t)^2$ and $-\delta(t)v_1(\psi_t) \leq \frac{k_2}{2}\delta(t)^2 + \frac{1}{2k_2}v_1(\psi_t)^2$.

Next, consider the Lyapunov functional

$$V_2(\eta(t), \delta(t), \psi_t) = U_1(\eta(t), \delta(t)) + \frac{b_2}{2}G(\psi_t)^2 = \frac{1}{2}(\eta(t)^2 + b_1\delta(t)^2 + b_2G(\psi_t)^2) \quad (58a)$$

where $b_2 > 0$ is a constant to be chosen and G is defined in (32).

Using Lemma 1 and definition (32), it holds that

$$|v_1(\psi_t)| \leq \exp(\sigma A)G(\psi_t), \quad \forall t \geq 0. \quad (59)$$

Using the above estimate, (57), (33) and defining $b_1 = \frac{4}{k_2 k_1}$, $b_2 = \left(\frac{k_1}{\sigma} + b_1 \frac{c_1 k_1^2}{\sigma k_2}\right) \exp(2\sigma A)$, we obtain the differential inequality

$$D^+ V_2(\eta(t), \delta(t), \psi_t) \leq -\sigma_1 V_2(\eta(t), \delta(t), \psi_t), \quad \forall t \geq 0 \quad (60)$$

where $\sigma_1 = \min\left(\frac{1}{2}k_1, \frac{1}{2}k_2, \sigma\right) > 0$. Since estimate (60) implies that all solutions stay bounded for all times for which they exist, we can conclude existence for all times.

The rest of the proof is exactly the same with the proof of Theorem 1. ■

6 | GLOBAL STABILIZATION WITH STATE CONSTRAINTS

The proposed controller (12a–c) unfortunately does not ensure that the dilution rate $D(t)$ remains positive. This can be observed in an example simulation in Figure 1. Whenever the signed control error $y(t) - y^*$ takes large negative values, the controller tries to “add population.”

A classical approach to guarantee positivity of the dilution rate is to introduce a control barrier function (CBF)³⁷

$$h(\eta, D, \psi) = D, \quad (61)$$

which imposes a positivity constraint on the state D , and where the task of the control law is not only to stabilize the desired equilibrium but to also maintain the positivity of the CBF in the process. The common approach to maintaining the positivity of a CBF is to “wrap” a safety filter around the nominal control law $u_0 = u_c + u_s$, so that the overall control is given by

$$u = u_0 + u_p = u_c + u_s + u_p \quad (62)$$

where u_p is the safety filter/override component of the controller that “penalizes” the negativity of the dilution and overrides the nominal feedback u_0 so that the dilution is kept positive.

The safety filter for a system that has actuator dynamics $\dot{D} = u$ and CBF $h = D$ is particularly simple and given in Reference 37

$$u_p = \max\{0, -u_0 - k_3 D\}, \quad k_3 > 0, \quad (63)$$

which ensures that

$$\dot{h}(t) \geq -k_3 h(t), \quad (64)$$

namely, that $\dot{D}(t) \geq -k_3 D(t)$, that is, $D(t) \geq D(0) \exp(-k_3 t) > 0$ for $D(0) > 0$.

The representative example simulation in Figure 3 shows that the safety filter ensures the positivity of $D(t)$ without impacting the convergence to the desired equilibrium. However, proving that the region of attraction of an equilibrium contains the entire safe set in the presence of a safety filter is impossible in general and has eluded us with this particular system as well.

For this reason, we investigate the possibility of ensuring the positivity of $D(t)$ with a stabilizing controller different than the nominal control (12a–c). We next study system (1a–d) with state space $\mathcal{F} \times (\underline{D}, \bar{D})$, where $0 \leq \underline{D} < D^* < \bar{D}$ are positive constants. The values of the constants \underline{D}, \bar{D} are determined by the technical characteristics of the bioreactor but from a mathematical point of view the values of the constants \underline{D}, \bar{D} are considered to be arbitrary given constants.

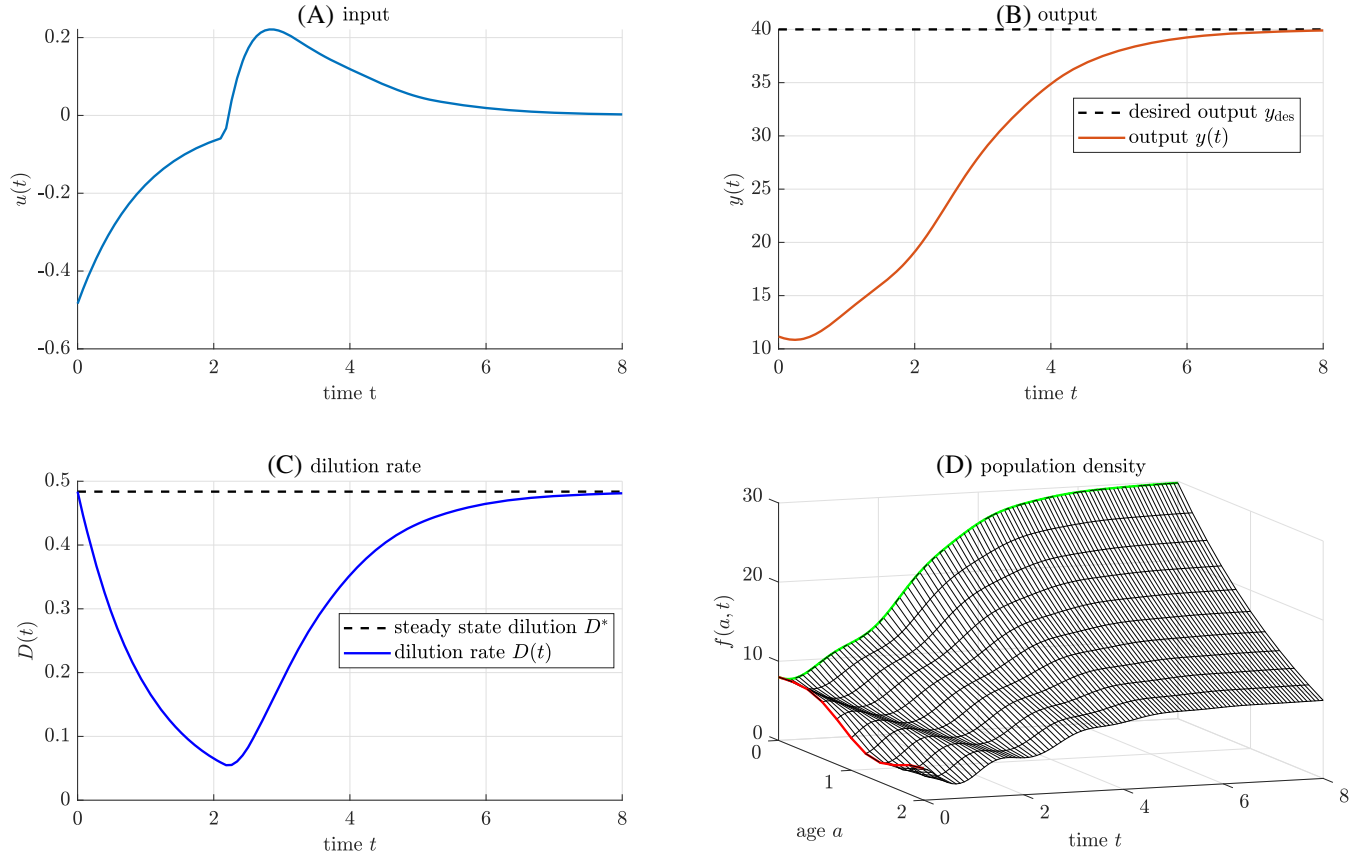


FIGURE 3 Simulation results of system (1a–d) with parameters and initial condition (16a,b) and controller (62) and (63) with gains $k_1 = 1$, $k_2 = 2$, $k_3 = 1$. Negative dilution rates are prevented and convergence to the desired output $y^* = y_{des}$ is achieved. (A) Input. (B) Output. (C) Dilution rate. (D) Population density.

Consider the diffeomorphism $\Phi : \mathbb{R} \rightarrow (\underline{D}, \bar{D})$ defined by

$$D = \Phi(\zeta) = \underline{D} + \frac{a_1 \exp(\zeta)}{a_2 + \exp(\zeta)} \quad (65)$$

with inverse $\Phi^{-1} : (\underline{D}, \bar{D}) \rightarrow \mathbb{R}$

$$\zeta = \Phi^{-1}(D) = \ln\left(\frac{a_2(D - \underline{D})}{\bar{D} - D}\right) \quad (66)$$

where

$$a_1 = \bar{D} - \underline{D} > 0, \quad a_2 = \frac{\bar{D} - D^*}{D^* - \underline{D}} > 0. \quad (67)$$

Notice that by virtue of (65), (66) and (67) it holds that $\Phi^{-1}(D^*) = 0$ and $\Phi(0) = D^*$.

Let $k_1, k_2, k_3 > 0$ be given arbitrary positive constants (the controller gains) and consider the static output feedback law

$$u(t) = \frac{(D(t) - \underline{D})(\bar{D} - D(t))}{\bar{D} - \underline{D}} \left[(k_1 + k_2)(D^* - D(t)) - k_3(\Phi^{-1}(D(t)) - k_2 \ln(y(t)/y^*)) \right]. \quad (68)$$

Our main result in this section is stated next.

Theorem 3 (Global asymptotic stabilization with dilution constrained to a finite positive interval). *Let Assumption 1 hold. Then for every $k_1, k_2, k_3 > 0$, there exists a non-increasing function $\varphi : \mathbb{R}_+ \rightarrow (0, +\infty)$ and a function $\alpha \in \mathcal{K}_\infty$ such that for every $(f_0, D_0) \in \mathcal{F} \times (\underline{D}, \overline{D})$ the unique solution $(f[t], D(t)) \in \mathcal{F} \times (\underline{D}, \overline{D})$ of the closed-loop system (1a–d) with (68) and initial condition $(f[0], D(0)) = (f_0, D_0)$ exists for all $t \geq 0$ and satisfies the following stability estimate for all $t \geq 0$*

$$R_2(f[t], D(t)) \leq \exp(-\varphi(R_2(f_0, D_0))t)\alpha(R_2(f_0, D_0)) \tag{69}$$

where

$$R_2(f, D) := \max_{a \in [0, A]} \left| \ln \frac{f(a)}{f^*(a)} \right| + |\Phi^{-1}(D)| \tag{70}$$

for all $(f, D) \in \mathcal{F} \times (\underline{D}, \overline{D})$.

Discussion of Theorem 3: The stability estimate (69) shows Global Asymptotic Stability of the equilibrium point (f^*, D^*) for the closed-loop system (1a–d) with (68). However, there are important differences with the corresponding stability estimate of Theorem 2.

1. The equilibrium point (f^*, D^*) for system (1a–d) with (68) is stabilized in a special measure: the measure $R_2(f, D) = \max_{a \in [0, A]} |\ln(f(a)/f^*(a))| + |\Phi^{-1}(D)|$ and not the measure $R_1(f, D) = \max_{a \in [0, A]} |\ln(f(a)/f^*(a))| + |D - D^*|$ that was used in Theorem 2. This is a consequence of the fact that the measure $R_1(f, D)$ does not take into account the state constraint for D . On the other hand, the measure $R_2(f, D)$ takes into account all state constraints (notice that $R_2(f, D)$ “blows up” when the state tends to a point on the boundary of the state space). In other words, the measure $R_2(f, D)$ is a size functional for system (1a–d) with (58a) and state space $\mathcal{F} \times (\underline{D}, \overline{D})$ in the sense of Reference 30, while the measure $R_1(f, D)$ is not a size functional.
2. An interesting special case of this result is the case where the dilution has no upper bound but it must remain positive, namely, $\underline{D} = 0, \overline{D} = +\infty$. Since $a_1/\overline{D} = 1$ and $a_2/\overline{D} = 1/D^*$, the transformation (66) in this case simplifies to $\zeta = \Phi^{-1}(D) = \ln(D/D^*)$, and the controller (68) simplifies to

$$u(t) = D(t) \left[(k_1 + k_2)(D^* - D(t)) + k_3 \ln \left(\frac{D^*}{D(t)} \left(\frac{y(t)}{y^*} \right)^{k_2} \right) \right], \tag{71}$$

whereas the state space becomes the “positive orthant” $\mathcal{F} \times (0, +\infty)$ and the measure R_2 becomes $R_2(f, D) = \max_{a \in [0, A]} |\ln(f(a)/f^*(a))| + |\ln(D/D^*)|$.

3. Theorem 3 guarantees Global Asymptotic Stabilization by means of the output feedback law (68) with exponential convergence rate exactly as Theorem 2 does. To see this, notice that estimate (69) implies that for every $\epsilon > 0$ and for every $(f_0, D_0) \in \mathcal{F} \times (\underline{D}, \overline{D})$ there exists $T \geq 0$ for which $R_2(f[T], D(T)) \leq \exp(-\varphi(R_2(f_0, D_0))T)\alpha(R_2(f_0, D_0)) \leq \epsilon$. Using the semigroup property and (69) we get the estimate

$$\begin{aligned} R_2(f[t], D(t)) &\leq \exp(-\varphi(\epsilon)(t - T))\alpha(R_2(f[T], D(T))) \\ &\leq \exp(-\varphi(\epsilon)(t - T))\alpha(\alpha(R_2(f_0, D_0))) \end{aligned} \tag{72}$$

for all $t \geq T$. Combining, we get

$$R_2(f[t], D(t)) \leq \exp(-\varphi(\epsilon)t) \left(1 + \frac{\alpha(R_2(f_0, D_0))}{\epsilon} \right)^{\frac{\varphi(\epsilon)}{\varphi(R_2(f_0, D_0))}} \alpha(\alpha(R_2(f_0, D_0))) \tag{73}$$

for all $t \geq 0$. The above estimate shows a uniform exponential convergence rate $\varphi(\epsilon) > 0$, for every $\epsilon > 0$. Consequently, the additional state constraint $D \in (\underline{D}, \overline{D})$, does not exclude the possibility of a uniform exponential convergence rate.

The proof of Theorem 3 shows that the controller gains $k_1, k_2, k_3 > 0$ strongly affect the convergence properties of the solutions of the closed-loop system (1a–d) with (68). Similarly, the parameters $\underline{D}, \overline{D}$ strongly affect the convergence

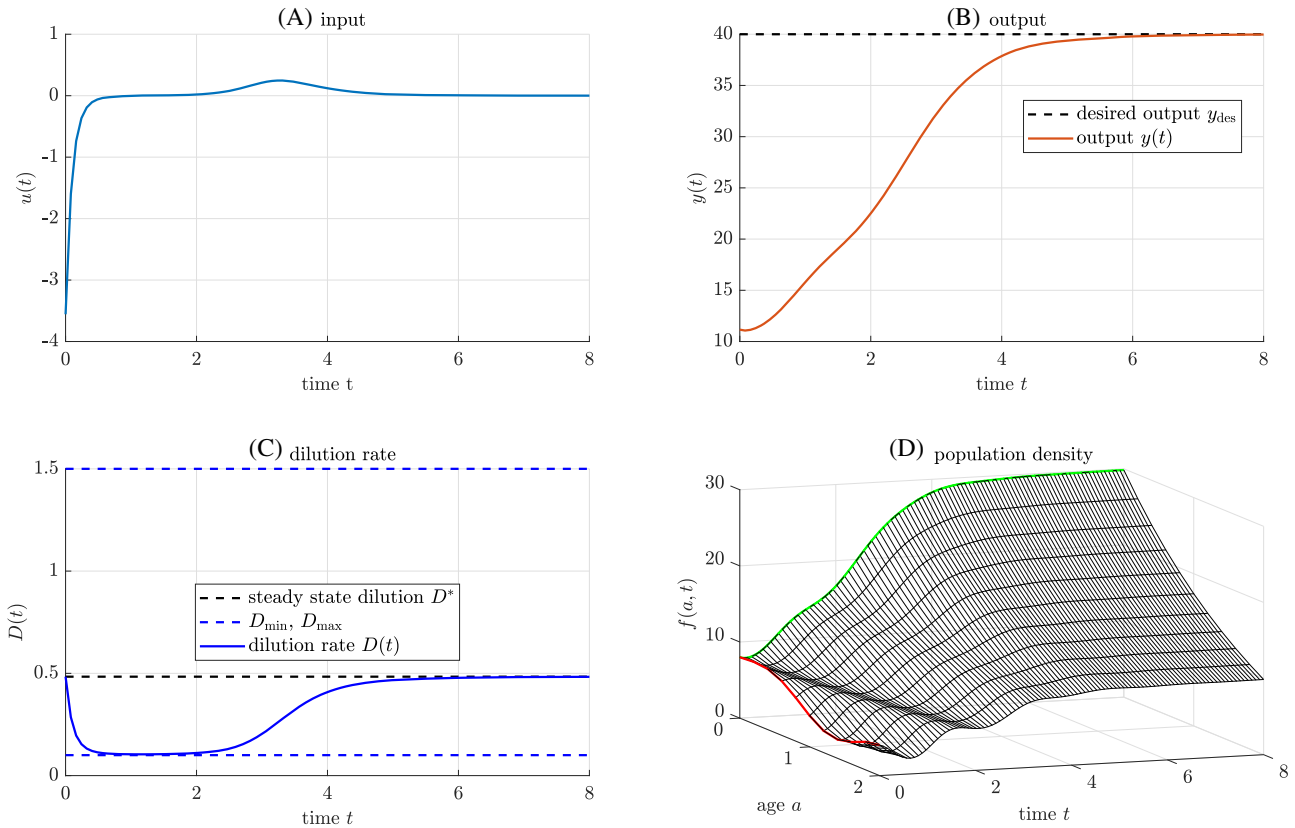


FIGURE 4 Simulation results of system (1a–d) with parameters and initial condition (16a,b) and controller (68) with gains $k_1 = 1$, $k_2 = 10$, $k_3 = 1$ and dilution interval $(\underline{D}, \overline{D}) = (D_{\min}, D_{\max}) = (0.1, 1.5)$. The controller constrains the dilution rate $D(t) \in (\underline{D}, \overline{D})$ and convergence to the desired output $y^* = y_{\text{des}}$ is achieved. (A) Input. (B) Output. (C) Dilution rate. (D) Population density.

properties of the solutions of the closed-loop system (1a–d) with (68): a tighter state constraint leads to slower convergence and higher overshoots. The behavior of the solutions of the closed-loop (1a–d) with (68) is illustrated by means of representative simulation example in Figure 4.

Having discussed Theorem 3 in detail, we next provide its proof.

Proof of Theorem 3. Using the transformations (17a,b), (18), (65) we get for the closed-loop system (1a–d) with (68):

$$\dot{\eta}(t) = \frac{a_1 a_2 (1 - \exp(\zeta(t)))}{(a_2 + 1)(a_2 + \exp(\zeta(t)))} := f_1(\zeta(t)) \quad (74a)$$

$$\dot{\zeta}(t) = (k_1 + k_2)f_1(\zeta(t)) - k_3(\zeta(t) - k_2\eta(t) - k_2v(\psi_t)) \quad (74b)$$

$$\psi(t) = \int_0^A \tilde{k}(a)\psi(t-a) da. \quad (74c)$$

where $v(\psi_t)$ is defined by (21) and (29). Again, like in (28), we know that the map $t \mapsto v(\psi_t)$ is well-defined and the closed-loop (74a–c) locally admits a unique solution. Consider the functional $G(\psi_t)$ defined by (32) and define the function

$$U_3(\eta, \zeta) = \frac{1}{2}\eta^2 + \frac{b_1}{2}(\zeta - k_2\eta)^2 \quad (75)$$

where $b_1 = \frac{1}{k_1 k_2}$. Using definition (75) and Equations (74a), (74b), we find that

$$\frac{d}{dt}U_3(\eta(t), \zeta(t)) = \frac{1}{k_2}\zeta(t)f_1(\zeta(t)) - b_1 k_3(\zeta(t) - k_2\eta(t))^2 + b_1 k_2 k_3(\zeta(t) - k_2\eta(t))v(\psi_t) \quad (76)$$

for all $t \geq 0$ for which the solution of (74a-c) exists. Equation (76) in conjunction with the inequality $2k_2(\zeta - k_2\eta)v(\psi) \leq (\zeta - k_2\eta)^2 + k_2^2v(\psi)^2$, gives for all $t \geq 0$ for which the solution of (74a-c) exists:

$$\frac{d}{dt} U_3(\eta(t), \zeta(t)) \leq \frac{1}{k_2} \zeta(t) f_1(\zeta(t)) - \frac{1}{2} b_1 k_3 (\zeta(t) - k_2 \eta(t))^2 + \frac{1}{2} b_1 k_2^2 k_3 v(\psi_t)^2. \tag{77}$$

Using (34) we obtain from (77) the following differential inequality

$$\frac{d}{dt} U_3(\eta(t), \zeta(t)) \leq \frac{1}{k_2} \zeta(t) f_1(\zeta(t)) - \frac{1}{2} b_1 k_3 (\zeta(t) - k_2 \eta(t))^2 + \frac{b_1 k_2^2 k_3}{2} \exp(2\sigma A) G(\psi_t)^2 \tag{78}$$

for all $t \geq 0$ for which the solution of (74a-c) exists. On the other hand, the differential inequality (33) in conjunction with lemma 2.12 on pp. 77-78 in Reference 32 implies the following estimate

$$G(\psi_t) \leq \exp(-\sigma t) G(\psi_0) \tag{79}$$

for all $t \geq 0$ and consequently, we obtain from (78), (79), the following differential inequality that holds for all $t \geq 0$ for which the solution of (74a-c) exists:

$$\frac{d}{dt} U_3(\eta(t), \zeta(t)) \leq \frac{1}{k_2} \zeta(t) f_1(\zeta(t)) - \frac{1}{2} b_1 k_3 (\zeta(t) - k_2 \eta(t))^2 + \frac{b_1 k_2^2 k_3}{2} \exp(-2\sigma(t - A)) G(\psi_0)^2. \tag{80}$$

Notice that by virtue of the fact that $f_1(\zeta) = \frac{a_1 a_2 (1 - \exp(\zeta))}{(a_2 + 1)(a_2 + \exp(\zeta))}$ (which implies that $\zeta f_1(\zeta) \leq 0$ for all $\zeta \in \mathbb{R}$), we obtain from (80) the following estimate for all $t \geq 0$ for which the solution of (74a-c) exists:

$$\frac{d}{dt} U_3(\eta(t), \zeta(t)) \leq \frac{b_1 k_2^2 k_3}{2} \exp(-2\sigma(t - A)) G(\psi_0)^2. \tag{81}$$

The above estimate in conjunction with lemma 2.12 on pp. 77-78 in Reference 32 implies that

$$U_3(\eta(t), \zeta(t)) \leq U_3(\eta(0), \zeta(0)) + \frac{b_1 k_2^2 k_3}{2\sigma} \exp(2\sigma A) G(\psi_0)^2 \tag{82}$$

for all $t \geq 0$ for which the solution of (74a-c) exists. For the positive definite quadratic function U_3 defined by (75), there exist constants $\underline{c}, \bar{c} > 0$ such that for all $(\eta, \zeta) \in \mathbb{R}^2$ it holds that

$$\underline{c}(\eta^2 + \zeta^2) \leq U_3(\eta, \zeta) \leq \bar{c}(\eta^2 + \zeta^2). \tag{83}$$

Inequalities (83), (82) show that the component $(\eta(t), \zeta(t))$ of the solution of (74a-c) is bounded for all times $t \geq 0$ for which the solution exists. Thus, the solution of (74a-c) exists for all $t \geq 0$ and satisfies

$$\eta^2(t) + \zeta^2(t) \leq \frac{\bar{c}}{\underline{c}} (\eta^2(0) + \zeta^2(0)) + \frac{b_1 k_2^2 k_3}{2\sigma \underline{c}} \exp(2\sigma A) G(\psi_0)^2 \tag{84}$$

for all $t \geq 0$. The fact that $f_1(\zeta) = \frac{a_1 a_2 (1 - \exp(\zeta))}{(a_2 + 1)(a_2 + \exp(\zeta))}$ and (75), (83) imply the existence of a non-increasing, positive mapping $\varphi(s) > 0$ defined for all $s \geq 0$ with the property that for all $s \geq 0$ the following estimate holds for all $(\eta, \zeta) \in \mathbb{R}^2$ with $\zeta^2 \leq \frac{\bar{c}}{\underline{c}} s^2 + \frac{b_1 k_2^2 k_3}{2\sigma \underline{c}} \exp(2\sigma A) s^2$:

$$\frac{1}{k_2} \zeta f_1(\zeta) - \frac{1}{2} b_1 k_3 (\zeta - k_2 \eta)^2 \leq -2\varphi(s) U_3(\eta, \zeta). \tag{85}$$

It follows from (80) and (84), (85) that the following estimate holds for all $t \geq 0$:

$$\frac{d}{dt} U_3(\eta(t), \zeta(t)) \leq -2\varphi(p_0) U_3(\eta(t), \zeta(t)) + \frac{b_1 k_2^2 k_3}{2} \exp(-2\sigma(t - A)) G(\psi_0)^2 \tag{86}$$

where $p_0 := |\eta(0)| + |\zeta(0)| + G(\psi_0)$. Without loss of generality, we may assume that $\varphi(s) \leq \sigma$ for all $s \geq 0$. The differential inequality (86) in conjunction with lemma 2.12 on pp. 77–78 in Reference 32 implies the following estimate for all $t \geq 0$:

$$\exp(2\varphi(p_0)t)U_3(\eta(t), \zeta(t)) \leq U_3(\eta(0), \zeta(0)) + \frac{b_1 k_2^2 k_3}{4\varphi(p_0)} \exp(2\sigma A)G(\psi_0)^2. \quad (87)$$

Combining (87), (83), (79), we get for all $t \geq 0$

$$|\eta(t)| + |\zeta(t)| + \exp(\sigma A)G(\psi_t) \leq K(p_0) \exp(-\varphi(p_0)t)(|\eta(0)| + |\zeta(0)| + \exp(\sigma A)G(\psi_0)) \quad (88)$$

where $K(s)$ is the non-decreasing function defined for $s \geq 0$ by the equation

$$K(s) := 3\sqrt{\frac{\bar{c}}{c}} + \sqrt{\frac{b_1 k_2^2 k_3}{c\varphi(s)}}. \quad (89)$$

Using (45), (47), (66), (89), the fact that $p_0 := |\eta(0)| + |\zeta(0)| + G(\psi_0)$ and definition (70), we obtain the stability estimate (69) for an appropriate $\alpha \in \mathcal{K}_\infty$. The proof is complete. ■

7 | FULL-STATE STABILIZATION UNDER STATE CONSTRAINTS

The design that we just presented is mindful of three practical requirements:

1. dilution must remain above a given positive lower bound $\underline{D} > 0$;
2. dilution must obey a given upper bound $\bar{D} < +\infty$;
3. only a bulk concentration $y(t)$ is available for measurement, rather than an age-structured density $f(a, t)$.

The price we pay for meeting all these practical requirements is a design that is quite complicated and that offers little insight and generalizability to other situations. In the remainder of this section we present an alternative design, which fails to obey two of the above requirements but is clear, elegant, and systematic.

First, we dispose of the requirement for a strictly positive lower bound $\underline{D} > 0$ and only require the dilution to remain positive. This is practically reasonable. Dilution/harvesting can be easily completely shut off. Second, we lift the fixed upper bound requirement $\bar{D} < +\infty$ and require the dilution to merely be bounded.

Third, we allow the measurement of the full state of the system, namely, of the age-structured density $f(a, t)$. This is a stronger requirement as the age distribution of the population cannot be measured. However, the size distribution of the population, which is proportional to the age distribution can be measured. We allow the full-state measurement only for pedagogical reasons, and without loss of generality. The analysis is much cleaner, clearer, and exact when the full $f(a, t)$ is measured, as opposed to when only $y(t)$ is measured.

So, we start by setting $\underline{D} = 0$ and $\bar{D} = +\infty$. Then, we recall that

$$\eta = \ln \Pi(f) \quad (90)$$

$$\zeta = \ln \frac{D}{D^*}. \quad (91)$$

Next, we introduce a backstepping transformation

$$z = \zeta - c_1 \eta, \quad c_1 > 0. \quad (92)$$

Straightforward calculation then yields

$$\begin{aligned} \dot{\eta} &= D^*(1 - \exp(\zeta)) \\ &= D^*(1 - \exp(c_1 \eta)) + D^* \exp(c_1 \eta)(1 - \exp(z)) \end{aligned} \quad (93)$$

$$\dot{\zeta} = \frac{u}{D} \tag{94}$$

$$\dot{z} = \frac{u}{D} - c_1 D^* (1 - \exp(\zeta)). \tag{95}$$

Before we design a controller, we introduce two positive definite radially unbounded functions,

$$\omega(q) = \exp(q) - 1 - q \tag{96}$$

$$\mu(q) = \sinh^2\left(\frac{q}{2}\right). \tag{97}$$

Next, we introduce two Lyapunov functions,

$$V_1 = \omega(-c_1 \eta) \tag{98}$$

$$V_2 = \omega(\zeta - c_1 \eta) = \omega(z) \tag{99}$$

and the overall Lyapunov function

$$V = \theta V_1 + V_2 = \theta \omega(-c_1 \eta) + \omega(\zeta - c_1 \eta), \quad \theta > 0. \tag{100}$$

Noting that $\omega'(z) = \exp(z) - 1$, as well as that

$$(\exp(z) - 1)(\exp(-z) - 1) = -4\sinh^2(z/2), \tag{101}$$

after a lengthy calculation, with intermediate steps that produce

$$\dot{V}_1 = -4D^* c_1 \mu(-c_1 \eta) - D^* c_1 (\exp(z) - 1)(\exp(c_1 \eta) - 1) \tag{102}$$

$$\dot{V}_2 = D^* (\exp(z) - 1) \left(\frac{u}{D^* D} - c_1 (1 - \exp(\zeta)) \right), \tag{103}$$

we note that the feedback law

$$u = D^* D \left\{ c_1 \left[\theta (\exp(c_1 \eta) - 1) + 1 - \exp(\zeta) \right] + c_2 (\exp(c_1 \eta - \zeta) - 1) \right\}, \tag{104}$$

with $c_2 > 0$, produces a particularly elegant Lyapunov derivative,

$$\dot{V} = -4D^* [\theta c_1 \mu(-c_1 \eta) + c_2 \mu(\zeta - c_1 \eta)], \tag{105}$$

which is negative definite and radially unbounded. Global asymptotic stability of the equilibrium $\eta = \zeta = 0$ then follows. With the global exponential stability of the decoupled ψ -system, the global asymptotic stability of the (η, ψ, ζ) -system follows.

Theorem 4. *The controller (104), rewritten in the original (f, D) -variables as*

$$u = D^* D \left\{ c_1 \left[\theta ((\Pi(f))^{c_1} - 1) + 1 - \frac{D}{D^*} \right] + c_2 \left(\frac{D^*}{D} (\Pi(f))^{c_1} - 1 \right) \right\}, \tag{106}$$

with gains $c_1, c_2, \theta > 0$, guarantees that there exists a class \mathcal{KL} function β such that

$$\max_{a \in [0, A]} \left| \ln \frac{f(a, t)}{f^*(a)} \right| + \left| \ln \frac{D(t)}{D^*} \right| \leq \beta \left(\max_{a \in [0, A]} \left| \ln \frac{f_0(a)}{f^*(a)} \right| + \left| \ln \frac{D_0}{D^*} \right|, t \right), \quad \forall t \geq 0 \tag{107}$$

for all $f_0 \in \mathcal{F}$ and $D_0 > 0$.

This design with $D \in (0, +\infty)$ calls for a reexamination of the more difficult problem where $D \in (\underline{D}, \bar{D})$ and $0 \leq \underline{D} < D^* < \bar{D}$. We omit much of the detail and summarize the design and analysis.

Let us denote

$$\delta_1 = \frac{D^* - \underline{D}}{D^*}, \quad n = \frac{D^* - \underline{D}}{\underline{D} - D^*}. \quad (108)$$

One gets

$$\eta = D^* \delta_1 \frac{1 - \exp(\zeta)}{1 + n \exp(\zeta)}, \quad \zeta = \ln\left(\frac{1}{n} \frac{D - \underline{D}}{\underline{D} - D}\right) \quad (109)$$

$$\dot{\zeta} = \frac{\underline{D} - D}{(D - \underline{D})(\underline{D} - D)} u \quad (110)$$

and

$$\begin{aligned} \dot{V}_1 &= -4D^* c_1 \frac{\delta_1}{1 + n \exp(c_1 \eta)} \mu(-c_1 \eta) \\ &\quad - D^* c_1 \frac{\delta_1(1 + n)}{(1 + n \exp(c_1 \eta))^2} (\exp(c_1 \eta) - 1)(\exp(\zeta) - 1). \end{aligned} \quad (111)$$

With further calculations, one obtains

$$\dot{V} = -4D^* \left[\theta c_1 \frac{\delta_1}{1 + n \exp(c_1 \eta)} \mu(-c_1 \eta) + c_2 \mu(\zeta - c_1 \eta) \right] \quad (112)$$

with the controller

$$\begin{aligned} u &= \frac{D^*}{\underline{D} - \underline{D}} (D - \underline{D})(\underline{D} - D) \left\{ c_1 \left[\theta \frac{\delta_1(1 + n)}{(1 + n \exp(c_1 \eta))^2} (\exp(c_1 \eta) - 1) + \frac{1 - \exp(\zeta)}{1 + n \exp(\zeta)} \right] \right. \\ &\quad \left. + c_2 (\exp(c_1 \eta) - \zeta) - 1 \right\} \\ &= \frac{D^*}{\underline{D} - \underline{D}} (D - \underline{D})(\underline{D} - D) \left\{ c_1 \left[\theta \frac{\delta_1(1 + n)}{(1 + n(\Pi(f)))^{c_1}} ((\Pi(f))^{c_1} - 1) + 1 - \frac{1}{n} \frac{D - \underline{D}}{\underline{D} - D} \right] \right. \\ &\quad \left. + c_2 \left(n \frac{\underline{D} - D}{\underline{D} - \underline{D}} (\Pi(f))^{c_1} - 1 \right) \right\}. \end{aligned} \quad (113)$$

This is clearly a considerably more complicated controller than (68) but the simplicity of the negative definite, radially unbounded (112) makes this controller worth consideration.

Theorem 5. *The controller (113) with gains $c_1, c_2, \theta > 0$, guarantees that there exists a class \mathcal{KL} function β such that*

$$\begin{aligned} &\max_{a \in [0, A]} \left| \ln \frac{f(a, t)}{f^*(a)} \right| + \left| \ln \left(\frac{D(t) - \underline{D}}{D^* - \underline{D}} \frac{\underline{D} - D^*}{\underline{D} - D(t)} \right) \right| \\ &\leq \beta \left(\max_{a \in [0, A]} \left| \ln \frac{f_0(a)}{f^*(a)} \right| + \left| \ln \left(\frac{D_0 - \underline{D}}{D^* - \underline{D}} \frac{\underline{D} - D^*}{\underline{D} - D_0} \right) \right|, t \right), \quad \forall t \geq 0 \end{aligned} \quad (114)$$

for all $f_0 \in \mathcal{F}$ and $D_0 \in (\underline{D}, \bar{D})$.

8 | CONCLUSION

Let us now systematize the catalog of controllers presented:

1. Controller in Reference 4 is simply a saturated (for positivity of dilution) static proportional feedback of the logarithmically scaled output, where the logarithmic scaling is not needed but used only to achieve exponential stability of the first mode of the population concentration age profile.
2. Controller (12a–c) is a standard backstepping extension of the controller from Reference 4, using full-state feedback from the chemostat PDE.
3. Controller (54) relaxes the full-state feedback requirement of (12a–c) and simply augments the controller from Reference 4 with proportional feedback of the dilution regulation error.
4. Controller (68) is the paper's most general design, achieving global stabilization with only output feedback, while compelling the dilution to remain within any positive interval that contains the setpoint dilution.
5. Controller (106) is a full-state design for which positivity of dilution and global stabilization are both achieved with a Lyapunov analysis that is the least conservative (no majorizations involved) and clearest.

The interest in further extending the foundational design and analysis results in Reference 4 goes in many directions. Among them, the most interesting at this stage are in incorporating additional dynamics, which may arise for a variety of reasons (the presence of actuator dynamics, a substrate, input delay, additional species, etc.). In this paper we made what is probably most natural non-trivial step—incorporating actuator dynamics in the form of a single state. Compensating these actuator dynamics was not exceptionally difficult but ensuring that, in addition to the population density remaining positive, the state of the actuator dynamics remains positive as well, or even remains within a given positive interval, is far from elementary and charts a path towards further generalizations.

Among the further generalizations are those that bring into the model additional infinite-dimensional states. One such addition is an input delay, which can be compensated using predictor feedback. Other additions of infinite dimensional states are additional species. Even two species can be interconnected in several ways, of which some require no innovations in the control design, while other types of interconnections do. Such generalizations of the chemostat problem into population systems, of which epidemiology is one possible application, open exciting possibilities for future research.

AUTHOR CONTRIBUTIONS

All the authors have contributed to conceiving the problems and writing the article. The simulations were produced by Paul-Erik Haacker.

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CONFLICT OF INTEREST STATEMENT

The authors declare no potential conflict of interests.

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Research data are not shared.

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REFERENCES

1. Kuritz K, Stöhr D, Pollak N, Allgöwer F. On the relationship between cell cycle analysis with ergodic principles and age-structured cell population models. *J Theor Biol.* 2017;414:91-102.
2. Billy F, Clairambault J, Delaunay F, Feillet CA, Robert N. Age-structured cell population model to study the influence of growth factors on cell cycle dynamics. *Math Biosci Eng.* 2012;10:1-17.

3. Rong L, Feng Z, Perelson AS. Mathematical analysis of age-structured HIV-1 dynamics with combination antiretroviral therapy. *SIAM J Appl Math*. 2007;67(3):731-756.
4. Karafyllis I, Krstic M. Stability of integral delay equations and stabilization of age-structured models. *ESAIM: Control Optim Calcul Var*. 2017;23(4):1667-1714.
5. Kurth AC, Schmidt K, Sawodny O. Tracking-control for age-structured population dynamics with self-competition governed by integro-PDEs. *Automatica*. 2021;133:109850.
6. Kurth AC, Sawodny O. Control of age-structured population dynamics with intraspecific competition in context of bioreactors. *Automatica*. 2023;152:110944.
7. De Leenheer P, Aeyels D. Stabilization of positive linear systems. *Syst Control Lett*. 2001;44(4):259-271.
8. De Leenheer P, Aeyels D. Stabilization results for positive systems with first integrals. *IFAC Proc Vol*. 2001;34(6):881-886.
9. Inaba H. *Age-Structured Population Dynamics in Demography and Epidemiology*. Springer; 2017.
10. Martcheva M. *An Introduction to Mathematical Epidemiology*. Vol 61. Springer; 2015.
11. Smith HL, Thieme HR. Chemostats and epidemics: competition for nutrients/hosts. *Math Biosci Eng*. 2013;10:1635-1650.
12. Toth D, Kot M. Limit cycles in a chemostat model for a single species with age structure. *Math Biosci*. 2006;202(1):194-217.
13. McKendrick AG. Applications of mathematics to medical problems. *Proc Edinburgh Math Soc*. 1925;44:98-130.
14. Brauer F, Castillo-Chavez C. *Mathematical Models in Population Biology and Epidemiology*. Vol 2. Springer; 2012.
15. Kermack WO, McKendrick AG. A contribution to the mathematical theory of epidemics. *Proc R Soc London Series A Contain Pap Math Phys Charac*. 1927;115(772):700-721.
16. Boucekkine R, Hritonenko N, Yatsenko Y. *Optimal Control of Age-Structured Populations in Economy, Demography, and the Environment*. Routledge; 2011.
17. Charlesworth B. *Evolution in Age-Structured Populations*. Vol 2. Cambridge University Press; 1994.
18. Rundnicki R, Mackey MC. Asymptotic similarity and Malthusian growth in autonomous and nonautonomous populations. *J Math Anal Appl*. 1994;187(2):548-566.
19. Smith HL, Waltman P. *The Theory of the Chemostat: Dynamics of Microbial Competition*. Vol 13. Cambridge University Press; 1995.
20. Inaba H. A semigroup approach to the strong ergodic theorem of the multistate stable population process. *Math Popul Stud*. 1988;1(1):49-77.
21. Inaba H. Asymptotic properties of the inhomogeneous Lotka-Von Foerster system. *Math Popul Stud*. 1988;1(3):247-264.
22. Feichtinger G, Tragler G, Veliov VM. Optimality conditions for age-structured control systems. *J Math Anal Appl*. 2003;288(1):47-68.
23. Sun B. Optimal control of age-structured population dynamics for spread of universally fatal diseases II. *Appl Anal*. 2014;93(8):1730-1744.
24. Schmidt K, Karafyllis I, Krstic M. Yield trajectory tracking for hyperbolic age-structured population systems. *Automatica*. 2018;90:138-146.
25. Karafyllis I, Kravaris C, Syrou L, Lyberatos G. A vector Lyapunov function characterization of input-to-state stability with application to robust global stabilization of the chemostat. *Eur J Control*. 2008;14(1):47-61.
26. Karafyllis I, Kravaris C, Kalogerakis N. Relaxed Lyapunov criteria for robust global stabilisation of non-linear systems. *Int J Control*. 2009;82(11):2077-2094.
27. Gouze JL, Robledo G. Robust control for an uncertain chemostat model. *Int J Robust Nonlinear Control*. 2006;16(3):133-155.
28. De Leenheer P, Smith H. Feedback control for chemostat models. *J Math Biol*. 2003;46(1):48-70.
29. Dimitrova N, Krastanov M. Nonlinear adaptive stabilizing control of an anaerobic digestion model with unknown kinetics. *Int J Robust Nonlinear Control*. 2012;22(15):1743-1752.
30. Sontag ED. Remarks on input to state stability of perturbed gradient flows, motivated by model-free feedback control learning. *Syst Control Lett*. 2022;161:105138.
31. Khalil HK. *Nonlinear Control*. Vol 406. Pearson New York; 2015.
32. Karafyllis I, Jiang ZP. *Stability and Stabilization of Nonlinear Systems*. Springer Science & Business Media; 2011.
33. Toth D. Strong resonance and chaos in a single-species chemostat model with periodic pulsing of resource. *Chaos Solitons Fract*. 2008;38(1):55-69.
34. Toth D. Bifurcation structure of a chemostat model for an age-structured predator and its prey. *J Biol Dyn*. 2008;2(4):428-448.
35. Kurth AC, Schmidt K, Sawodny O. Inversion-based and optimal feedforward control for population dynamics with input constraints and self-competition in chemostat reactor applications. *J Dyn Syst Meas Control*. 2021;143(5):051003.
36. Schmidt K, Sawodny O. Efficient simulation of semilinear populations models for age-structured bio reactors. Paper presented at: 2017 IEEE Conference on Control Technology and Applications (CCTA), IEEE. 2017 1716-1721.
37. Krstic M. Inverse optimal safety filters. *IEEE Trans Automat Contr*. 2023;69(1):1-16. doi:10.1109/TAC.2023.3278788

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APPENDIX A. PROOF OF TECHNICAL LEMMAS

Proof of Lemma 1. We rewrite (50), by bringing the expression to a common denominator and rearranging terms, as

$$-v_1(\psi_t) = \frac{-1}{\int_0^A p(a)f^*(a)(1 + \psi(t-a))da} T_3(\psi_t) \quad (\text{A1})$$

where

$$T_3(\psi_t) = p(A)f^*(A)(T_4(\psi_t) - \psi(t-A)) - p(0)f^*(0)(T_4(\psi_t) - \psi(t)) \quad (\text{A2})$$

$$- \int_0^A \tilde{p}(a)f^*(a)da T_4(\psi_t) + \int_0^A \tilde{p}(a)f^*(a)\psi(t-a)da \quad (\text{A3})$$

$$T_4(\psi_t) = \frac{1}{y^*} \int_0^A p(a)f^*(a)\psi(t-a)da. \quad (\text{A4})$$

By means of the definition of y^* (5) and the nonnegativity of p, f^* on $[0, A]$, it holds that

$$|T_4(\psi_t)| \leq \max_{a \in [0, A]} |\psi(t-a)|. \quad (\text{A5})$$

Taking the absolute value of (A2) and using (A5) we arrive at

$$|T_3(\psi_t)| \leq \sqrt{c_1} y^* \max_{a \in [0, A]} |\psi(t-a)| \quad (\text{A6})$$

with

$$\frac{1}{2} \sqrt{c_1} y^* = p(A)f^*(A) + p(0)f^*(0) + \int_0^A |\tilde{p}(a)|f^*(a)da > 0. \quad (\text{A7})$$

We note, that c_1 is independent of the chosen setpoint y^* . With nonnegativity of $p(a)$ and $f^*(a)$ for $a \in [0, A]$ and $1 + \psi(t-a) > 0$ for all $(a, t) \in [0, A] \times \mathbb{R}_+$, we note that

$$|v_1(\psi_t)| = \frac{1}{\int_0^A p(a)f^*(a)(1 + \psi(t-a))da} |T_3(\psi_t)| \quad (\text{A8})$$

and

$$\int_0^A p(a)f^*(a)\psi(t-a)da \geq y^* \min_{a \in [0, A]} \psi(t-a) \quad (\text{A9})$$

yields (53) using (A6). ■