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Global stabilization of the chemostat with delayed and sampled measurements and control[★]

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Abstract: The classical model of the chemostat with one substrate, one species and a Haldane type growth rate function is considered. The input substrate concentration is supposed to be constant and the dilution rate is considered as the control. The problem of globally asymptotically stabilizing a positive equilibrium point of this system in the case where the measured concentrations are delayed and piecewise constant with a piecewise constant control is addressed. The result relies on the introduction of a dynamic extension of a new type.

1. INTRODUCTION

Biological systems suffer of a systematic lack of sensors and actuators. However, even more crucial is the fact that real monitoring systems like substrate or biomass measurements, when available, deliver discrete measures of these variables with delays which may be important with respect to the proper dynamics of the system. From the best of authors's knowledge, this problem has never been taken into account explicitly. In practice, the control laws that are designed using continuous models are discretized and users rely on the robustness of the control laws with respect to delays of the measurements to control the system effectively. But no rigorous theoretical study corroborates the results and only small delays and sampling period intervals are allowed.

These remarks motivate the present work. We consider the classical model of the chemostat described in Smith et al. [1995] with one substrate and one species, with a Haldane type growth rate, a constant input substrate concentration. The dilution rate is used as a control. Controlling this system is a challenging problem, mostly because it admits two equilibrium points when the dilution rate is constant. One is locally exponentially stable and the other is unstable. It has been considered, in a more general context, in Mazenc et al. [2010], when a pointwise delay is present in the input, under the assumption that both the dilution rate and the measured variables are continuous functions.

To the best of our knowledge, the case of piecewise constant inputs and retarded discrete measurements has never

been considered. We thus address the problem of globally asymptotically stabilizing, on the positive orthant, a positive equilibrium point of the system described above in the case where the measured concentrations are delayed and piecewise constant with a piecewise constant control with delay. No limitation on the size of the delay or the largest sampling interval is imposed. The proposed result relies on the introduction of a time-varying dynamic extension of a new type. It leads to Lipschitz continuous time-varying control laws. The control laws as well as the stability analysis we present are of a new type. In particular, they are very different from those of Mazenc et al. [2010], Gajardo et al. [2009], Robledo [2009], Mazenc et al. [2009], which do not seem to extend to the problem we consider.

The paper is organized as follows. The considered model of the chemostat is recalled in Section 2. The main result is stated and proved in Section 3. Simulations are presented in Section 4. Concluding remarks are given in Section 5.

Notation and definitions.

- Denote $|\cdot|$ the Euclidean norm of matrices and vectors of any dimension.
- Given $\phi : I \rightarrow \mathbb{R}^p$ defined on an interval I , denote its (essential) supremum over I by $|\phi|_I$.
- Let p be any positive integer. We denote $C_{\text{in}} = C([-\tau, 0], \mathbb{R}^p)$ the set of all continuous \mathbb{R}^p -valued functions defined on a given interval $[-\tau, 0]$.
- For a continuous function $\varphi : [-\tau, +\infty) \rightarrow \mathbb{R}^k$, for all $t \geq 0$, the function φ_t defined by $\varphi_t(\theta) = \varphi(t + \theta)$ for all $\theta \in [-\tau, 0]$ is sometimes called translation operator.

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- We say that an equilibrium point is globally asymptotically stable, if is locally stable and all the trajectories with initial conditions in the positive orthant converge to the equilibrium point.

- The notation will be simplified whenever no confusion can arise from the context.

2. MODEL OF CHEMOSTAT

Consider the model defined by

$$\begin{cases} \dot{S}(t) = D(t)[S_{in} - S(t)] - \mu(S(t))x(t), \\ \dot{x}(t) = [\mu(S(t)) - D(t)]x(t), \end{cases} \quad (1)$$

where $S \in \mathbb{R}$ is the substrate, $x \in \mathbb{R}$ is the biomass and S_{in} is a positive constant. The variable D represents a dilution rate, and thus all its values are nonnegative.

We assume that the function μ is of class C^1 and such that:

(i) $\mu(0) = 0$,

(ii) there exists a value

$$\bar{S} \in (0, S_{in}) \quad (2)$$

such that $\mu'(S) > 0$ for all $S \in (0, \bar{S})$ and $\mu'(S) \leq 0$ over $(\bar{S}, +\infty)$,

(iii) $\lim_{S \rightarrow +\infty} \mu(S) = 0$.

The properties of μ imply that the positive orthant is a positively invariant set of (1). Throughout the paper, we consider solutions with positive initial conditions i.e. $x(0) > 0$ and $S(\ell) > 0$ for all $\ell \in [-\tau, 0]$. It is worth noticing that Haldane functions, i.e. functions of the type

$$\mu(S) = \frac{aS}{b + S + cS^2}, \quad (3)$$

with $a > 0$, $b > 0$, $c > 0$ satisfy the requirements (i), (ii),

(iii) with $\bar{S} = \sqrt{\frac{b}{c}}$.

We introduce two sequences of asynchronous sampling instants t_i and m_i . We let $t_0 = 0$, $m_0 = 0$ and assume that there are two positive constants $\nu_1 > 0$, $\nu_2 > \nu_1$ such that, for all $i \in \mathbb{N}$,

$$t_{i+1} - t_i \in [\nu_1, \nu_2] \quad (4)$$

and

$$m_{i+1} - m_i \in [\nu_1, \nu_2]. \quad (5)$$

We consider the case where

$$D(t) = D(t_i), \quad \forall t \in [t_i, t_{i+1}) \quad (6)$$

and where the output is

$$y(t) = S(m_i - \tau), \quad \forall t \in [m_i, m_{i+1}), \quad (7)$$

where τ is a positive constant. Thus D has to be piecewise constant and y corresponds to discrete measurements with a constant delay.

3. MAIN RESULT

3.1 Control design

Let S_* be a constant in the interval $(0, \bar{S})$. Then, the fact that μ is increasing over $(0, \bar{S})$ ensures that $\mu(S_*) > 0$. Therefore, when $D(t)$ is identically equal to $D_* = \mu(S_*)$,

the point (x_*, S_*) with $x_* = S_{in} - S_*$ is an equilibrium point of (1) and $(x_*, S_*) \in (0, +\infty) \times (0, \bar{S})$. Observe for later use that since the function μ is increasing over $(0, \bar{S})$, the inequalities

$$0 < \mu(S_*) < \mu(\bar{S}) \quad (8)$$

are satisfied.

The control objective we consider is the stabilization of such a point (x_*, S_*) when the output is (7) and the control of the type (6).

To begin with, we define two functions. Let $\theta : \mathbb{R} \rightarrow [0, 1]$ be defined by

$$\theta(\ell) = \min \{ \max \{ 0, \ell \}, 1 \} \quad (9)$$

and $\varphi : \mathbb{R} \rightarrow [0, 1]$ be defined by

$$\varphi(\ell) = \min \left\{ \max \left\{ 0, \frac{\bar{S} - \ell}{\bar{S} - S_*} \right\}, 1 \right\}. \quad (10)$$

We introduce a constant

$$\mathfrak{T} = \frac{1}{D_*} \ln \left(\frac{\mu(\bar{S})S_{in}}{[\mu(\bar{S}) - D_*][S_{in} - \bar{S}]} \right) + \nu_2 + \tau > 0. \quad (11)$$

We are ready to state and prove the main result of the paper:

Theorem 1. Consider the system (1) with the dynamic extension:

$$\begin{cases} \dot{p}(t) = \varphi(y(t))\theta \left(\frac{t - 7\mathfrak{T}}{\mathfrak{T}} \right), \\ p(t) = 0, \quad \forall t \in [-\tau, 0] \end{cases} \quad (12)$$

with $y(t)$ defined in (7) and \mathfrak{T} in (11) and the feedback $D_f(t)$ defined, for all $t \in [t_i, t_{i+1})$, by:

$$\begin{aligned} D_f(t) = & \theta(p(t_i))\theta \left(\frac{t_i - \mathfrak{T}}{\mathfrak{T}} \right) D_* \\ & + \left[1 - \theta \left(\frac{t_i - \mathfrak{T}}{\mathfrak{T}} \right) \right] D_*, \end{aligned} \quad (13)$$

where D_* is the value such that $D_* = \mu(S_*)$. Then this systems admits the point (S_*, x_*) , $x_* = S_{in} - S_*$ as a globally asymptotically stable equilibrium point.

3.2 Proof of Theorem 1

Let us prove that the dynamic feedback (12)-(13) renders the point (S_*, x_*) globally attractive for (1).

Let $(S(t), x(t))$ be a positive solution of (1)-(13). We analyze its behavior. To begin with, we observe that the growth properties of the nonlinear terms imply that the finite escape time phenomenon does not occur.

Next, we consider a value of t such that $t \geq 3\mathfrak{T}$. Let $i \in \mathbb{N}$ be such that $t \in [t_i, t_{i+1})$. Since $\mathfrak{T} \geq \nu_2$, we deduce that $t_i \geq 2\mathfrak{T}$. Consequently $\frac{t_i - \mathfrak{T}}{\mathfrak{T}} \geq 1$. From the definition of θ , it follows that

$$D_f(t) = \theta(p(t_i))D_*. \quad (14)$$

Therefore we have, for all $t \geq 3\mathfrak{T}$

$$\begin{cases} \dot{S}(t) = \theta(p(t_i))D_*[S_{in} - S(t)] - \mu(S(t))x(t), \\ \dot{x}(t) = [\mu(S(t)) - \theta(p(t_i))D_*]x(t), \\ \dot{p}(t) = \varphi(S(m_i - \tau))\theta \left(\frac{t - 7\mathfrak{T}}{\mathfrak{T}} \right), \text{ when } t \in [m_i, m_{i+1}). \end{cases} \quad (15)$$

Since, for all $t \in [0, 7\mathfrak{T}]$, $\theta\left(\frac{t-7\mathfrak{T}}{\mathfrak{T}}\right) = 0$, and $p(t) = 0$ for all $t \in [-\tau, 0]$, we deduce that, for all $t \in [-\tau, 7\mathfrak{T}]$, $p(t) = 0$. Let \mathfrak{k} be the integer such that $5\mathfrak{T} \in [m_{\mathfrak{k}}, m_{\mathfrak{k}+1})$. It follows that, for all $t \in [-\tau, m_{\mathfrak{k}}]$, $p(t) = 0$. Moreover, from the definitions of \mathfrak{k} and the inequality $\mathfrak{T} \geq \nu_2$, it follows that $m_{\mathfrak{k}} \geq 4\mathfrak{T}$. Consequently, for all $t \geq 3\mathfrak{T}$,

$$\begin{cases} \dot{S}(t) = \theta(p(t_i))D_*[S_{in} - S(t)] - \mu(S(t))x(t), \\ \dot{x}(t) = [\mu(S(t)) - \theta(p(t_i))D_*]x(t), \\ \dot{p}(t) = \varphi(S(m_i - \tau))\theta\left(\frac{t-7\mathfrak{T}}{\mathfrak{T}}\right), \text{ when } t \in [m_i, m_{i+1}), \\ p(t) = 0, \text{ when } t \in [3\mathfrak{T}, m_{\mathfrak{k}}], \end{cases} \quad (16)$$

Now, to prove that $S(t)$ cannot be always larger than \bar{S} , we proceed by contradiction. We assume that $S(t) \geq \bar{S}$ for all $t \geq m_{\mathfrak{k}} - \tau$ and we show that a contradiction occurs.

Let us consider $t \geq m_{\mathfrak{k}}$. Then there is an integer l such that $t \in [m_l, m_{l+1})$. Then $m_l - \tau \geq m_{\mathfrak{k}} - \tau$. Therefore our assumption implies that $S(m_l - \tau) \geq \bar{S}$. From the definition of φ , it follows that $\varphi(S(m_l - \tau)) = 0$. We deduce that, for all $t \geq m_{\mathfrak{k}}$, $\dot{p}(t) = 0$. Since $p(m_{\mathfrak{k}}) = 0$, it follows that, for all $t \geq m_{\mathfrak{k}}$, $p(t) = 0$. Consequently, for all $t \geq m_{\mathfrak{k}}$,

$$\begin{cases} \dot{S}(t) = -\mu(S(t))x(t), \\ \dot{x}(t) = \mu(S(t))x(t). \end{cases} \quad (17)$$

Therefore both the inequalities $S(t) > 0$ and $\dot{S}(t) \leq 0$ are satisfied for all $t \geq m_{\mathfrak{k}}$. We deduce that $S(t)$ converges to a nonnegative value S_{∞} . Since $S(t) \geq \bar{S}$ for all $t \geq m_{\mathfrak{k}}$, it follows that $S_{\infty} > 0$. Consequently, $x(t)$ goes to $+\infty$ because (17) there exists $T_L \geq m_{\mathfrak{k}}$ such that $\mu(S(t)) \geq \frac{\mu(S_{\infty})}{2}$ for all $t \geq T_L$, which implies that $x(t) \geq e^{\frac{\mu(S_{\infty})}{2}(t-T_L)}x(T_L)$ for all $t \geq T_L$. On the other hand, a consequence of (17) is that $x(t) + S(t) = x(m_{\mathfrak{k}}) + S(m_{\mathfrak{k}})$ for all $t \geq m_{\mathfrak{k}}$. It follows that $x(t) \leq x(m_{\mathfrak{k}}) + S(m_{\mathfrak{k}})$ for all $t \geq m_{\mathfrak{k}}$. This yields a contradiction.

We conclude that there exists a value $r \geq m_{\mathfrak{k}} - \tau$ such that $S(r) < \bar{S}$.

Next, we establish that for all $t \geq r$, $S(t) < \bar{S}$. From $m_{\mathfrak{k}} \geq 4\mathfrak{T}$ and the inequality $\mathfrak{T} \geq \tau$, it follows that $r \geq 4\mathfrak{T} - \tau \geq 3\mathfrak{T}$.

Now, observe that, we establish in Appendix A the following result

Lemma 1. Let

$$z = S + x. \quad (18)$$

Then, for all $t \geq \mathfrak{T}$, the inequality

$$[D_* - \mu(\bar{S})][S_{in} - \bar{S}] + \mu(\bar{S})[S_{in} - z(t)] < 0 \quad (19)$$

is satisfied.

We deduce from Lemma 1 and from the inequality $r > \mathfrak{T}$ that, for all $t \geq r$, the inequality

$$[D_* - \mu(\bar{S})][S_{in} - \bar{S}] + \mu(\bar{S})[S_{in} - z(t)] < 0 \quad (20)$$

is satisfied. Now, to prove that for all $t \geq r$, $S(t) < \bar{S}$, we proceed by contradiction. We assume that there is $\ell > r$ such that $S(\ell) = \bar{S}$ and, for all $t \in [r, \ell)$, $S(t) < \bar{S}$. Then, using $x = z - S$, we obtain

$$\dot{S}(\ell) = D_f(\ell)[S_{in} - S(\ell)] - \mu(S(\ell))[z(\ell) - S(\ell)].$$

Since $S(\ell) = \bar{S}$, it follows that

$$\dot{S}(\ell) = D_f(\ell)[S_{in} - \bar{S}] - \mu(\bar{S})[z(\ell) - \bar{S}].$$

This equality rewrites as

$$\dot{S}(\ell) = [D_f(\ell) - \mu(\bar{S})][S_{in} - \bar{S}] + \mu(\bar{S})[S_{in} - z(\ell)].$$

Since $S_{in} - \bar{S} > 0$ and $D_f(\ell) \leq D_*$, we deduce that

$$\dot{S}(\ell) \leq [D_* - \mu(\bar{S})][S_{in} - \bar{S}] + \mu(\bar{S})[S_{in} - z(\ell)].$$

Therefore, we deduce from (20) that $\dot{S}(\ell) < 0$. This yields a contradiction with the definition of ℓ .

Therefore we can conclude that, for all $t \geq r$, $S(t) < \bar{S}$.

The next part of the proof is devoted to the proof of the attractivity of the point (S_*, x_*) . To establish this result, we demonstrate first that the variable p goes to $+\infty$. We proceed by contradiction. We assume that p does not go to $+\infty$. Since p is non-decreasing over $[0, +\infty)$, then it converges to a finite value p_{∞} . Then, necessarily, $p_{\infty} > 0$ because, for all $t \geq r$, $S(t) < \bar{S}$, which implies that for all $t \geq 9\mathfrak{T} + r$, $\dot{p}(t) > 0$. Therefore, for all $t \geq 3\mathfrak{T}$,

$$\begin{cases} \dot{S}(t) = \theta(p_{\infty} + q(t))D_*[S_{in} - S(t)] - \mu(S(t))x(t), \\ \dot{x}(t) = [\mu(S(t)) - \theta(p_{\infty} + q(t))D_*]x(t), \end{cases} \quad (21)$$

with $q(t) = p(t_i) - p_{\infty}$ for all $t \in [t_i, t_{i+1})$. It follows that

$$\begin{cases} \dot{z}(t) = \theta(p_{\infty} + q(t))D_*[S_{in} - z(t)], \\ \dot{S}(t) = [\theta(p_{\infty} + q(t))D_* - \mu(S(t))][S_{in} - S(t)] \\ \quad + \mu(S(t))[S_{in} - z(t)]. \end{cases} \quad (22)$$

Since $p_{\infty} > 0$ and $q(t)$ converges to zero when t goes to $+\infty$, it follows that there is a value $t_a > 0$ such that, for all $t \geq t_a$, $\theta(p_{\infty} + q(t)) \in [\theta(\frac{1}{2}p_{\infty}), 1]$. It follows that $S_{in} - z(t)$ converges to zero when t goes to $+\infty$. Therefore the S -subsystem of (22) can be rewritten as

$$\dot{S}(t) = [\theta(p_{\infty})D_* - \mu(S(t))][S_{in} - S(t)] + h(t), \quad (23)$$

where

$$h(t) = [\theta(p_{\infty} + q(t)) - \theta(p_{\infty})]D_*[S_{in} - S(t)] \\ + \mu(S(t))[S_{in} - z(t)] \quad (24)$$

is a function which converges to zero when t goes to $+\infty$. From the definition of D_* and the fact that $\theta(p_{\infty}) \in (0, 1]$, we deduce that there is one and only one constant $S_l \in (0, S_*)$ such that $\mu(S_l) = \theta(p_{\infty})D_*$. Let us consider the Lyapunov function $V(S) = \frac{1}{2}[S - S_l]^2$. Its time derivative along (23) satisfies, for all $t \geq r$,

$$\dot{V}(t) = [S(t) - S_l][\mu(S_l) - \mu(S(t))][S_{in} - S(t)] \\ + [S(t) - S_l]h(t). \quad (25)$$

Since the fact that μ is increasing over $(0, \bar{S})$ ensures that $[S(t) - S_l][\mu(S_l) - \mu(S(t))] \leq 0$, it follows that

$$\dot{V}(t) \leq [S_{in} - \bar{S}][S(t) - S_l][\mu(S_l) - \mu(S(t))] \\ + [S(t) - S_l]h(t). \quad (26)$$

Since $\mu'(S) > 0$ for all $s \in (0, \bar{S})$, it follows that there is a constant $g > 0$ such that, for all $t \geq r$,

$$\dot{V}(t) \leq -g[S(t) - S_l]^2 + [S(t) - S_l]h(t). \quad (27)$$

From the triangle inequality, we deduce that

$$\dot{V}(t) \leq -gV(S(t)) + \frac{1}{2g}h(t)^2. \quad (28)$$

Since $h(t)$ converges to 0 when t goes to $+\infty$, we deduce that $V(S(t))$ converges to zero when t goes to $+\infty$. From this property, we deduce that $S(t)$ converges to $S_l \in (0, S_*)$ when t goes to $+\infty$. From the definition of the function φ , we deduce that there exists $T_a \geq r$ such

that for all $t \geq T_a$, the inequality $\dot{p}(t) \geq \frac{1}{2}$ is satisfied. We obtain a contradiction with the fact that $p(t)$ converges to a finite value.

We conclude that $p(t)$ goes to $+\infty$ when t goes to $+\infty$. Then there exists $T_b > 0$ such that, for all $t \geq T_b$

$$\begin{cases} \dot{S}(t) = D_*[S_{in} - S(t)] - \mu(S(t))x(t), \\ \dot{x}(t) = [\mu(S(t)) - D_*]x(t) \end{cases} \quad (29)$$

and $S(t) < \bar{S}$. Then, arguing as we did to prove the convergence of $S(t)$ to S_l , one can prove that the trajectory $(S(t), x(t))$ converges to (S_*, x_*) . Therefore (S_*, x_*) is globally attractive. In addition, one can easily prove that (S_*, x_*) is a locally exponentially stable equilibrium point of (29) by studying the linear approximation of this system around (S_*, x_*) . We deduce from the definition of global asymptotic stability we have adopted that (S_*, x_*) is a globally asymptotically stable equilibrium point of (1) in closed-loop with (12)-(13).

This concludes the proof.

4. SIMULATIONS

In this section, we illustrate our approach with simulations. The parameters of the chemostat model used in these simulations are given in Figure 1. The corresponding Haldane function is plotted in Figure 1. For the simulations which were performed over 300 time units, the delay in the measurement of S was 2 time units, the sampling period for the measurement was 4 time units while the sampled period for the control was chosen to be 1 time unit. It should be noticed that such values are quite realistic with respect to practical considerations about the dynamics of such a system.

Four simulations are presented. Two of these correspond to initial conditions $x_0 = 30$ and $S_0 = 0$ with or without noise and two other simulations were conducted with initial conditions given by $X_0 = 30$ and $S_0 = 90$. It should be noticed that for any of these initial conditions, the system is unstable in open loop. In all cases, the objective was to stabilize the substrate concentration around the setpoint defined as $S_* = 8$.

The simulations results are presented in Figure 2. Each line corresponds to one simulation with S in the first column, x in the second column and D in the last one. The first line corresponds to the noise free case for the initial condition $x_0 = 30$ and $S_0 = 0$. The second line has the same initial conditions but with a 0.1 noise over signal ratio added on the measurement of S . The last two rows represent simulations for the initial conditions $x_0 = 30$ and $S_0 = 90$. For the first column (the substrate concentration), both the continuous signal and the delayed and sampled one are represented.

$K (t^{-1})$	$g (l^2.mg^{-2})$	$L (mg.l^{-1})$	$S_{in} (mg.l^{-1})$
1.25	0.1111	7.65	100

Table 1. Model parameters

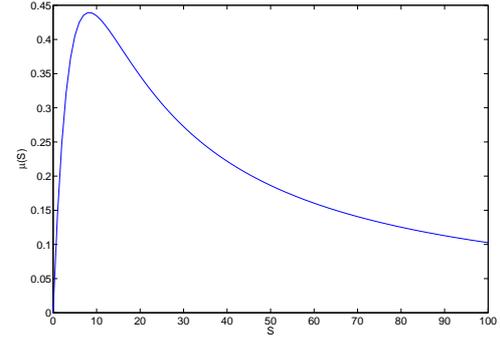


Fig. 1. The Haldane function.

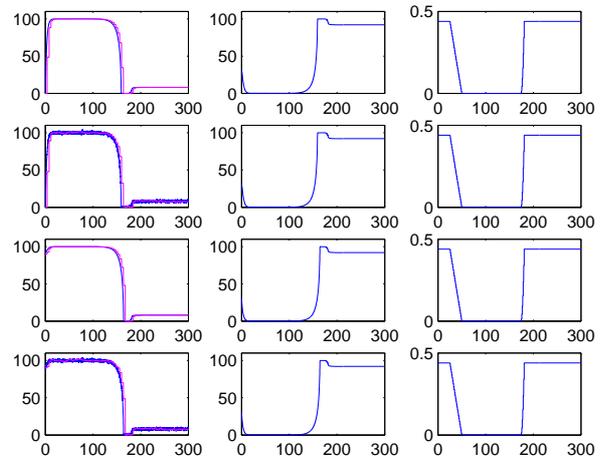


Fig. 2. Four simulations.

5. CONCLUSION

We have solved the problem of rendering globally asymptotically stable positive equilibrium points of a model of chemostat with a growth function of Haldane type, the substrate concentration as output in the case of retarded and sampled control and output. The key idea of the approach consists in the introduction of a dynamic extension which leads to a time-varying dynamic output feedback. Much remains to be done. In particular, the case where several species are present is of interest.

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Appendix A. PROOF OF LEMMA 1

The variable z satisfies

$$\dot{z}(t) = D_f(t)[S_{in} - z(t)], \quad (\text{A.1})$$

for all $t \geq 0$.

Now, we consider a value of t such that $t \in [0, \mathfrak{T}]$. Then, for all integer j such that $t_j \leq t$, the inequality $t_j - \mathfrak{T} \leq 0$ is satisfied. According to the definition of θ , it follows that

$$\dot{z}(t) = D_*[S_{in} - z(t)]. \quad (\text{A.2})$$

It follows that $S_{in} - z(t) = e^{-D_* t}[S_{in} - z(0)] \leq e^{-D_* t} S_{in}$ because $z(0) \geq 0$. Therefore

$$S_{in} - z(\mathfrak{T}) \leq e^{-D_* \mathfrak{T}} S_{in}. \quad (\text{A.3})$$

Now, observe that, for all $t \geq \mathfrak{T}$, the equality

$$S_{in} - z(t) = e^{-\int_{\mathfrak{T}}^t D_f(\ell) d\ell} [S_{in} - z(\mathfrak{T})]$$

is satisfied. This equality, in combination with (A.3), implies that, for all $t \geq \mathfrak{T}$,

$$S_{in} - z(t) \leq e^{-\int_{\mathfrak{T}}^t D_f(\ell) d\ell} e^{-D_* \mathfrak{T}} S_{in} \leq e^{-D_* \mathfrak{T}} S_{in}.$$

From the definition of \mathfrak{T} , it follows that

$$\begin{aligned} S_{in} - z(t) &\leq e^{-\ln\left(\frac{\mu(\bar{S})S_{in}}{[\mu(\bar{S}) - D_*][S_{in} - \bar{S}]}\right)} S_{in} \\ &= \frac{[\mu(\bar{S}) - D_*][S_{in} - \bar{S}]}{\mu(\bar{S})}. \end{aligned}$$

We deduce that, for all $t \geq \mathfrak{T}$,

$$\begin{aligned} [D_* - \mu(\bar{S})][S_{in} - \bar{S}] + \mu(\bar{S})[S_{in} - z(t)] \\ &< [D_* - \mu(\bar{S})][S_{in} - \bar{S}] \\ &+ [\mu(\bar{S}) - D_*][S_{in} - \bar{S}] = 0. \end{aligned} \quad (\text{A.4})$$