NONLINEAR CONTROL FOR ALGAE GROWTH MODELS IN THE CHEMOSTAT

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Abstract

We consider the control problem for a class of biological models of photo-synthetic algae growth in the chemostat. These models are "variable yield" models, on the contrary to classical bioprocess models that are "constant yield" ones. We develop then a nonlinear controller for a wide class of qualitatively known variable yield models and theoretically prove the global asymptotic stability of the resulting set point for the closed loop system. Finally some simulations for *Dunaliella tertiolecta* growth, with realistic parameters, illustrate this proof. Moreover, the controller appears to be robust to noise and algae concentration dynamics does not depend upon feeding nutrient concentration.

1 Introduction

Since Monod did the first model for microorganisms growth in continuous controlled laboratory devices [12], so-called chemostats, it appears that, especially for unicellular photosynthetic algae growth, the "Monod" like models do not fit so well experimental data. Later, Droop proposed a new one [4], taking into account nutrient supply accumulation in the cells, using two steps to model the unicellular algae growth on one limiting nutrient: first ingestion of the nutrient in the cell to make some cell supply, then metabolisation of these supplies by the cell to grow. These Droop like models are often called "variable yield models" [15], on the contrary to Monod like models that are of "constant yield" type.

In a previous work, we exhibited a new nonlinear feedback control for Monod like models, that needs only qualitative hypotheses on the microorganisms' growth rates [9, 10]. This contribution's subject is the study of these kind of non-linear feedback control for variable yield models of algae growth.

This paper is organized as follows: we first present the general variable yield model for unicellular algae growth in chemostats and we make some qualitative hypotheses about the algae's uptake and growth rates. Then we propose the nonlinear controller and prove the global asymptotic stability of the closed loop resulting system. Finally some simulations illustrate our approach.

2 The Variable Yield Model

2.1 The Model

The model variables are the extracellular limiting nutrient concentration (denoted s), the intra-cellular supply of limiting nutrient per unit of biomass (denoted cell quota q) and the biomass (denoted x). The function $\rho(.)$, depending on the extracellular limiting nutrient concentration s, is the uptake rate while the function $\mu(.)$, depending on the cell quota q, is the growth rate of the algae.

$$\begin{cases} \dot{s} = D(s_{in} - s) - \rho(s)x \\ \dot{q} = \rho(s) - \mu(q)q \\ \dot{x} = \mu(q)x - Dx \end{cases} \quad (1)$$

It is well known in biology that the most important problem in modelling these kind of biological phenomena is to give some reasonable expressions for the functions $\rho(.)$ and $\mu(.)$. As in [13], in order to relax this modelling difficulties, we only suppose qualitative hypotheses about these functions.

Hypothesis 1:
$\rho(0) = 0$ and $\rho(.)$ is a $\mathcal{C}^1$, increasing, bounded function of s
$\mu(.)$ is a $\mathcal{C}^1$, non-negative, increasing, bounded function of q
there exists $q_m > 0$ such that $\mu(q_m) = 0$

The qualitative hypotheses (H1) mean that: if there is some extracellular nutrient, then the cell takes it up to make some supplies. The parameter q_m is the minimum cell quota: when q drops below q_m there is insufficient internal nutrient to sustain the cell.

Throughout the paper we will only consider initial conditions for the state variables belonging to the set $\Omega = \{s > 0, q > q_m, x > 0\}$ which only has biological sense. Note that the closure of Ω is invariant by system (1).

In order to exhibit a better form of this system, we use a change of coordinates, so-called "first integral of Burmaster" [3, 13], $z = s + qx$ which represents the total amount of intra-cellular and extracellular limiting nutrient in the chemostat. Then we obtain the following system, which is easier to deal with:

$$\begin{cases} \dot{z} = D(s_{in} - z) \\ \dot{s} = D(s_{in} - s) - \rho(s)x \\ \dot{x} = \mu(\frac{z-s}{x})x - Dx \end{cases} \quad (2)$$

2.2 Behavior of the open loop model

It is well known that the asymptotic behavior of system (1) is of two different types, depending on the value of D compared to s_{in} [15, 8]: either there exists a positive equilibrium point towards each forward positive orbits initiated in Ω goes, either not and every forward orbit goes to the washout point corresponding to the disappearance of the algae from the chemostat (*i.e.* $x = 0$). Here our goal is to control the model in order to prevent the washout of the biomass and to impose the convergence of the state towards a positive equilibrium point. Specifically, we want to drive biomass concentration towards a chosen equilibrium. Moreover, chemostat devices sometimes suffers from uncertainty on the feeding substrate concentration s_{in}, that can destabilize the system so that the algae are washed out of the chemostat. Then it is important to guarantee that the biomass goes towards its chosen equilibrium value, independently from s_{in} variations.

3 Nonlinear Control Design

3.1 Statement of the control framework

Applied control of biological systems generally differs from the theoretical framework of control where it is generally assumed that the model is perfectly known and the state variables are outputs of the system [7]. To control biological systems, we have to take into account first that the model may be not fully or only qualitatively known, and second, that the outputs are not necessarily the full state and may be some qualitatively (badly) known nonlinear functions of the state variables. Moreover, inputs are considered free in classical control theory, whereas they usually fulfill some constraints (*e.g.* positivity) in biological systems.

Due to the high variability of biological phenomena, we consider here a qualitatively known model, qualitative outputs and constrained input and therefore we can not apply classical linearisation techniques (see *e.g.* [5]).

However, we still need to define the manipulated variables, *i.e.* the inputs, and the online available variables, *i.e.* the outputs. In chemostat-like systems, it is well known that the (non-negative) dilution rate D is easy to manipulate, thus we use it as the (constrained) input of the system. Now we define the outputs; here since we aim at applying results in a same way as in [10], and since this approach was based on gaseous measurements related to biomass growth, we suppose that our chemostat is instrumented with sensors that can measure, either the fixed carbon or the produced oxygen by the algae photosynthesis. Note that both of these quantities are proportional to the cells' growth rate and hence we assume that the output $y = \mu(q)x$ is available online from the plant. Note that y is of qualitatively known state function output type. Let us summarize these assumptions in the following hypothesis.

Hypothesis 2:
$D \geq 0$ is a constrained input of system (1)
$y = \mu(q)x$ is an output of the system (1)

3.2 Nonlinear Control Design

Here we will use the output y together with the input D to design a nonlinear controller for system (1). Let us denote by ξ the state vector.

Proposition 1:
Under assumptions (H1) and (H2), the nonlinear control law:

$$D(.) = \gamma y = \gamma \mu(q)x \text{ with } \gamma > \frac{q_m}{s_{in}} \tag{3}$$

globally stabilizes system (1) towards the single "positive" equilibrium $\xi^\star$, determined by the value of the gain γ.

By "positive" equilibrium point we mean that each coordinate of the point is positive. For instance the washout point that corresponds to the disappearance of algae from the chemostat (*i.e.* corresponding to $x = 0$ and $s = s_{in}$) is an equilibrium point of (1), but not a "positive" one. Moreover, note that with expression (3), the input $D(.)$ is non-negative and therefore fulfills its constraint.

Proof:
The control law (3) leads to the following closed loop system:

$$\begin{cases} \dot{z} = D(.)(s_{in} - z) \\ \dot{x} = D(.)(\frac{1}{\gamma} - x) \\ \dot{s} = D(.)(s_{in} - s) - \rho(s)x \end{cases} \tag{4}$$

We first want to show that for the closed loop system (4), both variables z and x converge (asymptotically) to s_{in} and $\frac{1}{\gamma}$ respectively. Therefore we need to prove that the quantity $\int_0^t D(\tau)d\tau$ diverges towards infinity as t tends to infinity. Let us integrate the two first equations of this system, we have:

$$\begin{cases} z(t) = s_{in} + (z(0) - s_{in})e^{-\int_0^t D(\tau)d\tau} \\ x(t) = \frac{1}{\gamma} + (x(0) - \frac{1}{\gamma})e^{-\int_0^t D(\tau)d\tau} \end{cases} \tag{5}$$

Since $D(.)$ is non-negative, it is straightforward that: $e^{-\int_0^t D(\tau)d\tau} \in [0,\ 1]$. Then, we have:

$$\forall t \geq 0 \begin{cases} \max(s_{in}, z(0)) \geq z(t) \geq \min(s_{in}, z(0)) > 0 \\ \max(\frac{1}{\gamma}, x(0)) \geq x(t) \geq \min(\frac{1}{\gamma}, x(0)) > 0 \end{cases} \tag{6}$$

Let us suppose that $\lim_{t\to+\infty} \int_0^t D(\tau)d\tau$ is bounded. Thus a necessary condition is that $\lim_{t\to+\infty} D(t) = 0$. From (6), since γ is positive and x lower bounded by a positive constant, it implies at least that:

$$\lim_{t\to+\infty} q(t) = q_m$$

Since $q(t)$ is a time-Lipschitz function ($\dot{q}$ is bounded) and using Barbalat's lemma [7], we show:

$$\lim_{t\to+\infty} \dot{q} = 0$$

that leads to: $\lim_{t\to+\infty} \rho(s(t)) = 0$ and thus:

$$\lim_{t\to+\infty} s(t) = 0$$

Note that, these points, corresponding to $q = q_m$ and $s = 0$, are equilibria for all values of the variable x. Since x is positively lower bounded, they are defined, for all $x > \min(\frac{1}{\gamma}, x(0))$, by:

$$\xi_u = (s = 0, q = q_m, x)^T$$

Now we want to show that these equilibria are not reachable from initial conditions belonging to the set Ω. To achieve this purpose, let us compute the Jacobian matrix at these equilibrium points, in the $(s, q, x)^T$ variables, we have:

$$\mathcal{J}(\xi_u) = \begin{pmatrix} -\rho'(0)x & \gamma\mu'(q_m)xs_{in} & 0 \\ \rho'(0) & -\mu'(q_m)q_m & 0 \\ 0 & \gamma\mu'(q_m)x(\frac{1}{\gamma} - x) & 0 \end{pmatrix} \quad (7)$$

It is straightforward that one of the eigenvalue is zero, with the associated eigenvector $(0, 0, 1)^T$, which corresponds to the fact that we have a continuum of equilibria that does not depend upon the variable x. Note that the only non zero term of the last line is different from zero, otherwise our proof is over (see equation (5)).

Now let us wonder about the two other eigenvalues. These are the same eigenvalues as the following matrix B:

$$B = \begin{pmatrix} -\rho'(0)x & \gamma\mu'(q_m)xs_{in} \\ \rho'(0) & -\mu'(q_m)q_m \end{pmatrix} \quad (8)$$

Remind that since (H1) hold, $\rho'(0)$ and $\mu'(q_m)$ are positive, then the trace of matrix B is obviously negative. Now we compute the determinant, we have:

$$\det B = \rho'(0)x\mu'(q_m)(q_m - \gamma s_{in})$$

This determinant is negative since $\gamma > \frac{q_m}{s_{in}}$, then there exist a positive real eigenvalue and unfortunately a negative real one. Now we focus only on the stable eigenspace, since the equilibrium points ξ_u can only be reached from this manifold. Hence, we want to show that the stable eigenvector, at ξ_u, does not point from the set Ω towards the point ξ_u, which will prove that ξ_u can not be reached from Ω.

Note that the matrix B is off-diagonal positive and irreducible. Then we apply Perron-Frobenius theorem, in fact the corollary 3.2 from chapter 4 in [14], what shows that the positive eigenvectors are associated only with the largest eigenvalue (here the positive one). Then the stable eigenvector of matrix B is non-positive.

From matrix B, since none of its components is zero, it is straightforward that the stable eigenvector has no zero component and then both components have different signs. Note that these components are the same as the two first components of the stable eigenvector of the Jacobian matrix $\mathcal{J}(\xi_u)$. Then, the stable eigenvector of the Jacobian matrix has no zero components and its first two components are of different signs, which proves that the tangent vector, at ξ_u, of the stable manifold does not point from the set Ω towards the point ξ_u, and therefore that the equilibrium points ξ_u are not reachable from the set Ω. Then $\lim_{t\to+\infty} \int_0^t D(\tau)d\tau$ cannot be bounded, and since $D(.) \geq 0$, we have:

$$\lim_{t\to+\infty} \int_0^t D(\tau)d\tau = +\infty \quad \square \quad (9)$$

Note that equation (9) together with (5) implies that:

$$\begin{cases} \lim_{t\to+\infty} z(t) = s_{in} \\ \lim_{t\to+\infty} x(t) = \frac{1}{\gamma} \end{cases} \quad (10)$$

Then all forward trajectories of system (4), converges towards the set $\mathcal{E} = \{\xi \in \Omega, z = s_{in}, x = \frac{1}{\gamma}, s < s_{in}\}$. Now let us consider the "reduced" system (4), in s, under the constraint $\xi \in \mathcal{E}$, we have:

$$\dot{s} = \mu(\gamma(s_{in} - s))(s_{in} - s) - \frac{\rho(s)}{\gamma} \quad (11)$$

which is equivalent to (see *e.g.*[6]):

$$\dot{s} = \gamma(s_{in} - s)\mu(\gamma(s_{in} - s)) - \rho(s) \quad (12)$$

Since $s \in]0, s_{in}[$, $\gamma > \frac{q_m}{s_{in}}$, and $\mu(.)$ is an increasing function, it is straightforward that $g(\gamma, s) = \gamma(s_{in} - s)\mu(\gamma(s_{in} - s))$ is a decreasing function of s on $]0, s_{in}[$. Note that $g(\gamma, s)$ is an increasing function of γ on $\mathbb{R}_*^+$. This situation corresponds to figure 1, which shows that there exists a single positive equilibrium $s^\star$ for (12) which is globally asymptotically stable on $]0, s_{in}[$. Moreover, note that $s^\star$ increases as γ increases.

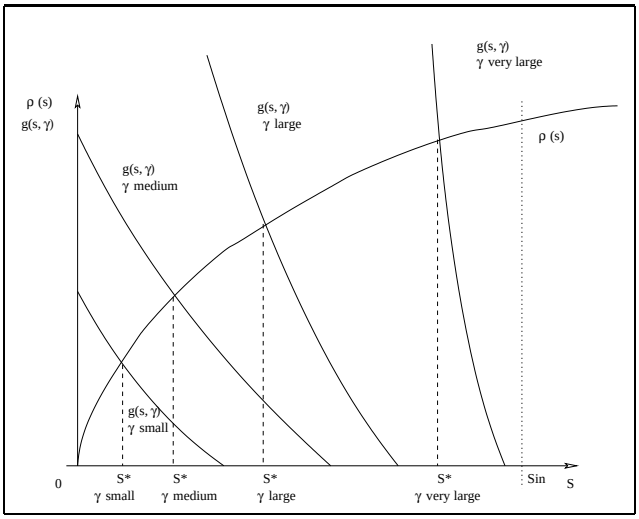

Figure 1: Existence, unicity and stability of $s^\star$ for system (12)

Then it is straightforward that system (4) has a single, positive, equilibrium denoted $\xi^\star = (s_{in}, \frac{1}{\gamma}, s^\star)^T$. Moreover, the choice of the gain γ allows to choose the desired equilibrium point $s^\star \in]0, s_{in}[$.

Now let us come back to system (4) and consider the $\dot{s}$ equation, injecting the solutions $z(t)$ and $x(t)$ initiated at $z(0)$ and

$x(0)$. Then, for each couple of initial conditions $z(0), x(0)$, we obtain the following non-autonomous system:

$$\dot{s} = D\big(s, z(t), x(t)\big)(s_{in} - s) - \rho(s)x(t) \qquad (13)$$

Remark that equation (9) implies that for each couple of initial conditions $z(0), x(0)$, the non-autonomous system (13) is "asymptotically autonomous" (in the sense of [11]) with limit equation (11). Applying corollary 4.3 from [16], we conclude that for each couple of initial conditions $z(0), x(0)$, each forward trajectory of system (13) converges towards the globally asymptotically stable equilibrium point $s^\star$ of the limit equation (11). Thus, for each initial state vector $\xi(0)$, the forward orbit of system (4) converges towards the point $\xi^\star = (s_{in}, \frac{1}{\gamma}, s^\star)^T$. Then we conclude that $\xi^\star$ is globally attractive on $\mathbb{R}^3_{+*}$.

Now let us compute the Jacobian matrix of the closed loop system (4) around the equilibrium point $\xi^\star$ in the $(z, x, s)^T$ coordinates. Remark that this matrix is lower triangular, then we only care about the diagonal terms of this matrix ($\bullet$ will stand for any possible term). We have:

$$\mathcal{J}^\star = \begin{pmatrix} -D(\xi^\star) & 0 & 0 \\ 0 & -D(\xi^\star) & 0 \\ \bullet & \bullet & -D(\xi^\star) - \frac{\partial \rho}{\partial s}(s^\star)\gamma^{-1} \end{pmatrix}$$

Since $\rho(.)$ is an increasing function, γ is positive and $D(\xi^\star) = \mu(\gamma(s_{in} - s^\star))$ is positive, it is straightforward that $\xi^\star$ is locally stable for system 4. Since $\xi^\star$ is globally attractive too, we conclude that $\xi^\star$ is a positive, globally asymptotically stable equilibrium point for the closed loop system (4). □

Remark 1: *Remind that the demonstration is not based on any analytical expression for the "biological" functions $\mu(.)$ and $\rho(.)$ what is particularly important regarding to the difficulty of modelling and identification of these functions.*

Remark 2: *It is important to note that the asymptotic behavior of biomass concentration x does not depend on parameter s_{in}. Then, even for a time varying parameter $s_{in}(t)$, biomass concentration x will asymptotically converge towards $\frac{1}{\gamma}$, provided that for all time $\gamma > \frac{q_m}{s_{in}(t)}$.*

4 Simulations

We consider as an example *Dunaliella tertiolecta* growth; this is a chlorophilian phytoplanktonic green microalga. Then according to [1], the uptake and growth rates are (for all simulations):

$$\rho(s) = \frac{\rho_m s}{k + s} \text{ and } \mu(q) = \max(0, \mu_m(1 - \frac{q_m}{q}))$$

Liters are denoted L, micro grams of nitrogen μg, number of cells c and days d. The parameters are according to [1] (for all the simulations):

ρ_m	k	μ_m	q_m	γ
1.5	0.06	1.6	0.15	0.1
$10^{-6}\mu$g.c^{-1}.d^{-1}	μg.L^{-1}	d^{-1}	$10^{-6}\mu$g.c^{-1}	10^{-6}L.c^{-1}

On figure 2, the parameter s_{in} equals 20 μg.L^{-1}, while on figure 4 s_{in} varies from 5 to 40 μg.L^{-1}. On the figures, extracellular nutrient concentration axis is graduated in μg.L^{-1}, particular nutrient axis in μg.L^{-1}, biomass axis in 10^6cell.L^{-1} and time axis in days.

We show on figure 2 some numerical simulations of the closed loop plant. From biologists' point of view, the control law (3) drives the state variables towards the desired equilibrium determined by the value of the feedback gain γ. Note that the behavior of the closed loop plant is quite simple and agrees with the predicted theoretical behavior.

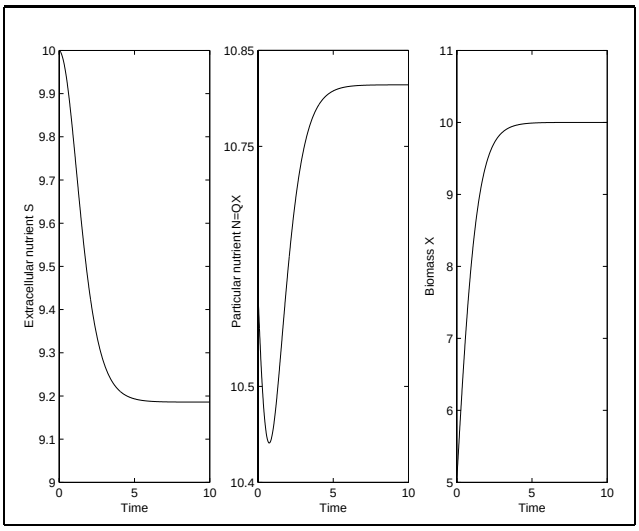

Figure 2: Simulation of the closed loop system; constant s_{in}

On figure 3, we show some noisy simulations: we put a 15% white noise on the output y to check the controller robustness. Results are good, especially for biomass concentration that filters almost all the noise.

Moreover, to illustrate the fact that time variations of influent substrate concentration s_{in} do not change the behavior of the biomass concentration x, we put a piecewise constant time-dependent s_{in}; the results are shown on figure 4. We check that, despite fast and large s_{in} variations, the behavior of the variable x remains the same than with fixed s_{in}: it converges towards its equilibrium $x^\star = \frac{1}{\gamma}$: in both of these simulations we had chosen $\gamma = 0.1$, hence $x^\star = 10$.

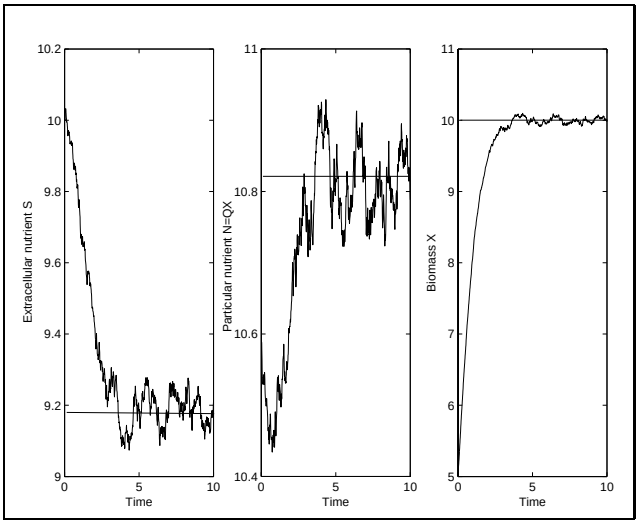

Figure 3: Simulation; constant s_{in}; 15% white noise on y

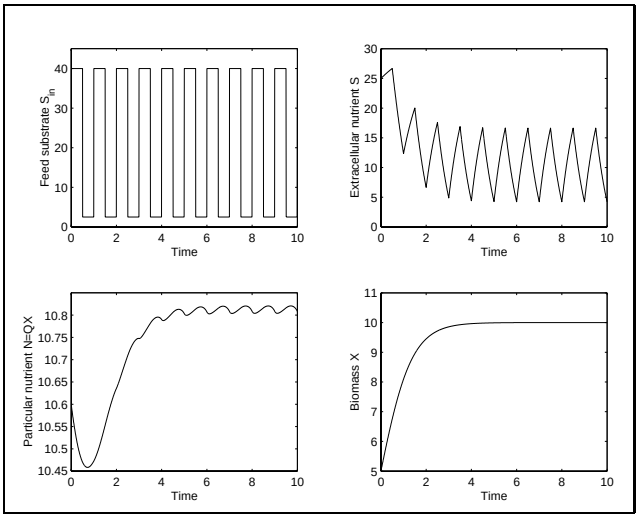

Figure 4: Simulation of the closed loop system; varying $s_{in}(t)$

Finally, from controllers' point of view, note that the only required knowledge from the plant for control is the output y and the feedback gain γ. It ensures (provided that $\gamma > \frac{q_m}{\min_t(s_{in}(t))}$) a very simple behavior for biomass concentration x that goes asymptotically towards $\frac{1}{\gamma}$ like a first order with moving gain, independently from $s_{in}(t)$, even for quick and/or large variations. Of course, since model (1) is not controllable, in the classical sense [7], the other variables change in time as x remains at equilibrium.

5 Conclusions

In this contribution, we have proposed a nonlinear controller able to globally stabilize algae growth biological models in the chemostat. The hypothesis assumed on the model are of qualitative and of structural type, therefore our approach would be suitable for a wide class of variable yield models for microorganisms growth in controlled laboratory devices as bioreactors. Some simulations with realistic parameters for *Dunaliella tertiolecta* growth had been performed and had shown the relevance of our approach. Moreover, the controller appears to be quite robust to noisy output.

A further step in this study could be to manipulate the feeding substrate concentration $s_{in}(t)$ in order to reconstruct a dynamical extracellular concentration signal $s^{\star}(t)$ whereas we keep biomass concentration at a constant level. It should be interesting for instance in the experimental laboratory study of algae meeting various limiting substrate concentrations as in the sea (see *e.g.* [2]).

Of course, this approach is, up to now, mainly theoretical and needs experimental tests to prove its interest in real life phenomena.

Acknowledgements

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