Nonlinear Control of Biotechnological Processes with Growth-Production Decoupling

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ABSTRACT

Nonlinear control design techniques for a class of continuous biological processes with growth and production decoupling are investigated. We establish, under realistic assumptions on the kinetics, that though neither the inlet substrate concentration nor the dilution rate can achieve linearization of the global dynamics, we can maximize the dimension of the linear system obtained after feedback and get stable zero dynamics by choosing output functions having a physical meaning. More precisely, if the manipulated variable is the inlet substrate concentration, then the output can be chosen as the biomass concentration. But if the chosen input is the dilution rate, then a suitable output corresponds to yields.

1. INTRODUCTION

During the last 20 years, theoretical control studies of biotechnological systems have mainly focused on the optimization of fed-batch processes and more precisely on the design of open-loop feeding strategies aiming at maximizing the productivity of reactors. However, as emphasized, for example, by Henson and Seborg [5], once optimal strategies have been determined, feedback control is often required to account for modeling uncertainties and disturbances.

Obviously, feedback control is even more relevant for processes for

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which continuous operation is inherently desirable, especially if they can have unstable steady states due, for instance, to substrate overloading. Typical examples involve biological wastewater treatment processes and continuous production of ethanol (as a benzine substitute).

Our concern in this paper is to examine the applicability of the techniques of partial linearization by feedback and diffeomorphism [8–12] to a class of biotechnological processes in continuous stirred tank reactors, characterized by a decoupling between the biomass growth and the product formation.

The issue of feedback linearizing control of biological reactors has been previously considered in three papers ([6] and [7] by Hoo and Kantor and the recent paper [5] by Henson and Seborg, published as this paper was being reviewed). Our contribution in the present paper (see also [3]–[4]) differs from these previous works on two points:

(1) In [5]–[7], the authors consider specific processes (a fermentation on methanol in [6], a mixed culture with inhibition in [7], and a special case of the biological system (1)–(3) in [5]) where the kinetic expressions are completely defined by given rational functions. In this paper, we present a set of conditions of feedback stabilizability for a large class of systems that require only a qualitative knowledge of the structure of the kinetics but not a prior full specification of the kinetic expressions.

(2) In [6] and [7], the authors restricted their analysis to biological systems that are fully state feedback-linearizable (that is, with zero dynamics restricted to the origin, in the terminology of [9]). In this paper, as in [5], we are concerned with a class of biological systems that are only *partially* feedback-linearizable. However, our purpose differs from that of [5] since we explicitly state the dimension of the largest linearizable subsystem and characterize the output functions that guarantee the maximization of this linearization dimension while preserving the local stability of the zero dynamics.

In Section 2, we present a class of dynamic models of bioreactors with growth–production decoupling, and we state the feedback stabilization problem addressed in the sequel. The local stability of the equilibrium states of these systems is analyzed in Section 3. The existence of structural instability conditions motivates the search for stabilizing feedback controllers. A theoretical review of the problem of partial feedback linearization with local stability is then presented in Section 4. Our main result in Sections 5 and 6 is a characterization of the choice of output functions that ensure both the maximization of the linearizable subsystem and the local stability of the zero dynamics when either substrate concentration or dilution rate is taken as the control input. Two examples are presented in Section 7.

2. PROBLEM STATEMENT

We consider biotechnological processes characterized by a decoupling between biomass growth and product formation. By this, we mean that two different biological reactions basically take place in the reactor, namely a reaction of microbial growth and a reaction of enzymatic synthesis, and that these reactions do *not* proceed at the same rate. In other words, the enzyme-catalyzed formation of the product is *not* associated to the growth.

The dynamics of such processes, in continuous stirred tank bioreactors, are commonly described by a state-space model of the following form:

$$\dot{X} = \mu(X,S,P)X - DX, \tag{1}$$

$$\dot{S} = -\alpha\mu(X,S,P)X - \beta\nu(X,S,P)X - DS + DS_{\text{in}}, \tag{2}$$

$$\dot{P} = \nu(X,S,P)X - DP, \tag{3}$$

where X, S, and P represent the biomass, substrate, and product concentrations, respectively; $\mu(X,S,P)$ and $\nu(X,S,P)$ represent the specific growth and production rates, respectively; $\alpha^{-1} \triangleq Y_{X/S}$ and $\beta^{-1} \triangleq Y_{P/S}$ are the biomass–substrate yield constant and the product–substrate yield constant, respectively; D is the dilution rate; and S_{in} is the influent substrate concentration. Note that in [5] the specific growth rate μ is assumed independent of the biomass X [and is therefore of the form $\mu(S,P)$] and the specific production rate ν is an affine function of the specific growth rate, namely $\nu(S,P) \triangleq \alpha\mu(S,P) + \beta$, with α and β given constants.

The equilibrium states of the system (1)–(3) are of two types, parametrized by the *constant* influent substrate concentration $\bar{S}_{\text{in}}$ and the *constant* dilution rate $\bar{D}$:

- Equilibria (E.1) defined by

$$\bar{X} = 0, \qquad \bar{S} = \bar{S}_{\text{in}}, \qquad \bar{P} = 0; \tag{4}$$

- Equilibria (E.2) implicitly defined by

$$\mu(\bar{X},\bar{S},\bar{P}) = \bar{D}, \tag{5}$$

$$\bar{D}(\bar{S}_{\text{in}} - \bar{S}) = \alpha\mu(\bar{X},\bar{S},\bar{P})\bar{X} + \beta\nu(\bar{X},\bar{S},\bar{P})\bar{X}, \tag{6}$$

$$\bar{D}\bar{P} = \nu(\bar{X},\bar{S},\bar{P})\bar{X}. \tag{7}$$

Straightforward calculations show that both equilibria (E.1) and (E.2) satisfy the relation

$$\alpha\bar{X} + \beta\bar{P} + \bar{S} = \bar{S}_{\text{in}}. \tag{8}$$

We note that (8) is independent of the dilution rate D and the kinetic functions $\mu(X,S,P)$ and $\nu(X,S,P)$.

Equilibria (E.1) correspond to reactor washout. Therefore only equilibria (E.2) are of practical interest. They can be attractive or repulsive, depending on the particular form of the kinetic functions $\mu(X,S,P)$ and $\nu(X,S,P)$, as we shall see in Section 3.

Our concern is to stabilize the system locally around equilibria (E.2) by state feedback. We discuss the design of single-input control laws when either the influent substrate concentration S_{in} (Section 5) or the dilution rate D (Section 6) is the control input.

Our main contributions are to show that

(1) The single-input system is not full state linearizable by feedback and diffeomorphism whatever the structure of the kinetic functions $\mu(X,S,P)$ and $\nu(X,S,P)$ and the choice of input (S_{in} or D).

(2) The largest feedback-linearizable subsystem has dimension 2 whatever the single control input (S_{in} or D).

(3) The maximization of the dimension of the feedback-linearizable subsystem can be achieved with local stabilization of the zero dynamics by a proper choice of the output functions under realistic assumptions on the structure of the kinetic functions.

3. STABILITY OF EQUILIBRIUM STATES

We now analyze the stability of equilibria (E.2) defined by relations (5)–(7) for given constant inputs $\bar{D}$ and $\bar{S}_{\text{in}}$.

We introduce the following functions:

$$\varphi_0(X,S) \triangleq \frac{\bar{S}_{\text{in}} - S - \alpha X}{\beta}, \tag{9}$$

$$\mu_0(X,S) \triangleq \mu(X,S,\varphi_0(X,S)), \tag{10}$$

$$\nu_0(X,S) \triangleq \nu(X,S,\varphi_0(X,S)), \tag{11}$$

$$\gamma_0(X,S) \triangleq \alpha\mu_0(X,S) + \beta\nu_0(X,S). \tag{12}$$

We remark that, according to (8), $\varphi_0(\bar{X},\bar{S}) = \bar{P}$ at any equilibrium point and hence $\mu_0(\bar{X},\bar{S}) = \mu(\bar{X},\bar{S},\bar{P})$ and $\nu_0(\bar{X},\bar{S}) = \nu(\bar{X},\bar{S},\bar{P})$.

The local stability of system (1)–(3) at an equilibrium (E.2) is studied via the eigenvalues of its tangent linear approximation. To facilitate the eigenvalues computation, we introduce the following change of coordinates parametrized by $\bar{S}_{\text{in}}$:

$$\xi = \alpha X + \beta P + S - \bar{S}_{\text{in}} \qquad \text{and}$$

$$\phi(\mathrm{X},\mathrm{S},\xi,\bar{\mathrm{S}}_{in}) = \frac{\xi - \alpha \mathrm{X} - \mathrm{S} + \bar{\mathrm{S}}_{in}}{\beta}.$$

Obviously, we have $P = \phi(X, S, \xi, \bar{S}_{\text{in}})$, and the transformation $(X, S, P) \to (X, S, \xi)$ is a diffeomorphism for every $\bar{S}_{\text{in}}$. In these new coordinates, system (1)–(3) can be rewritten as

$$\dot{X} = \tilde{\mu}(X, S, \xi, \bar{S}_{\text{in}})X - \bar{D}X, \tag{13}$$

$$\dot{S} = -\alpha\tilde{\mu}(X, S, \xi, \bar{S}_{\text{in}})X - \beta\tilde{\nu}(X, S, \xi, \bar{S}_{\text{in}})X - \bar{D}S + \bar{D}\bar{S}_{\text{in}}, \tag{14}$$

$$\dot{\xi} = -\bar{D}\xi, \tag{15}$$

with $\tilde{\mu}(X, S, \xi, \bar{S}_{\text{in}}) = \mu(X, S, \phi(X, S, \xi, \bar{S}_{\text{in}}))$ and $\tilde{\nu}(X, S, \xi, \bar{S}_{\text{in}}) = \nu(X, S, \phi(X, S, \xi, \bar{S}_{\text{in}}))$. An equilibrium (E.2) in these coordinates is thus characterized by $\bar{\xi} = 0$ and $\bar{X}$ and $\bar{S}$ defined as before. Notice that we have $\tilde{\mu}(\bar{X}, \bar{S}, 0, \bar{S}_{\text{in}}) = \mu_0(\bar{X}, \bar{S})$, $\tilde{\nu}(\bar{X}, \bar{S}, 0, \bar{S}_{\text{in}}) = \nu_0(\bar{X}, \bar{S})$.

It is then easily shown that the linear approximation of system (13)–(15) [or equivalently (1)–(3)] around an equilibrium (E.2) has three eigenvalues $\lambda_1, \lambda_2, \lambda_3$ defined by

$$\lambda_1 = -\bar{D}, \tag{16}$$

$$\lambda_2 + \lambda_3 = \frac{\partial\mu_0}{\partial X}\bar{X} - \frac{\partial\gamma_0}{\partial S}\bar{X} - \bar{D} \tag{17}$$

and

$$\lambda_2 \times \lambda_3 = -\bar{D}\bar{X}\frac{\partial\mu_0}{\partial x} + \bar{X}^2\left(\frac{\partial\mu_0}{\partial S}\frac{\partial\gamma_0}{\partial X} - \frac{\partial\mu_0}{\partial X}\frac{\partial\gamma_0}{\partial S}\right) + \bar{D}(\bar{S}_{\text{in}} - \bar{S})\frac{\partial\mu_0}{\partial S}, \tag{18}$$

where all the partial derivatives are evaluated at the equilibrium point. The equilibrium state (E.2) is locally asymptotically stable if and only if $\lambda_2 \times \lambda_3 > 0$ and $\lambda_2 + \lambda_3 < 0$. Otherwise it is repulsive in at least one direction. Furthermore, if $\lambda_2 \times \lambda_3 < 0$, the equilibrium state is a saddle point, while there is a saddle–node bifurcation (with respect to the parameter $\bar{D}$ or $\bar{S}_{\text{in}}$) if $\lambda_2 + \lambda_3 \neq 0$ and $\lambda_2 \times \lambda_3 = 0$.

The fact that the equilibrium state may be unstable, depending on the kinetic structure, motivates the search for stabilizing feedback controllers.

Remark 1. The apparent decoupling between the dynamics of (X, S) and ξ at an equilibrium (E.2) in Equations (13)–(15) fails to hold as soon as S_{in} and D are time-varying functions, namely in the case of interest for control. In the general case, it is straightforward to verify that $\dot{\xi} = -D\xi + D(S_{in} - \bar{S}_{in})$ with D and S_{in} arbitrary time-varying functions. This indicates in particular that system (1)–(3) cannot be simply treated as a two-dimensional system.

4. FEEDBACK LINEARIZATION WITH STABILITY: A THEORETICAL REVIEW

In the subsequent sections of this paper, we address the problem of the local state feedback stabilization of biotechnological systems of the form (1)–(3). This control problem is solved by using a feedback-linearization technique (e.g., [10], [8], [9, chapter 4], or [12, chapter 6]) that is briefly reviewed in the present section.

We consider the class of single-input nonlinear systems of the form

$$\dot{x} = f(x) + g(x)u, \tag{19}$$

where $u \in \mathbb{R}$ is the control input, $x \in \mathbb{R}^n$ is the state vector, and $f(\cdot)$ and $g(\cdot)$ are n-dimensional smooth functions from $\mathbb{R}^n$ to $\mathbb{R}^n$. In the particular case of the biological model (1)–(3), state x is the set of concentrations $x \triangleq (X, S, P)^T$ and the control input may be either the dilution rate $u \triangleq D$ or the influent substrate concentration $u \triangleq S_{in}$.

The problem we address in this paper is that of finding a static state feedback control law of the form

$$u(x) \triangleq \alpha(x) + \beta(x)v, \tag{20}$$

where v is an external reference signal and α and β are smooth in a neighborhood of (E.2), with $\beta(x) \neq 0$ for all x in this neighborhood, such that the closed-loop system obtained by applying (20) to (19),

$$\dot{x} = f(x) + g(x)[\alpha(x) + \beta(x)v], \tag{21}$$

is locally stabilizable around the equilibrium points (E.2).

DEFINITION 1

The nonlinear system (19) *is said to be* partially linearizable *by state feedback* (20) *and diffeomorphism if there exists a smooth change of*

coordinates defined in a neighborhood of an equilibrium point (*E*.2),

$$\begin{pmatrix} z_1 \\ z_2 \end{pmatrix} = \Phi(x) \tag{22}$$

with $\Phi(\cdot)$ *a diffeomorphism such that, in the new coordinates, the closed-loop system* (21) *takes the form*

$$\dot{z}_1 = A_c z_1 + B_c v, \tag{23}$$

$$\dot{z}_2 = a(z_1, z_2) \tag{24}$$

with (A_c, B_c) *a controllable pair.*

Let us recall the definition of the Lie bracket of the vector fields f and g: $[f,g]=(\partial g/\partial x)f-(\partial f/\partial x)g$. The notation $\mathrm{ad}_f g=[f,g]$ is often introduced because it can be used iteratively as $\mathrm{ad}_f^i g=[f,\mathrm{ad}_f^{i-1}g]$, with the convention $\mathrm{ad}_f^0 g = g$. We introduce the distributions

$$Q^0 = \mathrm{Span}\{g\} \tag{25}$$

$$Q^i = \mathrm{Span}\left\{\mathrm{ad}_f^i g, \overline{Q}^{i-1}\right\}, \qquad i \geqslant 1 \tag{26}$$

where $\overline{Q}^k$ denotes the involutive closure of Q^k, that is, the smallest involutive distribution containing Q^k.

THEOREM 1 (Marino [11])

The dimension m of the largest linearizable subsystem is

$$m = \dim Q^{n-1} + \sum_{i=0}^{n-2} \left(\dim Q^i - \dim \overline{Q}^i\right). \tag{27}$$

The proof of this theorem is constructive and provides explicitly the change of coordinates:

$$\begin{pmatrix} z_1 \\ z_2 \end{pmatrix} = \begin{pmatrix} \Phi_1(x) \\ \Phi_2(x) \end{pmatrix}, \tag{28}$$

which allows us to put the system in the form (23), (24). In particular, it can be shown that there exists a smooth scalar function $h(x)$, called the

output function, such that

$$z_1 = \Phi_1(x) = \begin{pmatrix} h(x) \\ L_f h(x) \\ L_f^2 h(x) \\ \vdots \\ L_f^{m-1} h(x) \end{pmatrix}, \tag{29}$$

where the notation $L_f h$ stands for the Lie derivative of the smooth function h from $\mathbb{R}^n$ to $\mathbb{R}$ with respect to f; that is,

$$L_f h(x) = \sum_{i=1}^{n} f_i(x) \frac{\partial h}{\partial x_i}(x),$$

and where $L_f^k h = L_f(L_f^{k-1} h)$ denotes the kth iteration of the Lie derivative of h. The integer m is called the *relative degree* of the system associated to the output $h(x)$.

Once a nonlinear system has been partially linearized by state feedback and diffeomorphism, it is decomposed into two subsystems, (23) and (24). The first subsystem (23) is linear and controllable and can therefore be stabilized by classical methods. The second subsystem is nonlinear, and its stability analysis requires additional developments.

Let an equilibrium point be denoted $(\bar{z}_1, \bar{z}_2)$ in the new coordinates. The dynamics of the nonlinear subsystem (24), with z_1 fixed at its equilibrium value $\bar{z}_1$, are called *zero dynamics*:

$$\dot{z}_2 = a(\bar{z}_1, z_2). \tag{30}$$

The system (23), (24) is then said to have locally asymptotically stable zero dynamics at the equilibrium $(\bar{z}_1, \bar{z}_2)$ if $z_2 = \bar{z}_2$ is an attractive equilibrium point of (30) for every z_1 in a neighborhood of $\bar{z}_1$.

The following fundamental property follows from these definitions.

THEOREM 2 (see, e.g. [9, Chapter 4])

The nonlinear system (19) *is locally stabilizable by static state feedback if it is partially linearizable by state feedback and diffeomorphism with locally asymptotically stable zero dynamics.*

We show in Sections 5 and 6 that Theorems 1 and 2 both hold together for biotechnological systems of the form (1)–(3), that is, there exists a choice of output functions $h(x)$ that maximizes the dimension of the linearizable subsystem with locally asymptotically stable zero dynamics.

5. FEEDBACK STABILIZATION WITH S_{in} AS CONTROL INPUT

We consider the state-space model (1)–(3) of a stirred-tank bioreactor with a constant dilution rate D and the influent substrate concentration S_{in} as control input. Our concern is to stabilize this system at an equilibrium point (E.2) by state feedback.

The system (1)–(3) is in the general form $\dot{x} = f(x) + g(x)u$, with

$$x \triangleq (X, S, P)^T, \qquad u \triangleq S_{in}, \tag{31}$$

$$f(x) \triangleq \begin{pmatrix} [\mu(X,S,P) - D]X \\ -\alpha\mu(X,S,P)X - \beta\nu(X,S,P)X - DS \\ \nu(X,S,P)X - DP \end{pmatrix}, \tag{32}$$

$$g(x) \triangleq \begin{pmatrix} 0 \\ D \\ 0 \end{pmatrix}. \tag{33}$$

For this system, we calculate the distributions Q^i defined by (25), (26). We have

$$Q^0 = \mathrm{Span}\{g\} = \begin{pmatrix} 0 \\ D \\ 0 \end{pmatrix}, \qquad D \text{ constant}, \tag{34}$$

and hence $\dim \overline{Q}^0 = \dim Q^0 = 1$,

$$Q^1 = \mathrm{Span}\{g, \mathrm{ad}_f g\}, \tag{35}$$

with

$$\mathrm{ad}_f g = -D \begin{pmatrix} X\,\partial\mu/\partial S \\ -\alpha X\,\partial\mu/\partial S - \beta X\,\partial\nu/\partial S - D \\ X\,\partial\nu/\partial S \end{pmatrix}. \tag{36}$$

Under the conditions

$$X \neq 0, \qquad \frac{\partial\mu}{\partial S} \neq 0 \quad \text{or} \quad \frac{\partial\nu}{\partial s} \neq 0, \qquad \frac{\partial\mu}{\partial S}\frac{\partial^2\nu}{\partial S^2} \neq \frac{\partial\nu}{\partial S}\frac{\partial^2\mu}{\partial S^2}, \tag{37}$$

it is easily checked that Q^1 is not involutive, that $\dim Q^1 = 2$ and $\dim \overline{Q}^1 = 3$, and consequently that the system is *not* fully state linearizable.

According to Theorem 1, the dimension of the largest linearizable subsystem is thus given by

$$m = \dim Q^2 + \dim Q^1 - \dim \bar{Q}^1 + \dim Q^0 - \dim \bar{Q}^0$$
$$= 3+2-3+1-1=2. \tag{38}$$

From this analysis we have the following result.

Result 1. For the biological system (1)–(3) with the influent substrate concentration S_{in} as control input, if conditions (37) are satisfied, the dimension of the largest feedback-linearizable subsystem is $m = 2$.

The following result then gives conditions for the choice of output functions that maximize the dimension of the linearizable subsystem with *stability* in a neighborhood of the equilibrium point (E.2).

Result 2. Consider the biological system (1)–(3) with the influent substrate concentration S_{in} as control input. Assume that conditions (37) are satisfied in a neighborhood of $(\bar{X}, \bar{S}, \bar{P})$ defined by (E.2). Then

- If

$$\frac{\partial \mu}{\partial S}(\bar{X}, \bar{S}, \bar{P}) \neq 0, \qquad \left[\frac{\partial \nu}{\partial P} - \left(\frac{\partial \mu}{\partial S}\right)^{-1} \frac{\partial \mu}{\partial P} \frac{\partial \nu}{\partial S}\right](\bar{X}, \bar{S}, \bar{P}) < \frac{\bar{D}}{\bar{X}} \tag{39}$$

and the output function is selected as $h(X, S, P) \triangleq X$,

- Or if at the point $(\bar{X}, \bar{S}, \bar{P})$,

$$\frac{\partial \nu}{\partial S}(\bar{X}, \bar{S}, \bar{P}) \neq 0, \qquad \left[\left(\frac{\partial \nu}{\partial S}\right)^{-1} \frac{\partial \mu}{\partial S}\left(\nu + \bar{X}\frac{\partial \nu}{\partial \bar{X}}\right) - \bar{X}\frac{\partial \mu}{\partial \bar{X}}\right](\bar{X}, \bar{S}, \bar{P}) > 0 \tag{40}$$

and the output function is selected as $h(X, S, P) \triangleq P$,

then the system has relative degree 2 with locally asymptotically stable zero dynamics at the equilibrium $(\bar{X}, \bar{S}, \bar{P})$.

The proof of this result is given in Appendix B. Let us just mention that we use a property presented in [1], namely, the fact that the local stability of the zero dynamics is related to the stability of the zeros of the linear approximation of the system at the equilibrium point.

With Result 2, we have shown that the feedback stabilization of a biological reactor with growth–production decoupling can be achieved by the regulation of the biomass X or the product P concentrations. The choice of the output to be regulated (X or P) depends on the

structure of the rate functions $\mu(X,S,P)$ and $\nu(X,S,P)$. For example, condition (39) is satisfied if μ and ν do not depend on P in a neighborhood of (E.2), and, symmetrically, condition (40) holds if, for example, μ and ν do not depend on X in a neighborhood of (E.2).

We conclude this section by giving the expressions of the change of coordinates (diffeomorphism) and the state feedback leading to the system with relative degree 2 and locally asymptotically stable zero dynamics in both situations.

For $h(X,S,P) \triangleq X$, the change of coordinates is

$$\xi_1 = X - X^*, \tag{41}$$

$$\xi_2 = \left[\mu(X,S,P) - \bar{D}\right]X, \tag{42}$$

$$\xi_3 = P, \tag{43}$$

where X^* denotes the *set point* of the biomass concentration.

The condition $\partial\mu/\partial S \neq 0$ of (39) implies that this change of coordinates is a diffeomorphism. The inverse transformation can be written

$$X = \xi_1 + X^*, \tag{44}$$

$$S = \sigma(\xi_1, \xi_2, \xi_3), \tag{45}$$

$$P = \xi_3, \tag{46}$$

with the function σ, a solution of the implicit equation

$$\xi_2 - \left[\mu(\xi_1 + X^*, \sigma(\xi_1, \xi_2, \xi_3), \xi_3) - \bar{D}\right](\xi_1 + X^*) = 0.$$

The state feedback is given by

$$S_{\text{in}} = \frac{-L_f^2 h}{L_g L_f h} + \frac{1}{L_g L_f h} v \tag{47}$$

with

$$L_g L_f h = \bar{D} X \frac{\partial \mu}{\partial S},$$

$$L_f^2 h = X^2(\mu - \bar{D})\frac{\partial \mu}{\partial X} - X(X\gamma + \bar{D}S)\frac{\partial \mu}{\partial S} + X(\nu X - \bar{D}P)\frac{\partial \mu}{\partial P} + X(\mu - \bar{D})^2$$

and with

$$v \triangleq -k_1 \xi_1 - k_2 \xi_2, \qquad k_1, k_2 > 0.$$

If the control law (47) is applied to the biological system (1)–(3), the resulting closed loop is governed by the following equations in the new coordinates ξ_1, ξ_2, ξ_3:

$$\dot{\xi}_1 = \xi_2, \tag{48}$$

$$\dot{\xi}_2 = -k_1 \xi_1 - k_2 \xi_2, \tag{49}$$

$$\dot{\xi}_3 = \nu_0(\xi_1, \xi_2, \xi_3)(\xi_1 + X^*) - \bar{D}\xi_3, \tag{50}$$

where $\nu_0(\xi_1, \xi_2, \xi_3) \triangleq \nu(\xi_1 + X^*, \sigma(\xi_1, \xi_2, \xi_3), \xi_3)$. We note that the control signal v is chosen in order to place the poles of the linear second-order subsystem (48), (49). We have $\xi_1 = 0$, that is, $X = X^*$, and $\xi_2 = 0$ at the equilibrium point of the closed loop. The corresponding zero dynamics, which are therefore written as

$$\dot{\xi}_3 = \nu_0(0,0,\xi_3) X^* - \bar{D}\xi_3,$$

are proved to be stable in Appendix B.

For $h(X,S,P) \triangleq P$, the change of coordinates is $\xi_1 = P - P^*$, $\xi_2 = \nu X - \bar{D}P$, $\xi_3 = X$. The state feedback is again given by (47) with $L_g L_f h = \bar{D}X \partial \nu / \partial S$ and

$$L_f^2 h = X(\mu - \bar{D})\left(\nu + X\frac{\partial \nu}{\partial X}\right) - X(\gamma X + \bar{D}S)\frac{\partial \nu}{\partial S}$$

$$+ \left(X\frac{\partial \nu}{\partial P} - \bar{D}\right)(\nu X - \bar{D}P).$$

The analysis follows the same lines as before.

6. FEEDBACK STABILIZATION WITH D AS CONTROL INPUT

We consider the state-space model (1)–(3) of a stirred-tank bioreactor with a constant influent substrate concentration $\bar{S}_{in}$ and the dilution rate D as control input. Our concern is again to stabilize this system locally around an equilibrium point (E.2) by state feedback.

The system (1)–(3) is in the general form $\dot{x} = f(x) + g(x)u$ with the following definitions:

$$x \triangleq (X, S, P)^T, \qquad u \triangleq D, \tag{51}$$

$$f(x) \triangleq \begin{pmatrix} \mu(X,S,P)X \\ -\alpha\mu(X,S,P)X - \beta\nu(X,S,P)X \\ \nu(X,S,P)X \end{pmatrix}, \tag{52}$$

$$g(x) \triangleq \begin{pmatrix} -X \\ \bar{S}_{\text{in}} - S \\ -P \end{pmatrix}. \tag{53}$$

We first calculate the linear approximation of the system around an equilibrium point (E.2). It is represented by the linear system

$$\dot{x} = Fx + Gd, \tag{54}$$

with $d = D - \bar{D}$, $x \triangleq (X - \bar{X}, S - \bar{S}, P - \bar{P})^T$, and

$$F \triangleq \begin{pmatrix} \frac{\partial\mu}{\partial X}\bar{X} & \bar{X}\frac{\partial\mu}{\partial S} & \bar{X}\frac{\partial\mu}{\partial P} \\ -\bar{X}\frac{\partial\gamma}{\partial X} - \gamma & -\bar{X}\frac{\partial\gamma}{\partial S} - \bar{D} & -\bar{X}\frac{\partial\gamma}{\partial P} \\ \frac{\partial\nu}{\partial X}\bar{X} + \nu & \bar{X}\frac{\partial\nu}{\partial S} & \bar{X}\frac{\partial\nu}{\partial P} - \bar{D} \end{pmatrix}, \tag{55}$$

where $\gamma(X,S,P) = \alpha\mu(X,S,P) + \beta\nu(X,S,P)$ and

$$G \triangleq \begin{pmatrix} -\bar{X} \\ \bar{S}_{\text{in}} - \bar{S} \\ -\bar{P} \end{pmatrix}. \tag{56}$$

Linear system (54) is not controllable. Indeed, using relation (8) satisfied by equilibria (E.2), it is straightforward to verify that $\det(G, FG, F^2G) = 0$ and $\text{rk}(G, FG, F^2G) = 2$. This implies that the biological model (1)–(3) is not fully state linearizable with D as control input and that the largest linearizable subsystem has dimension $m = 2$ (see, e.g., [9, chapter 4, remarks 2.7 and 2.8]).

The following result then gives conditions for the choice of output functions that maximize the dimension of the linearizable subsystem with local stability.

Result 3. Consider the biological system (1)–(3) with the dilution rate D as control input.

- If the rate functions μ and ν are independent of P and the output function is selected as

$$h(X,S,P) \triangleq \frac{X}{S-\bar{S}_{\text{in}}}$$

- Or if the rate functions μ and ν are independent of X and the output function is selected as

$$h(X,S,P) \triangleq \frac{X}{P},$$

then the system has relative degree 2 and is partially state feedback-linearizable with locally asymptotically stable zero dynamics.

The proof of this result is given in Appendix C. We just mention that the two above output functions are found by solving the first-order partial differential equation $L_g h = 0$ (which ensures that the control input does not appear directly in the output and in its first derivative with respect to time), that is,

$$X\frac{\partial h}{\partial X} + (S-\bar{S}_{\text{in}})\frac{\partial h}{\partial S} + P\frac{\partial h}{\partial P} = 0. \tag{57}$$

Obviously, $h = X/(S-\bar{S}_{\text{in}})$ and $h = X/P$ are two independent solutions of this partial differential equation. When $h = X/(S-\bar{S}_{\text{in}})$, the change of coordinates is selected as

$$\xi_1 = X/(S-\bar{S}_{\text{in}}), \tag{58}$$

$$\xi_2 = \mu(X,S)\frac{X}{S-\bar{S}_{\text{in}}} + [\alpha\mu(X,S) + \beta\nu(X,S)]\left(\frac{X}{S-\bar{S}_{\text{in}}}\right)^2, \tag{59}$$

$$\xi_3 = X/P, \tag{60}$$

and the state feedback is given by

$$D = \frac{-L_f^2 h}{L_g L_f h} + \frac{1}{L_g L_f h}v \tag{61}$$

with

$$L_g L_f h = \xi_1 L_g \mu + \xi_1^2 (\alpha L_g \mu + \beta L_g \nu),$$
$$L_f^2 h = \xi_1 (\mu^2 + L_f \mu) + \xi_1^2 [3\mu(\alpha\mu + \beta\nu) + (\alpha L_f \mu + \beta L_f \nu)] + 2(\alpha\mu + \beta\nu)^2 \xi_1^3.$$

When $h = X/P$, the change of coordinates is selected as

$$\xi_1 = X/P, \tag{62}$$

$$\xi_2 = \mu(S,P)\frac{X}{P} - \nu(S,P)\frac{X^2}{P^2}, \tag{63}$$

$$\xi_3 = X/(S - \bar{S}_{\text{in}}), \tag{64}$$

and the derivation of the state feedback follows the same lines as above.

7. EXAMPLES

To illustrate the foregoing theory, we now apply the results of Section 5 to two specific examples.

7.1. *EXAMPLE* 1

We consider the state-space model (1)–(3) of a stirred-tank bioreactor with a constant dilution rate and the influent substrate concentration S_{in} as control input. We assume that the specific growth rate is represented by a Contois model,

$$\mu(X,S) = \mu^* S/(K_1 X + S)$$

and the specific growth rate by a model with inhibition by the product

$$\nu(S,P) = \nu^* S/(K_2 + P).$$

The various derivatives needed for the analysis are calculated as follows:

$$\frac{\partial\mu}{\partial X} = -\frac{\mu^* K_1 S}{(K_1 X + S)^2}, \qquad \frac{\partial\mu}{\partial S} = \frac{\mu^* K_1 X}{(K_1 X + S)^2}, \qquad \frac{\partial\mu}{\partial P} = 0,$$

$$\frac{\partial\nu}{\partial X} = 0, \qquad \frac{\partial\nu}{\partial S} = \frac{\nu^*}{K_2 + P}, \qquad \frac{\partial\nu}{\partial P} = -\frac{\nu^* S}{(K_2 + P)^2},$$

$$\frac{\partial^2\mu}{\partial S^2} = -\frac{2K_1 S X}{(K_1 X + S)^3}, \qquad \frac{\partial^2\nu}{\partial S^2} = 0.$$

We immediately observe that conditions (37) are satisfied everywhere in the region of interest (that is, for all $X > 0$, $S > 0$, $P > 0$).

Furthermore, condition (39) is satisfied, since

$$\frac{\partial \mu}{\partial S} - \frac{\mu^* K_1 \bar{X}}{\left(K_1 \bar{X} + \bar{S}\right)^2} \neq 0$$

and

$$\left[\frac{\partial \nu}{\partial P} - \left(\frac{\partial \mu}{\partial S}\right)^{-1} \frac{\partial \mu}{\partial P} \frac{\partial \nu}{\partial S}\right] = -\frac{\nu^* \bar{S}}{\left(K_2 + \bar{P}\right)^2} < 0.$$

We can thus select X as an output function to stabilize the process at any equilibrium point. Moreover, condition (40) is also satisfied, since

$$\frac{\partial \nu}{\partial S} = \frac{\nu^*}{K_2 + \bar{P}} \neq 0$$

and

$$\left[\left(\frac{\partial \nu}{\partial S}\right)^{-1} \frac{\partial \mu}{\partial S}\left(\nu + \bar{X}\frac{\partial \nu}{\partial X}\right) - \bar{X}\frac{\partial \mu}{\partial X}\right] = \frac{2\mu^* K_1 \bar{X}\bar{S}}{\left(K_1 \bar{X} + \bar{S}\right)^2} > 0.$$

We can thus also select P as an output function to stabilize the process at any equilibrium point.

7.2. *EXAMPLE* 2

We now slightly modify the previous example by adding substrate inhibition in the specific growth rate,

$$\mu(X, S) = \mu^* S / \left(K_1 X + S^2\right),$$

and keeping the same model of the specific production rate.

This example is of interest because with these reaction models the system may now be *unstable* in an open loop. Indeed, it is easy to show that the equilibria $(\bar{X}, \bar{S}, \bar{P})$ that satisfy the inequality

$$\bar{S}^2 \geqslant K_1 \bar{X}$$

are unstable.

The partial derivatives of μ are modified as follows:

$$\frac{\partial \mu}{\partial X} = -\frac{\mu^* K_1 S}{\left(K_1 X + S^2\right)^2}, \qquad \frac{\partial \mu}{\partial S} = \frac{\mu^*\left(K_1 X - S^2\right)}{\left(K_1 X + S\right)^2}, \qquad \frac{\partial \mu}{\partial P} = 0,$$

$$\frac{\partial^2 \mu}{\partial S^2} = -\frac{2\mu^* S\left(3S^2 - K_1 X\right)}{\left(K_1 X + S^2\right)^3}.$$

Conditions (37) are satisfied everywhere in the state-space except at the single point

$$\bar{S}^2 = K_1 \bar{X}/3.$$

We observe that this equilibrium point is stable in an open loop. If our concern is primarily to stabilize the unstable equilibria of the process by feedback, it is clear that this singularity can be ignored in the analysis.

Condition (39) is expressed as

$$\bar{S}^2 \neq K_1 \bar{X} \qquad \text{and} \qquad -\frac{\nu^* \bar{S}}{\left(K_2 + \bar{P}\right)^2} < \frac{\bar{D}}{\bar{X}}.$$

It follows that X can be selected as an output function to stabilize all the unstable equilibria except those that satisfy the condition $\bar{S}^2 = K_1 \bar{X}$.

Moreover, condition (40) is expressed as

$$\frac{\mu^* \bar{S}\left(2K_1 \bar{X} - \bar{S}^2\right)}{\left(K_1 \bar{X} + \bar{S}^2\right)^2} > 0.$$

It follows that P can be selected as an output function for all the unstable equilibria that satisfy

$$\bar{S}^2 < 2K_1 \bar{X}.$$

Consequently, all the unstable equilibria of the process can be stabilized by feedback, provided that the output functions are selected according to Table 1.

TABLE 1

Stabilizing Output Functions

Unstable equilibria	Stablilizing output function
$K_1 \bar{X} \leqslant \bar{S}^2 < 2K_1 \bar{X}$	P
$K_1 \bar{X} < \bar{S}^2$	X

8. SOME FINAL COMMENTS

We have discussed in this paper the single-input control of a class of biological systems with growth–production decoupling when either the influent substrate concentration S_{in} or the dilution rate D is the control input.

In both cases, we have shown that the maximization of the dimension of the feedback-linearizable subsystem can be achieved with local asymptotic stabilization of the zero dynamics under simple structural conditions.

It is worth noting that these conditions on the structure of the rate functions are very realistic and are satisfied in most models available in the literature for this kind of application. In particular, we have shown that the local feedback stabilization is guaranteed in various instances summarized in Table 2.

Moreover, the output functions have a clear physical meaning. When S_{in} is the control input, the local feedback stabilization is obtained through the regulation of the biomass X or the product P concentrations; when D is the control input, the local feedback stabilization is obtained by the regulation of the biomass/substrate or biomass/product yield ratios of the process.

We note also that a trivial consequence of our results is that the system is fully state feedback linearizable in the multivariable case with two control inputs D and S_{in}.

There are, however, important limitations to these techniques:

- The expression of the linearizing feedback explicitly depends on the rate functions μ and ν, and the potential modeling uncertainties have to be compensated by an appropriate choice of the poles of the linear closed-loop system, according to robustness considerations.
- The presence of zero dynamics makes the stability analysis around arbitrary time-varying reference trajectories very difficult, and, even around an equilibrium point, global stability of the closed-loop system is not guaranteed.

TABLE 2

Choice of Output Function for Guaranteed Stabilization

Control input	Rate functions μ and ν independent of	Output function
S_{in}	P	X
	X (if furthermore $\partial\mu/\partial S$ or $\partial\nu/\partial S > 0$)	P
D	P	$X/S - \bar{S}_{in}$
	X	X/P

- A real-time knowledge of the state is needed to implement the feedback control law, which often requires the use of an observer when the state is not directly measured (see, e.g., [2]). Such an observer may degrade the overall performance of the feedback.

The importance of these limitations can be studied on simulations in practical applications.

APPENDIX A: Lie Brackets and Distributions of Vector Fields

Let f be a smooth vector field on $\mathbb{R}^n$ and h a smooth function from $\mathbb{R}^n$ to $\mathbb{R}$. The *Lie derivative of h with respect to f*, denoted by $L_f h$, is defined by

$$L_f h(x) = \frac{d}{dt} h(x(t))|_{t=0},$$

where $x(t)$ is the solution of the differential equation $\dot{x}(t) = f(x(t))$ starting from $x(0) = x$ at time $t = 0$. If $f = (f_1, \ldots, f_n)^T$ is given in local coordinates, it is easily checked that

$$L_f h(x) = \sum_{i=1}^{n} f_i(x) \frac{\partial h}{\partial x_i}(x).$$

Note that this relation implies that every vector field f is associated in a one-to-one way to the first-order differential operator

$$L_f = \sum_{i=1}^{n} f_i \frac{\partial}{\partial x_i}.$$

Given two smooth vector fields f and g on $\mathbb{R}^n$, one defines a new vector field, called the *Lie bracket of f and g* and denoted $[f, g]$, by the formula

$$L_{[f,g]} h = L_f L_g h - L_g L_f h$$

for every smooth function h from $\mathbb{R}^n$ to $\mathbb{R}$. It can be easily checked that, in local coordinates,

$$[f, g] = \frac{\partial g}{\partial x} f - \frac{\partial f}{\partial x} g.$$

The notation $\mathrm{ad}_f g = [f, g]$ is often adopted because it can be used iteratively as follows: $\mathrm{ad}_f^i g = [f, \mathrm{ad}_f^{i-1} g]$ for every $i \geqslant 1$, with the convention $\mathrm{ad}_f^0 g = g$.

A *distribution of vector fields* Q is a mapping from $\mathbb{R}^n$ to its tangent space for which every x of $\mathbb{R}^n$ is associated to $Q(x)$, a linear subspace of the tangent space of $\mathbb{R}^n$. A distribution is called *smooth with constant rank k* if there exist k smooth independent vector fields $g_1,\ldots,g_k$ that locally generate Q, namely, $Q(x) = \text{Span}\{g_1(x),\ldots,g_k(x)\}$ for every x in a given open subset of $\mathbb{R}^n$. A distribution Q is called *involutive* if the Lie bracket of two arbitrary vector fields of Q is an element of Q. In other words, Q is involutive if and only if $[Q,Q] \subset Q$. If, on the contrary, Q is not involutive, one can define its *involutive closure*, denoted $\overline{Q}$, as the smallest involutive distribution containing Q. The involutive closure of an arbitrary distribution Q necessarily exists, because Q is a subset of the tangent space $T\mathbb{R}^n$ of $\mathbb{R}^n$, which is involutive by definition.

APPENDIX B: Proof of Result 2

By linearizing the open-loop nonlinear system (1)–(3) around the equilibrium (E.2) with S_{in} as control input, we obtain the linearized system,

$$\dot{x} = Fx + Gs_{\text{in}}, \tag{65}$$

with $s_{\text{in}} = S_{\text{in}} - \overline{S}_{\text{in}}$,

$$x = \begin{pmatrix} X - \overline{X} \\ S - \overline{S} \\ P - \overline{P} \end{pmatrix}, \tag{66}$$

$$F \triangleq \begin{pmatrix} \dfrac{\partial \mu}{\partial X}\overline{X} & \overline{X}\dfrac{\partial \mu}{\partial S} & \overline{X}\dfrac{\partial \mu}{\partial P} \\ -\overline{X}\dfrac{\partial \gamma}{\partial X} - \gamma & -\overline{X}\dfrac{\partial \gamma}{\partial S} - \overline{D} & -\overline{X}\dfrac{\partial \gamma}{\partial P} \\ \dfrac{\partial \nu}{\partial X}\overline{X} + \nu & \overline{X}\dfrac{\partial \nu}{\partial S} & \overline{X}\dfrac{\partial \nu}{\partial P} - \overline{D} \end{pmatrix}, \tag{67}$$

and

$$G = \begin{pmatrix} 0 \\ \overline{D} \\ 0 \end{pmatrix}. \tag{68}$$

We recall that $\gamma(X,S,P) = \alpha\mu(X,S,P) + \beta\nu(X,S,P)$ in matrix F above and that all partial derivatives appearing in F are evaluated at the equilibrium point $(\overline{X},\overline{S},\overline{P})$.

Standard computations show that the pair (F,G) is controllable. In fact,

$$\det(G,FG,F^2G) = \bar{D}^3\bar{X}^2\left\{\bar{X}\frac{\partial\nu}{\partial S}\left(\frac{\partial\mu}{\partial X}\frac{\partial\mu}{\partial S}+\frac{\partial\mu}{\partial P}\frac{\partial\nu}{\partial S}\right)\right.$$
$$\left.-\frac{\partial\mu}{\partial S}\left[\left(\frac{\partial\mu}{\partial S}\frac{\partial\nu}{\partial X}+\frac{\partial\nu}{\partial S}\frac{\partial\nu}{\partial P}\right)\bar{X}+\nu\frac{\partial\mu}{\partial S}-\mu\frac{\partial\nu}{\partial S}\right]\right\} \quad (69)$$

is nonzero in a neighborhood of (E.2). Hence we can use the property presented in [1], namely the fact that the eigenvalues of the gradient of the zero dynamics at an equilibrium point are the finite linear zeros of the linearized system, in order to find the output functions $h(X,S,P)$ leading to local stability.

We are looking for a function $h(X,S,P)$ such that for the transfer function

$$H(sI-F)^{-1}G = \frac{R(s)}{\det(sI-F)} \quad (70)$$

with

$$H = \left(\frac{\partial h}{\partial X},\frac{\partial h}{\partial S},\frac{\partial h}{\partial P}\right) = (h_1,h_2,h_3), \quad (71)$$

the polynomial $R(s)$ (s denoting the Laplace complex variable as usual) has all its roots in the left half of the complex plane.

This polynomial is expressed as

$$R(s) = h_2s^2+\left[h_1\bar{X}\frac{\partial\mu}{\partial S}+h_2\left(\bar{D}-\bar{X}\frac{\partial\nu}{\partial P}-\bar{X}\frac{\partial\mu}{\partial\bar{X}}\right)+h_3\bar{X}\frac{\partial\nu}{\partial S}\right]s$$
$$+h_1\left[\bar{X}\bar{D}\frac{\partial\mu}{\partial S}+\bar{X}^2\left(\frac{\partial\mu}{\partial P}\frac{\partial\nu}{\partial S}-\frac{\partial\mu}{\partial S}\frac{\partial\nu}{\partial P}\right)\right]+h_2\left[-\bar{D}\bar{X}\frac{\partial\mu}{\partial\bar{X}}\right.$$
$$\left.+\bar{X}^2\left(\frac{\partial\mu}{\partial\bar{X}}\frac{\partial\nu}{\partial P}-\frac{\partial\mu}{\partial P}\frac{\partial\nu}{\partial\bar{X}}\right)\right]+h_3\left[\bar{X}^2\left(\frac{\partial\mu}{\partial S}\frac{\partial\nu}{\partial X}-\frac{\partial\mu}{\partial X}\frac{\partial\nu}{\partial S}\right)+\bar{X}_\nu\frac{\partial\mu}{\partial S}\right], \quad (72)$$

where the partial derivatives of μ and ν are evaluated at (E.2).

For $h(X,S,P)=X$, we have $H=(h_1,h_2,h_3)=(1,0,0)$ and

$$R(s) = \bar{X}\frac{\partial\mu}{\partial S}s+\bar{X}\bar{D}\frac{\partial\mu}{\partial S}+\bar{X}^2\left(\frac{\partial\mu}{\partial P}\frac{\partial\nu}{\partial S}-\frac{\partial\mu}{\partial S}\frac{\partial\nu}{\partial P}\right). \quad (73)$$

The single root of $R(s)$ is given by

$$s = -\left(\frac{\partial \mu}{\partial \bar{S}}\right)^{-1}\left[\bar{D}\frac{\partial \mu}{\partial \bar{S}} + \bar{X}\left(\frac{\partial \mu}{\partial P}\frac{\partial \nu}{\partial \bar{S}} - \frac{\partial \mu}{\partial \bar{S}}\frac{\partial \nu}{\partial P}\right)\right], \tag{74}$$

and condition (39) follows.

For $h(X,S,P) = P$, we have $H = (h_1, h_2, h_3) = (0,0,1)$ and

$$R(s) = \bar{X}\frac{\partial \nu}{\partial \bar{S}}s + \left[\bar{X}^2\left(\frac{\partial \mu}{\partial \bar{S}}\frac{\partial \nu}{\partial \bar{X}} - \frac{\partial \mu}{\partial \bar{X}}\frac{\partial \nu}{\partial \bar{S}}\right) + \bar{X}\nu\frac{\partial \mu}{\partial \bar{S}}\right]. \tag{75}$$

The single root of $R(s)$ is given by

$$s = -\left(\frac{\partial \nu}{\partial \bar{S}}\right)^{-1}\left[\nu\frac{\partial \mu}{\partial \bar{S}} + \bar{X}\left(\frac{\partial \mu}{\partial \bar{S}}\frac{\partial \nu}{\partial \bar{X}} - \frac{\partial \mu}{\partial \bar{X}}\frac{\partial \nu}{\partial \bar{S}}\right)\right], \tag{76}$$

and condition (40) follows.

APPENDIX C: Proof of Result 3

For $h(X,S,P) \triangleq X/(S - \bar{S}_{\text{in}})$, we assume that the rate functions μ and ν are independent of P, and we consider the following change of coordinates:

$$\xi_1 = X/\left(S - \bar{S}_{\text{in}}\right),$$

$$\xi_2 = \mu(X,S)\frac{X}{S - \bar{S}_{\text{in}}} + \left[\alpha\mu(X,S) + \beta\nu(X,S)\right]\left(\frac{X}{S - \bar{S}_{\text{in}}}\right)^2,$$

$$\xi_3 = X/P.$$

This transformation is a diffeomorphism provided that the following inequality holds in a neighborhood of the equilibrium point:

$$\left(1 + \alpha\frac{X}{S - \bar{S}_{\text{in}}}\right)L_g\,\mu(X,S) + \beta\frac{X}{S - \bar{S}_{\text{in}}}L_g\,\nu(X,S) \neq 0,$$

where g is the input vector field (53).

The inverse transformation of coordinates may be written as

$$X = \phi_1(\xi_1, \xi_2), \qquad S = \phi_2(\xi_1, \xi_2), \qquad P = \frac{\phi_1(\xi_1, \xi_2)}{\xi_3}$$

with appropriate definitions of ϕ_1 and ϕ_2.

In the new coordinates (ξ_1, ξ_2, ξ_3), with the state feedback (61), the closed-loop dynamics are written

$$\dot{\xi}_1 = \xi_2, \qquad \dot{\xi}_2 = v, \qquad \dot{\xi}_3 = \mu_0(\xi_1, \xi_2)\xi_3 - \nu_0(\xi_1, \xi_2)\xi_3^2,$$

with

$$\mu_0(\xi_1, \xi_2) \triangleq \mu(\phi_1(\xi_1, \xi_2), \phi_2(\xi_1, \xi_2)),$$
$$\nu_0(\xi_1, \xi_2) \triangleq \nu(\phi_1(\xi_1, \xi_2), \phi_2(\xi_1, \xi_2)),$$

and $v(\xi_1, \xi_2)$ is chosen to place the poles of the input–output transfer function $v \to \xi_1$.

The equilibrium point of the closed loop may be written

$$\bar{\xi}_1 = \text{set point of the yield } \frac{X}{S - S_{\text{in}}},$$

$$\bar{\xi}_2 = 0, \qquad \bar{\xi}_3 = \frac{\mu_0(\bar{\xi}_1, 0)}{\nu_0(\bar{\xi}_1, 0)}.$$

Finally the zero dynamics are written

$$\dot{\xi}_3 = \mu_0(\bar{\xi}_1, 0)\xi_3 - \nu_0(\bar{\xi}_1, 0)\xi_3^2$$

and have the following stable linearization around the equilibrium (with $\tilde{\xi}_3 = \xi_3 - \bar{\xi}_3$):

$$\dot{\tilde{\xi}}_3 = -\mu_0(\bar{\xi}_1, 0)\tilde{\xi}_3.$$

Hence, we have shown that, provided that the rate functions are independent of P, we can design a feedback controller that maximizes the dimension of the linearizable subsystem while preserving the local stability of the zero dynamics.

For $h(X, S, P) \triangleq X/P$, the proof follows exactly the same lines.

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