ZERO DYNAMICS OF CONTINUOUS AND FED-BATCH BIOREACTORS

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Abstract

The zero dynamics of simple continuous and fed-batch bioreactors is investigated in this paper for different input and output selections. A function λ generating the necessary coordinates transformation has been determined analytically for each case solving a simple PDE, and the resulting coordinates transformations have found to be invertible on the physically meaningful operating region.

It is shown that that the investigated continuous and fed-batch bioreactors are globally minimum phase systems with the examined reaction rate function if the manipulable input is the inlet feed flow rate and the output is the substrate concentration.

It is also shown that the zero dynamics may have multiple (locally stable and unstable) equilibria if the input is the inlet feed flow rate and the output is the biomass concentration.

1 Introduction

Fermentation processes are widely used in the biochemical industries for producing either biomass of a certain type or the by-product of biomass growth. Baker's yeast, beer and certain antibiotics are typical products of bioreactors.

Two basic operation types of fermentation processes can be distinguished:

- In *continuous fermenters* the liquid volume in the bioreactor is held constant which means that the inlet feed flow rate is equal to the outlet flow rate in each time instant.
- In *fed-batch fermenters* the substrate is gradually fed into the reactor, and the whole product is taken away at the end of the process.

Even in the simplest case it is unavoidable to carefully perform dynamic analysis, because fermentation processes are known to be highly nonlinear both in the continuous and fed-batch operation mode with difficult and sometimes unusual open-loop dynamic properties. They may have narrow open-loop stability region near desired operation points [11] and traditional linear techniques, such as LQR or pole-placement may completely fail when designed on their linearized models. In addition, fed-batch fermenters may exhibit lack of reachability if the usual input variable, the fed-batch feed flowrate is applied (see e.g. [3] or [10]). There is a broad literature available on dynamics of fermentation processes, the reader is referred e.g. to the excellent papers [2] and [5] for mainly control-oriented results.

It is well-known that, in a globally minimum phase system (i.e. a system having globally asymptotically stable zero dynamics), system trajectories can be driven to an arbitrary small neighborhood of the origin by using high-gain output feedback (see e.g. [9] or [1]). Since certain state variables (typically, the biomass concentrations) are rarely measurable on-line in bioreactors, it is of significant practical interest, what system configurations result in a locally or globally asymptotically stable (or unstable) zero dynamics. Furthermore, the zero dynamics analysis results are useful for designing nonlinear controllers or controller-observer structures for bioprocesses.

The outline of the paper is the following. In Section 2, the most important concepts and tools are described that are used later on. Section 3 and 4 contain the main results about the continuous and fed-batch case, respectively. Finally, the paper is closed by some conclusions in Section 5.

2 The zero dynamics

The necessary definitions and notations are briefly summarized in this section based on [6].

Consider a nonlinear single-input single-output dynamical system in the following input-affine state-space form

$$\dot{x} = f(x) + g(x)u \quad (1)$$
$$y = h(x) \quad (2)$$

where $x \in \mathbb{R}^n$ is the state vector, $u \in \mathbb{R}$ is the input, $y \in \mathbb{R}$ is the output, f and g are smooth $\mathbb{R}^n$-valued mappings, $f(0) = 0$ and h is a smooth $\mathbb{R}$-valued mapping.

It is said that (1) has relative degree r at the equilibrium $x^0 = 0$ if $L_g L_f^k h(x) = 0$ for all x in a neighborhood of x^0 and all $k < r-1$, and $L_g L_f^{r-1} h(x^0) \neq 0$.

After a suitable coordinates transformation $z = \Phi(x)$ where $z_i = \phi_i(x) = L_f^{i-1} h(x)$ for $1 \le i \le r$ and $L_g \phi_i(x) = 0$ for $r+1 \le j \le n$ the state-space model (1) with relative degree r can be rewritten as

$$\begin{aligned}
\dot{z}_1 &= z_2 \\
\dot{z}_2 &= z_3 \\
&\dots \\
\dot{z}_{r-1} &= z_r \\
\dot{z}_r &= b(\xi,\eta) + a(\xi,\eta)u \\
\dot{\eta} &= q(\xi,\eta)
\end{aligned} \quad (3)$$

where $\xi = [z_1 \ \dots \ z_r]^T$, $\eta = [z_{r+1} \ \dots \ z_n]^T$, $a(\xi,\eta) = L_g L_f^{r-1} h(\Phi^{-1}(\xi,\eta))$ and $b(\xi,\eta) = L_f^r h(\Phi^{-1}(\xi,\eta))$.

The *Problem of Zeroing the Output* is to find, if it exists, pairs consisting of an initial state x^* and input function u defined for all t in a neighborhood of $t = 0$, such that the corresponding output $y(t)$ of the system is identically zero for all t in a neighborhood of $t = 0$. For any fixed initial state x^* the input function u can be determined as follows. Let us set the output to be identically zero, then the system's behavior is governed by the differential equation

$$\dot{\eta}(t) = q(0,\eta(t)). \quad (4)$$

The dynamics (4) describes the internal behavior of the system when the output is forced to be zero and it is called the *zero dynamics*. The initial state of the system must be set to a value such that $\xi(0) = 0$, while $\eta(0) = \eta^0$ can be chosen arbitrarily. Furthermore, the input must be set as

$$u(t) = -\frac{b(0,\eta(t))}{a(0,\eta(t))} \quad (5)$$

where $\eta(t)$ denotes the solution of (4) with initial condition $\eta(0) = \eta^0$.

In the forthcoming sections we will examine models with 2 state variables, therefore it is useful to briefly describe how the zero dynamics analysis can be simplified in this special case. Consider a nonlinear coordinates-transformation of the state variables in the following form

$$z = \Psi(x), \quad (6)$$

Table 1: Variables and parameters of the bioreactor model

X	biomass concentration		$[\frac{g}{l}]$
S	substrate concentration		$[\frac{g}{l}]$
F	feed flow rate		$[\frac{l}{h}]$
V	volume	4	$[l]$
S_F	substrate feed concentration	10	$[\frac{g}{l}]$
Y	yield coefficient	0.5	-
μ_{max},	kinetic parameter	1	$[\frac{1}{h}]$
K_1	kinetic parameter	0.03	$[\frac{g}{l}]$
K_2	kinetic parameter	0.5	$[\frac{l}{g}]$

where

$$z_1 = y = h(x) \quad (7)$$
$$z_2 = \lambda(x), \quad (8)$$

and λ is calculated such that

$$L_g \lambda(x) = \frac{\partial \lambda}{\partial x} g(x) = 0. \quad (9)$$

Then the second state equation in the transformed coordinates reads

$$\dot{z}_2 = \frac{\partial \lambda}{\partial x}\dot{x} = \frac{\partial \lambda}{\partial x}(f(x) + g(x)u) = L_f \lambda(x) + \underbrace{L_g \lambda(x)}_{0} u = L_f \lambda(x) = L_f(\Psi^{-1}(z)), \quad (10)$$

and the zero dynamics can be examined independently of the input by setting $z_1 = 0$ (or constant) in (10). Note that this method requires the solution of the PDE $\frac{\partial \lambda}{\partial x} g(x) = 0$ and the coordinates-transformation Ψ to be analytically invertible.

3 The continuous case

The dynamics of the isotherm continuous bioreactor is given by the state space model

$$\frac{dX}{dt} = \mu(S)X - \frac{XF}{V} \quad (11)$$
$$\frac{dS}{dt} = -\frac{\mu(S)X}{Y} + \frac{(S_F - S)F}{V} \quad (12)$$
$$\text{where} \quad \mu(S) = \mu_{max}\frac{S}{K_2 S^2 + S + K_1} \quad (13)$$

The first equation originates from the biomass component mass balance, while the second is from the substrate component mass balance. They are coupled by the nonlinear reaction rate function $\mu(S)X$ which is the main source of the nonlinearity and uncertainty in this simple model. Note that the source of the difficulties in the nonlinear dynamics is the non-monotonous character of the function $\mu(S)$ which has a maximum in the operation region of interest.

The variables and parameters of the model together with their units and parameter values are given in Table 1. The parameter values are taken from [7]. It is stressed, that in this case, the volume V is constant.

3.1 Control input: feed flow rate

The continuous model (11)-(13) can easily be written in standard input-affine form with the centered state vector $x = [x_1 \ x_2]^T = [X - X_0 \ S - S_0]^T$ consisting of the centered biomass and substrate concentrations. The centered input flowrate is chosen as manipulable input variable $u = F - F_0$. The vector fields in the state equations are

$$f(x) = \begin{bmatrix} \mu(x_2+S_0)(x_1+X_0) - \frac{(x_1+X_0)F_0}{V} \\ -\frac{\mu(x_2+S_0)(x_1+X_0)}{Y} + \frac{(S_F-(x_2+S_0))F_0}{V} \end{bmatrix},$$
$$g(x) = \begin{bmatrix} -\frac{(x_1+X_0)}{V} \\ \frac{(S_F-(x_2+S_0))}{V} \end{bmatrix} \quad (14)$$

with (X_0, S_0, F_0) being a steady-state operating point. A typical control problem is to operate the system at the point where the outlet biomass mass flow rate $X \cdot F$ is maximal.

From the state equations (11)-(12) it can be calculated that at any non-washout equilibrium point

$$XF = (S_F - S)\mu(S)VY. \quad (15)$$

From (15), the maximizing equilibrium value of S (and then that of X and F) can be calculated. From now on, we assume that X_0, S_0 and F_0 correspond to this optimal operating point (although some of the presented results do not depend on the selection of the operating point) which is at

$$S_0 = \frac{1}{2}\frac{-2K_1 + 2\sqrt{K_1^2 + S_F^2K_1K_2 + S_FK_1}}{S_FK_2+1} \quad (16)$$
$$X_0 = (S_F - S_0)Y \quad (17)$$
$$F_0 = \mu(S_0)V. \quad (18)$$

The coordinates transformation generator function The continuous model (11)-(13) has clearly two state variables and the PDE $\frac{\partial \lambda}{\partial x}g(x) = 0$ can be solved analytically for this case to obtain a function λ that satisfies the condition in (9)

$$\lambda(x) = \mathscr{F}\left(\frac{V(-S_F + x_2 + S_0)}{x_1 + X_0}\right), \quad (19)$$

where $\mathscr{F}$ is an arbitrary continuously differentiable function (a class C^1 function).

3.1.1 Choosing the substrate concentration as output

If the substrate concentration is chosen as output, i.e.

$$y = h(x) = x_2 \quad (20)$$

then the coordinates-transformation Ψ and it's inverse is given by

$$\begin{bmatrix} z_1 \\ z_2 \end{bmatrix} = \begin{bmatrix} x_2 \\ \frac{V(-S_F+x_2+S_0)}{x_1+X_0} \end{bmatrix} = \Psi(x) \quad (21)$$

and

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} \frac{-z_2X_0 - S_FV + Vz_1 + S_0V}{z_2} \\ z_1 \end{bmatrix} = \Psi^{-1}(z). \quad (22)$$

This results in the zero dynamics governed by the differential equation

$$\dot{z}_2 = L_f\lambda(\Psi^{-1}(0, z_2)) = -\frac{(z_2Y + V)S_0\mu_{max}}{Y(K_2 + S_0^2 + S_0 + K_1)} \quad (23)$$

which is *linear and globally stable* (considering that the constant parameters of the system are always positive). The equilibrium state of the zero dynamics is at $z_2^* = -\frac{V}{Y}$ which, together with $z_1 = 0$, corresponds to the desired equilibrium state $x_1 = 0, x_2 = 0$ in the original coordinates.

The above analysis shows that *if we manage to stabilize the substrate concentration either by a full state feedback or by an output feedback (partial state feedback) or even by a dynamic controller then the overall system will be stable.*

3.1.2 Choosing the biomass concentration as output

The output in this case is the biomass concentration:

$$z_1 = y = h(x) = x_1 \quad (24)$$

The zero dynamics of the system is given by

$$\dot{z_2} = -\frac{V\mu_{max}(z_2^2YX_0 + z_2(YVS_F + VX_0) + S_FV^2))}{(K_2X_0^2z_2^2 + z_2(2K_2X_0S_FV + VX_0) + V^2(K_2S_F^2 + S_F + K_1))Y}, \quad (25)$$

which describes a nonlinear dynamics and is only locally stable around the desired equilibrium state. The stability region can be determined using the parameters of the system.

The right hand side of (25) is visible in Fig. 1 using the parameter values of Table 1. It can be seen that the zero dynamics has two equilibrium points: the equilibrium point corresponding to the optimal operating point ($z_2 = -V/Y = -8$) is stable and the other one is unstable.

3.2 Control input: inlet substrate concentration

In this case we assume that the inlet feed flow rate (F) is constant and the manipulable input variable is the inlet substrate concentration (S_F). We assume that $F = F_0$ (see Eq. (18)). Let us introduce the following centered variables similarly to the previous case:

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} X - X_0 \\ S - S_0 \end{bmatrix}, \quad u = S_F - S_{f0}, \quad (26)$$

where (X_0, S_0) is again a steady state operating point defined by the nominal input value S_{f0}.

Using the above notations, the f and g vector fields in the input-affine form of the model defined by (11)-(13) is the following:

$$f(x) = \begin{bmatrix} \mu(x_2+S_0)(x_1+X_0) - \frac{(x_1+X_0)F}{V} \\ -\frac{\mu(x_2+S_0)(x_1+X_0)}{Y} + \frac{(S_{f0}-S_0-x_2)F}{V} \end{bmatrix},$$
$$g(x) = \begin{bmatrix} 0 \\ \frac{F}{V} \end{bmatrix} \quad (27)$$

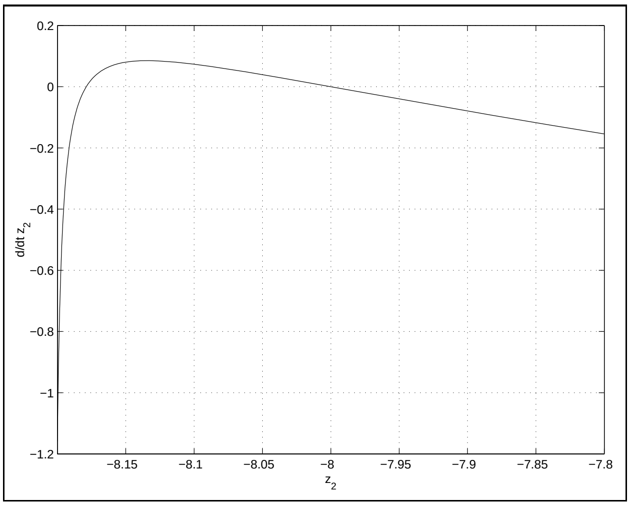

Figure 1: The zero dynamics in the transformed coordinates: continuous bioreactor, input: inlet feed flow rate, output: biomass concentration

3.2.1 Choosing the substrate concentration as output

There is no need for a coordinates-transformation here ($h(x) = x_2$), because the first state equation is not affected by the input. Therefore we can simply set $x_2 = 0$ in the first state equation which gives

$$\dot{x}_1 = \left(\mu(S_0) - \frac{F}{V}\right) x_1 = 0, \tag{28}$$

since it is visible from (11) that in any non-washout equilibrium point $\mu(S_0) = \frac{F}{V}$.

3.2.2 Choosing the biomass concentration as output

In this case, the investigated output is $h(x) = x_1$, and the system has relative degree 2 around the optimal operating point, since

$$L_g h(x) = \begin{bmatrix} 1 & 0 \end{bmatrix} \begin{bmatrix} 0 \\ \frac{F}{V} \end{bmatrix} = 0. \tag{29}$$

and

$$L_g L_f h(0) = \frac{\partial f_1}{\partial x}(0) \cdot g(0) \neq 0. \tag{30}$$

Therefore the system is exactly linearizable with this output selection and it has no zero dynamics.

4 The fed-batch case

In the fed batch case the volume V is not constant any more, therefore the model (11)-(13) is extended by one additional differential equation, namely

$$\frac{dV}{dt} = F \tag{31}$$

The inlet feed flowrate F is chosen as the only input variable for this case. Then the standard input-affine form (1) of the model equations (11)-(31) is given by

$$x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = \begin{bmatrix} X \\ S \\ V \end{bmatrix} \quad , \quad u = F \tag{32}$$

$$f(x) = \begin{bmatrix} \mu(x_2)x_1 \\ -\frac{1}{Y}\mu(x_2)x_1 \\ 0 \end{bmatrix} = \begin{bmatrix} \frac{\mu_{max}x_2x_1}{K_1+x_2+K_2x_2^2} \\ -\frac{\mu_{max}x_2x_1}{(K_1+x_2+K_2x_2^2)Y} \\ 0 \end{bmatrix}$$
$$g(x) = \begin{bmatrix} -\frac{x_1}{x_3} \\ \frac{S_F-x_2}{x_3} \\ 1 \end{bmatrix} \tag{33}$$

4.1 Reachability and the minimal realization of fed-batch bioreactors

It's easy to check from the model equations (33) that the function

$$\gamma(x) = x_3\left(-\frac{1}{Y}x_1 - x_2 + S_F\right) \tag{34}$$

is constant in time under any input i.e. $\frac{d}{dt}\gamma = \frac{\partial\gamma}{\partial x}\dot{x} = 0$ (see e.g. [8] or [10] for a complete control Lie-algebraic derivation).

Using the calculated γ function, it's possible to give a minimal state space realization of fed-batch fermentation processes in the temperature-independent case. Since the reachability hypersurface defined by γ is two-dimensional, the minimal realization will contain two state variables (i.e. the input-to-state behaviour of the system can be described by two differential equations). It's clear from the above that

$$\gamma(x(t)) = -\frac{1}{Y}x_1(t)x_3(t) - (x_2(t)x_3(t) - S_Fx_3(t)) = \tag{35}$$
$$= -\frac{1}{Y}x_1(0)x_3(0) - (x_2(0)x_3(0) - S_Fx_3(0)) = \gamma(x(0)).$$

Therefore we can express the volume x_3 from the above equation in the following way:

$$x_3 = \frac{\gamma(x(0))}{-\frac{1}{Y}x_1 + S_F - x_2}, \quad -\frac{1}{Y}x_1 + S_F - x_2 \neq 0 \tag{36}$$

and the minimal state space model reads

$$\dot{x} = f_{min}(x) + g_{min}(x)u, \tag{37}$$

where

$$x = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix}, \quad f_{min}(x) = \begin{bmatrix} \frac{\mu_{max}x_2x_1}{K_1+x_2+K_2x_2^2} \\ -\frac{\mu_{max}x_2x_1}{(K_1+x_2+K_2x_2^2)Y} \end{bmatrix}$$
$$g_{min}(x) = \begin{bmatrix} \frac{\frac{1}{Y}x_1^2+x_1(x_2-S_F)}{\gamma(x(0))} \\ \frac{(-\frac{1}{Y}x_1+S_F-x_2)(S_F-x_2)}{\gamma(x(0))} \end{bmatrix} \tag{38}$$

We can see by expressing x_3 from γ that the structure of the reaction rate function in f_{min} remains unchanged. It's also important to note that the function g_{min} in the minimal realization (38) depends on the initial state of the system. However, the following results on the zero dynamics are independent of the initial conditions.

4.2 The zero dynamics of the minimal realization

The coordinates transformation generator function Now again, we have two state variables in the minimal realization model (38). The PDE $\frac{\partial \lambda}{\partial x} g(x) = 0$ can be solved analytically for this case to obtain a function λ that satisfies the condition in (9)

$$\lambda(x) = \mathscr{F}\left(\ln\left(\frac{x_1}{S_F - x_2}\right)\right), \qquad (39)$$

where $\mathscr{F}$ is an arbitrary function of the class C^1. Note that this solution requires the assumption $S_F - x_2 > 0$ which always holds under physically meaningful operating and initial conditions. It's important to note that λ does not depend on γ containing the initial conditions.

4.2.1 Choosing the substrate concentration as output

Now we choose $z_1 = y = h(x) = x_2$. Because λ does not depend on γ, the following coordinates-transformation is valid for all initial states:

$$\begin{bmatrix} z_1 \\ z_2 \end{bmatrix} = \begin{bmatrix} x_2 \\ \ln\left(\frac{x_1}{S_F - x_2}\right) \end{bmatrix} = \Psi(x) \qquad (40)$$

This results in the inverse transformation:

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} \exp(z_2)(S_F - z_1) \\ z_1 \end{bmatrix} = \Psi^{-1}(z). \qquad (41)$$

Then the zero dynamics reads

$$\dot{z}_2 = \dot{\lambda} = \frac{\partial \lambda}{\partial x}\dot{x} = \frac{1}{x_1} f_1(x) + \frac{1}{S_F - x_2} f_2(x), \qquad (42)$$

which gives

$$\dot{z}_2 = \mu(x_2)\left(1 - \frac{x_1}{(S_F - x_2)Y}\right) \qquad (43)$$

If we apply the inverse coordinates-transformation given by (41), the μ function remains in the expression and this gives

$$\dot{z}_2 = \mu(z_1)\left(1 - \frac{\exp(z_2)}{Y}\right) \qquad (44)$$

It's easy to calculate that the equilibrium point of (44) is at $z_2^* = \ln(Y)$ independently of how z_1 (the substrate concentration) is set (if $z_1 > 0$). This means that *if the substrate concentration is kept on any constant value (by manipulating the input feed flow rate), then the biomass concentration always converges to the corresponding equilibrium value on the $x_1 - x_2$ plane independently of the reaction rate function μ.*

4.2.2 Choosing the biomass concentration as output

In this case $z_1 = y = h(x) = x_1$ and the coordinates-transformation is:

$$\begin{bmatrix} z_1 \\ z_2 \end{bmatrix} = \begin{bmatrix} x_1 \\ \ln\left(\frac{x_1}{S_F - x_2}\right) \end{bmatrix} = \Psi(x) \qquad (45)$$

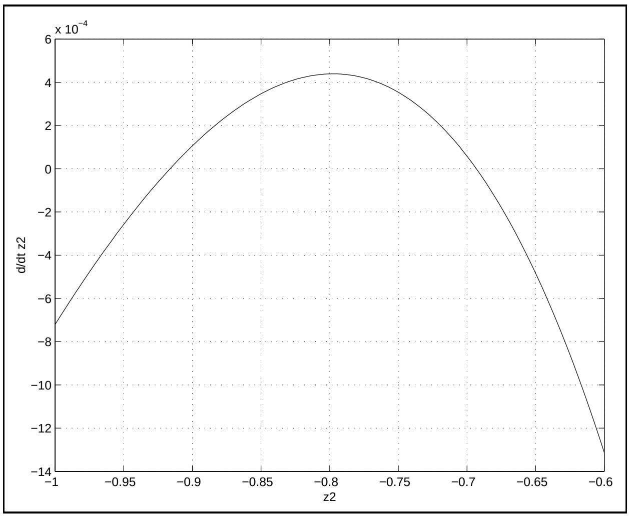

Figure 2: The zero dynamics in the transformed coordinates: fed-batch bioreactor, input: inlet feed flow rate, output: biomass concentration, $z_1 = 4\frac{g}{l}$

Its inverse transformation is in the following form:

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} z_1 \\ \frac{\exp(z_2)S_F - z_1}{\exp(z_2)} \end{bmatrix} = \Psi^{-1}(z) \qquad (46)$$

The zero dynamics in the new coordinates is then:

$$\dot{z}_2 = \frac{\mu_{max}(\exp(z_2)S_F - z_1)\exp(z_2)(Y - \exp(z_2))}{(\exp(2z_2)(K_1 + S_F + K_2 S_F^2) - \exp(z_2)(z_1 - 2K_2 S_F z_1) + K_2 z_1^2)Y} \qquad (47)$$

The right hand side of Eq. (47) is shown in Fig. 2 for a fixed value of $z_1 = 4\frac{g}{l}$. It is visible, that in this case the zero dynamics have two equilibria, one of which is independent of z_1 and is locally asymptotically stable ($z_2^* = \ln(Y) \approx -0.6931\frac{g}{l}$), and the other one is unstable. It means that a high gain feedback of the biomass concentration may move the biomass concentration itself out of the desirable range, similarly to the continuous case (see section 3.1.2).

5 Conclusions

The zero dynamics of a simple fermenter both in continuous and fed-batch operation mode is investigated. The manipulable input variables were the inlet feed flow rate and the inlet substrate concentration in the continuous case and only the inlet feed flow rate in the fed-batch case. The minimal realization of fed-batch bioreactors was used for the investigations based on former reachability results. The selection of the substrate as well as the biomass concentration as the output was investigated in all cases.

It was shown that the investigated continuous and fed-batch bioreactors are globally minimum phase systems if the manipulable input is the inlet feed flow rate and the output is the substrate concentration.

It was also shown that the zero dynamics may have multiple (locally stable and unstable) equilibria if the input is the inlet feed flow rate and the output is the biomass concentration. Furthermore, continuous bioreactors with the inlet substrate concentration as input have relative degree 2 if the output is the biomass concentration, and they are typically (but not necessarily) non-minimum phase systems if the substrate concentration is selected as output.

A function λ generating the necessary coordinates transformation has been determined analytically for each case solving a simple PDE, and the resulting coordinates transformations have found to be invertible on the physically meaningful operating region.

Further work will be directed towards the application of the zero dynamics analysis results for nonlinear controller structure selection by choosing controlled or performance outputs as well as for feedback linearization and observer design.

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