Extremum seeking control for a mass structured cell population balance model in a bioreactor

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Abstract: This paper is concerned with the design of an adaptive extremum seeking control scheme for a mass structured cell population balance model in a bioreactor. The feed substrate concentration is considered as the manipulated input to drive system states to the desired setpoints that maximize the value of an objective function of the cell density. We assume limited knowledge on the objective function and we use the substrate concentration measurements to estimate this function. We use the Lyapunov's stability theorem and a persistency of excitation condition to show that the proposed adaptive extremum seeking control achieves the exponential convergence to the desired set points. Numerical simulation has been performed to illustrate the performance of the proposed approach.

Keywords: Extremum seeking, Adaptive control, Cell population model, Lyapunov theory, Integro-partial differential equation.

1. INTRODUCTION

The design of a control algorithms, the analysis of the dynamical properties, and the analysis of numerical schemes for a mass structured cell population balance model has become an active area of research over the last decades (see e.g. Mantzaris et al (2007), Mantzaris et al (1999) and references therein). The dynamics of such processes is described by a nonlinear partial integro-differential equation with a nonlinear boundary condition for the cell growth coupled with a nonlinear ordinary integro-differential equation accounting for substrate consumption, see Mantzaris et al (2007), Mantzaris et al (1999).

Several control approaches have been developed for this class of systems by controlling the different moments in order to achieve a cell mass distribution with the maximum possible for zeroth and first moments and the minimum possible for second moment. Mantzaris et al (2007) have developed a nonlinear linearizing controller to control the different cell distribution moments, Mantzaris et al (2002) have proposed nonlinear and linear schemes to control the productivity for multi-staged cell population, and Beniich, Dochain (2009) have developed a nonlinear constrained controller based on the Lyapunov design to stabilize a steady state of the cell distribution. In this work, we are particularly interested in maximizing an objective function of the zeroth moment described by a nonlinear integro-ordinary differential equation with limited knowledge of the integral term. We assume that measurements of the substrate concentration are available to estimate the objective function. In the literature, the used approach to solve the similar control problem, where some parameters are unknowns and where the objective function is not available for measurement, is known as the extremum seeking control approach.

The main purpose of the extremum seeking control design is to find the operating setpoints that maximize or minimize an objective function, we refer to Guay et al (1990), Hudon et al (2008), Zhang et al (2007), Zhang (2012) and references therein for a complete review of the control algorithms and the stability analysis developed for linear unknown systems and a class of general nonlinear systems.

In our approach, a Lyapunov-based adaptive learning control technique is used to approximate the unknown state and to steer the system to its unknown extremum. We show that a certain level of persistence of excitation condition is necessary to guarantee the convergence of the extremum seeking mechanism.

The paper is organized as follows. Section 1 presents the mathematical model, its parameters, and the problem formulation. In section 2, and extremum seeking algorithm design is developed. Numerical simulation is shown in Section 3 followed by brief conclusions in Section 4.

2. MATHEMATICAL MODEL

Let us consider a cell population growing in a continuous stirred tank reactor. The cells are distinguishable from each other in terms of their mass or any other property

Manuscript 575 submitted to 21st IFAC World Congress, 2020.
Received October 29, 2019.

of the cell, which obeys the conservation law. Let $N(m,t)$ be the number of cells which have a mass m at time t. The cells are considered to grow with a rate $r(m,S)$ that depends on their mass and on the concentration of the limiting substrate S. We also assume that the value of the mass is standardized and that $m \in [0,1]$. The cell division and the birth processes of the cell population are described by the division rate $\Gamma(m,S)$ defined as follows (see Mantzaris et al (2007); Mantzaris et al (1999)):

$$\Gamma(m,S) = \frac{f(m)}{1-\int_0^m f(m')dm'} r(m,S) = \gamma(m) r(m,S) \quad (1)$$

where $f(m)$ is the division probability density function which is assumed to depend only on the cell mass, and is taken to be a left hand side truncated Gaussian distribution with the mean of μ_f and standard deviation of σ_f.

We also assume that the probability p that a mother cell of mass m will give birth to a daughter cell of mass m' is independent of substrate concentration. This function should further satisfy the following normalization condition

$$\int_0^{m'} p(m,m')dm = 1 \quad (2)$$

and should also be such that the biomass is conserved at cell division, i.e.:

$$p(m,m') = p(m'-m,m') \quad (3)$$

We finally assume that the probability function is a symmetrical beta distribution with a parameter q defined by the following equation:

$$p(m,m') = \frac{1}{B(q,q)} \times \frac{1}{m'} \left(\frac{m}{m'}\right)^{q-1} \left(1-\frac{m}{m'}\right)^{q-1} \quad (4)$$

We assume also that no cell death occurs and that cells grow in a continuous reactor from which they exit with a dilution rate of D. Under these assumptions, the cell population dynamics are described by the following integro-differential equations:

$$\frac{\partial N(m,t)}{\partial t} + \frac{\partial}{\partial m}\left[r(m,S)N(m,t)\right] + \Gamma(m,S)N(m,t) = -DN(m,t) + 2\int_m^1 \Gamma(m',S)p(m,m')N(m',t)dm' \quad (5)$$

subject to the initial condition:

$$N(m,0) = N_0 \quad (6)$$

completed by the following boundary conditions:

$$r(1,S) \times N(1,t) = r(0,t) \times N(0,t) = 0 \quad (7)$$

The behavior of the cell population depends on the substrate concentration, the source of nutrient for its growth. The mass balance equation for the substrate expresses in particular that the substrate consumption is proportional to the total biomass production $\int_0^1 r(m,S)N(m,t)dm$ with a yield coefficient Y which is the ratio of the biomass production rate over the substrate consumption rate, assumed to be constant. The substrate concentration mass balance then reads as follows:

$$\frac{dS}{dt} = D(S_f - S) - \frac{1}{Y}\int_0^1 r(m,S)N(m,t)dm \quad (8)$$

subject to the initial condition:

$$S(0) = S_0 \quad (9)$$

with S_f is the substrate concentration in the feed.

Here we address the problem of controlling the cell density (zeroth moment):

$$M_0 = \int_0^1 N(m,t)dm \quad (10)$$

by manipulating the substrate concentration in the feed.

By integrating both sides of (5) with respect to the mass m, we obtain:

$$\int_0^1 \frac{\partial N(m,t)}{\partial t}dm + \int_0^1 \frac{\partial}{\partial m}\left[r(m,S)N(m,t)\right]dm + \int_0^1 \Gamma(m,S)N(m,t)dm + D\int_0^1 N(m,t)dm = 2\int_0^1\int_m^1 \Gamma(m',S)p(m,m')N(m',t)dm'dm$$

by considering equations (2) and (7), we obtain:

$$\int_0^1\int_m^1 \Gamma(m',S)p(m,m')N(m',t)dm'dm = \int_0^1 \left(\int_0^{m'} p(m,m')dm\right)\Gamma(m',S)N(m',t)dm' = \int_0^1 \Gamma(m',S)N(m',t)dm'$$

Consequently,

$$\dot{M}_0(t) = -DM_0(t) + \int_0^1 \Gamma(m,S)N(m,t)dm \quad (11)$$

3. EXTREMUM SEEKING CONTROL DESIGN

Let us consider the problem of the design of the extremum seeking controller of the following model:

$$\dot{M}_0(t) = -DM_0(t) + \int_0^1 \Gamma(m,S)N(m,t)dm \quad (12)$$

$$\frac{dS}{dt} = DS_f - DS - \frac{1}{Y}\int_0^1 r(m,S)N(m,t)dm \quad (13)$$

with an objective function:

$$y = HM_0 \quad \text{where} \quad H \in R^{1\times n} \quad (14)$$

Our objective is to design a control law $u = DS_f$, with D is a constant, that maximizes the cell density, i.e that maximize the objective function

$$y = HM_0 \quad (15)$$

In practice, S_f should be positive, then $u = DS_f \geq 0$.

Due to the limited knowledge on the integral terms, we use the second mean theorem to reformulate the model.

This means that we consider that there exists a unique $m_1 \in [0,1]$ such that:

$$\int_0^1 \Gamma(m,S)N(m,t)dm = \gamma(m_1) \times m_1 \times r(S)\int_0^1 N(m,t)dm = \gamma(m_1) \times m_1 \times r(S) \times M_0 = C_1(S,M_0)$$

Manuscript 575 submitted to 21st IFAC World Congress, 2020.
Received October 29, 2019.

We obtain a similar result for $\frac{1}{Y}\int_0^1 r(m,S)N(m,t)dm$.

Therefore there exists a unique $m_2 \in [0,1]$ such that:

$$-\frac{1}{Y}\int_0^1 r(m,S)N(m,t)dm = -\frac{1}{Y}m_2 \times r(S)\int_0^1 N(m,t)dm$$
$$= -C_2(S,M_0)$$

The problem will be therefore defined by considering the following dynamical equations:

$$\dot{M}_0(t) = -DM_0(t) + C_1(S(t),M_0(t)) \quad (16)$$
$$\dot{S}(t) = -DS(t) + C_2(S(t),M_0(t)) + u(t) \quad (17)$$

with limited knowledge on $C_1(S,M_0)$.

The problem is solved by expressing the equilibrium as a function of the substrate concentration. We assume that there exists a vector valued function $\pi(S)$ solution of the following equation:

$$-D\pi(S) + C_1(S,\pi(S)) = 0 \quad (18)$$

The solution $\pi(S)$ is assumed to be continuous. More specifically, we require the following.

Assumption 1. The solution $\pi(S)$ is supposed continuous in a compact set of $\mathbb{R}^+$.

Assumption 2. The function $H\pi(S)$ is continuously differentiable and admits a maximum in $M_0 \in X \setminus \pi(S)$.

The substrate concentration dynamics equation subject to the equilibrium condition equation is writen as follows:

$$\dot{S} = -DS + C_2(S,M_0) + u + D\pi(S) - C_1(\pi(S),S) \quad (19)$$
$$= -DS + u + D\pi(S) + [C_2(S,M_0) - C_1(\pi(S),S)] \quad (20)$$

We assume that the following holds.

Assumption 3. For all M_0 in the compact set of R^+ and for all $S \in R^+$, there exists a positive nonzero constant L such that

$$||C_2(S,M_0) - C_1(\pi(S),S)|| \leq L||M_0 - \pi(S)||$$

Remark 1.

(1) **Assumption 1** is important for the approximation of the objective function.
(2) In **Assumption 2** , we consider only the cases where $H\pi(S)$ is continuously differentiable convex function of S.
(3) **Assumption 3** guarantees the convergence of M_0 to a neighborhood of the equilibrium $M_0 = \pi(S)$.

Our approach consists in approximating the equilibrium $\pi(S)$ using a linear approximation based on the radial basis function (RBF) presented in Hudon et al (2008).

A continuous function $f : \mathbb{R}^p \to \mathbb{R}$ can be approximated by using RBF technique as:

$$f(z) = W^{*T}Z(z) + \mu_l(t) \quad (21)$$

with $\mu_l(t)$ the approximation error, and $Z(z)$ is the radial basis function vector defined as follows:

$$Z(z) = [Z_1(z), Z_2(z), ..., Z_l(z)] \quad (22)$$
$$Z_i(z) = exp\left[\frac{-(z-\varphi_i)^T(z-\varphi_i)}{\sigma_i^2}\right] \quad (23)$$

with $i = 1,...,l$, and φ_i is the center of the receptive field, and σ_i is the width of the Gaussian function.

The ideal weight W^* is defined as

$$W^* := \arg\min_{W\in\Omega_\omega}\{\sup_{z\in\Omega}|W^TS(z) - f(z)|\} \quad (24)$$

where Ω is a compact set of $\mathbb{R}^p$ and

$$\Omega_\omega = \{W \mid \quad ||W|| \leq \omega_m\} \quad (25)$$

with positive constant ω_m to be chosen at the design stage.

We apply this method on our objective function to obtain an approximation as follows:

$$H\pi(S) = W_p^{*T}Z(S) + \mu_p(t) \quad (26)$$

where $\mu_p(t)$ is an approximation error, and we consider that

$$\pi(S) = H^TW_p^{*T}Z(S) + W_o^{*T}Z(S) + \mu_l(t) \quad (27)$$

We have the following assumption about the approximation error terms $\mu_p(t)$ and $\mu_l(t)$.

Assumption 4: The approximation errors satisfy $|\mu_p(t)| \leq \mu_1$ and $|\mu_l(t)| \leq \mu_2$ with constants $\mu_1 > 0$ and $\mu_2 > 0$ over the compact set Ω_ω.

At this stage, we first give the estimation algorithm of the unknown parameter vector W^*. Let us denote by $\hat{W}$ the estimate of the true parameter W^* and $\hat{S}$ the prediction of S. We have

$$\begin{aligned}
\dot{S} &= -DS + u + D\pi(S) + [C_2(S,M_0) - C_1(\pi(S),S)] \\
&= -DS + u + DH^TW_p^{*T}Z(S) + DW_o^{*T}Z(S) \\
&\quad + D\mu_l(t) + [C_2(S,M_0) - C_1(\pi(S),S)] \\
&= -DS + u + [DZ(S)^T, DH^TZ(S)^T]\begin{pmatrix} W_p^{*T} \\ W_o^{*T}\end{pmatrix} \\
&\quad + D\mu_l(t) + [C_2(S,M_0) - C_1(\pi(S),S)] \\
&= -DS + u + F(S)W^* + D\mu_l(t) \\
&\quad + [C_2(S,M_0) - C_1(\pi(S),S)]
\end{aligned}$$

where $W^{*T} = [W_p^{*T}, W_o^{*T}]$ and $F(S) = [DZ(S)^T, DH^TZ(S)^T]$

The predicted state $\hat{S}$ is generated by

$$\dot{\hat{S}} = -DS + u + F(S)\hat{W} + k_S(S - \hat{S}) + c_1(t)\dot{\hat{W}} \quad (28)$$

with gain function $k_S > 0$ and prediction error $e_S = S - \hat{S}$. The vector time varying function $c_1(t)$ is to be assigned. It follows that

$$\begin{aligned}
\dot{e}_S &= F(S)\tilde{W} + D\mu_l(t) - k_Se_S \\
&\quad + [C_2(S,M_0) - C_1(\pi(S),S)] - c_1(t)\dot{\hat{W}} \quad (29)
\end{aligned}$$

where $\tilde{W} = W^* - \hat{W}$.

The aim of the extremum seeking control is to stabilize the closed-loop system around a point where the gradient of $y = H\pi(S)$ with respect to S vanishes while attenuating the effect of the modeling uncertainty $\mu_l(t)$. Using the radial basis function approximation, the objective function is given by:

$$y = H\pi(S) = W_p^{*T}Z(S) + \mu_p(t) \quad (30)$$

is approximated by

$$y_e = \hat{W}_p^T Z(S) \tag{31}$$

where $\hat{W}_p$ is an estimate of the optimal weight W_p^*.

The estimated gradient of y_e with respect to S is given by

$$z = \frac{\partial y_e}{\partial S} = \hat{W}_p^T dZ(S) \tag{32}$$

where: $dZ(S) = \frac{\partial Z(S)}{\partial S}$.

The Hessian of y_e with respect to S is given by

$$\frac{\partial^2 y_e}{\partial S} = \hat{W}_p^T d^2 Z(S) = \Gamma_2 \tag{33}$$

where: $d^2 Z(S) = \frac{\partial^2 Z(S)}{\partial S^2}$

Let us define

$$z_S = \hat{W}_p^T dZ(S) - d(t) \tag{34}$$

where $d(t) \in C^1$ is an excitation signal to be assigned.

For the controller design, we define the following auxiliary signals

$$\eta_1 = e_S - c_1(t)^T \tilde{W} \tag{35}$$

$$\eta_2 = z_S - c_2(t)^T \tilde{W} \tag{36}$$

where $c_2(t)$ is a time-varying vector valued function to be assigned in the design.

And the dynamics of the time varying functions $c_1(t)$ and $c_2(t)$ are assigned as follows

$$\dot{c}_1(t)^T = -k_S c_1(t)^T + F(S) \tag{37}$$

$$\dot{c}_2(t)^T = -k_Z c_2(t)^T + \Gamma_2 F(S) \tag{38}$$

Let us consider the following Lyapunov function candidate

$$V = \frac{1}{2}\eta_1^2 + \frac{1}{2}\eta_2^2 \tag{39}$$

$$= V_1 + V_2 \tag{40}$$

We consider the control input u such that

$$u = DS - F(S)W^* - k_d d(t) \tag{41}$$

with the following dynamical equation for d:

$$\begin{aligned}\dot{d}(t) = {} & \dot{\hat{W}}_p^T dZ(S) + k_Z c_2(t)^T \tilde{W} + k_Z \eta_2 \\ & -\Gamma_2 F(S)\tilde{W} - c_2(t)^T \dot{\tilde{W}} - k_d \Gamma_2 d(t)\end{aligned} \tag{42}$$

where k_Z, k_d are positive gain functions to be assigned.

We have

$$\begin{aligned}\dot{V}_1 &= \eta_1 \dot{\eta}_1 \\ &= \eta_1(\dot{e}_S - \dot{c}_1(t)^T \tilde{W} - c_1(t)^T \dot{\tilde{W}}) \\ &= \eta_1\{F(S)\tilde{W} + D\mu_l(t) - k_S e_S + C_2(S, M_0) \\ &\quad -C_1(\pi(S), S) - c_1(t)\dot{\hat{W}} - \dot{c}_1(t)^T \tilde{W} - c_1(t)^T \dot{\tilde{W}}\} \\ &= \eta_1\{F(S)\tilde{W} + D\mu_l(t) - k_S e_S + C_2(S, M_0) \\ &\quad -C_1(\pi(S), S) - c_1(t)\dot{\hat{W}} + k_S c_1(t)^T \tilde{W} \\ &\quad -F(S)\tilde{W} - c_1(t)^T \dot{\tilde{W}}\} \\ &= \eta_1\{D\mu_l(t) - k_S(e_S - c_1(t)^T \tilde{W}) + C_2(S, M_0) \\ &\quad -C_1(\pi(S), S) - c_1(t)\dot{\hat{W}} - c_1(t)^T \dot{\tilde{W}}\} \\ &= \eta_1\{D\mu_l(t) - k_S \eta_1 + [C_2(S, M_0) - C_1(\pi(S), S)] \\ &\quad -c_1(t)\dot{\hat{W}} - c_1(t)^T \dot{\tilde{W}}\} \\ &= -k_S \eta_1^2 + \eta_1(D\mu_l(t) + [C_2(S, M_0) - C_1(\pi(S), S)]).\end{aligned}$$

And

We obtain

$$\dot{V}_1 = -k_S \eta_1^2 + \eta_1(D\mu_l(t) + [C_2(S, M_0) - C_1(\pi(S), S)]) \tag{43}$$

In a similar way, we obtain

$$\dot{V}_2 = -k_Z \eta_2^2 + \Gamma_2 \eta_2(D\mu_l(t) + [C_2(S, M_0) - C_1(\pi(S), S)]) \tag{44}$$

We finally have

$$\begin{aligned}\dot{V} &= -k_S \eta_1^2 + \eta_1(D\mu_l(t) + [C_2(S, M_0) - C_1(\pi(S), S)]) \\ &\quad -k_Z \eta_2^2 + \Gamma_2 \eta_2(D\mu_l(t) + [C_2(S, M_0) - C_1(\pi(S), S)]) \\ &= -k_S \eta_1^2 - k_Z \eta_2^2 + (\eta_1 + \Gamma_2 \eta_2)((D\mu_l(t) \\ &\quad +[C_2(S, M_0) - C_1(\pi(S), S)])\end{aligned}$$

from **Assumption 1**, it follows that

$$\sup ||M_0 - \pi(S)|| = C_S$$

exists and is finite.

By **Assumption 3**, we get

$$\begin{aligned}\dot{V} &\leq -k_S \eta_1^2 - k_Z \eta_2^2 + (\eta_1 + \Gamma_2 \eta_2) D\mu_l(t) \\ &\quad +(|\eta_1| + |\Gamma_2||\eta_2|)L \times \sup ||M_0 - \pi(S)|| \\ &= -k_S \eta_1^2 - k_Z \eta_2^2 + (\eta_1 + \Gamma_2 \eta_2) D\mu_l(t) \\ &\quad +(|\eta_1| + |\Gamma_2||\eta_2|)L \times C_S\end{aligned}$$

Completing the squares and applying the gain functions

$$k_S = k_{S0} + \frac{k_4}{2} D^2 \tag{45}$$

$$k_Z = k_{Z0} + \frac{k_7}{2} \Gamma_2^2 \tag{46}$$

we obtain the following inequality

$$\dot{V} \leq -k_{S0}\eta_1^2 - k_{Z0}\eta_2^2 + \frac{1}{2k_4} D^2 \mu_l(t) + \left(\frac{1}{2k_6} + \frac{1}{2k_7}\right) L^2 C_S \tag{47}$$

where k_{S0},k_{Z0},k_4,k_6 and k_7 are positive constants.

Remark 2. Equation (47) establishes that the state η converges to a small neighborhood of the origin.

It remains to show that the original state variables e_S, z_S and the parameter estimation errors $\tilde{W}$ converge to a small neighborhood of the origin. To this end, we derive a persistency of excitation condition that guarantees the convergence of the parameter estimates to the ideal weight W^*.

Consider the following matrix,

$$\Upsilon(t) = \begin{bmatrix} c_1(t)^T \\ c_2(t)^T \end{bmatrix}$$

By construction, this matrix solves the matrix differential equation

$$\dot{\Upsilon}(t) = -K(t)\Upsilon(t) + B(t) \tag{48}$$

where

$$K(t) = \begin{bmatrix} k_S & 0 \\ 0 & k_z \end{bmatrix}$$

And

$$B(t) = \begin{bmatrix} F(S) \\ \Gamma_2 F(S) \end{bmatrix}$$

Manuscript 575 submitted to 21st IFAC World Congress, 2020.
Received October 29, 2019.

A bound on the parameter estimates $\hat{W}$ can be ensured by choosing the following parameter update law.

$$\dot{\hat{W}} = \begin{cases} \gamma_w \Gamma & if\, ||\hat{W}|| \leq w_m\, or \\ & if\, ||\hat{W}|| = w_m \quad and \quad \hat{W}^T \leq 0 \\ \gamma_w \left(I - \dfrac{\hat{W}\hat{W}^T}{\hat{W}^T\hat{W}} \right) \Gamma & otherwise \end{cases} \tag{49}$$

where $\Gamma = \Upsilon(t)^T e$.

(49) is a projection algorithm which ensures that $||\hat{W}|| \leq w_m$. The convergence of the parameter estimation scheme is considered in the sequel.

By the property of projection algorithm and for the specific choice of basis function, it is possible to show that the norm of $B(t)$ is bounded.

Using the bound on $B(t)$, an explicit bound for the solution of (48) can be obtained as follows,

$$||\Upsilon(t)|| \leq C_3 e^{-\lambda_2(t-t_0)} + C_3 \frac{B_M}{\lambda_2} \tag{50}$$

where $C_2 = \Upsilon(t_0) > 0$ and $\lambda_2 > 0$ is a positive constant.

Next we want to show that the parameter estimation error $\tilde{W}$ converges to a neighborhood of the origin.

Substituting for $e = \eta + \Upsilon(t)\tilde{W}$, we obtain the dynamics

$$\dot{\tilde{W}} = -\gamma_w \Upsilon(t)^T \tilde{W} - \gamma_w \Upsilon(t)^T \eta$$

$$+ \begin{cases} 0 & if\, ||\hat{W}|| \leq w_m\, or \\ & if\, ||\hat{W}|| = w_m \quad and \quad \hat{W}^T \Upsilon(t)^T e \leq 0 \\ \gamma_w \left(\dfrac{\hat{W}\hat{W}^T}{\hat{W}^T\hat{W}} \right) (\Upsilon(t)^T \Upsilon(t) \tilde{W} + \Upsilon(t)^T \eta) & otherwise \end{cases}$$

To establish the convergence of the parameter estimation, we make the following persistency of excitation assumption.

Assumption 5. The solution of (48) is such that there exist positive constants $T > 0$ and $k_N > 0$ such that

$$\int_t^{t+T} \Upsilon(\tau)^T \Upsilon(\tau) d\tau \geq k_N I_N \tag{51}$$

where I_N is the N-dimensional identity matrix.

By a standard adaptive control argument, the persistency of excitation condition guarantees that the origin of the differential equation

$$\dot{\tilde{W}} = -\gamma_m \Upsilon(t)^T \Upsilon(t) \tilde{W} \tag{52}$$

is an exponentially stable equilibrium. Since $B(t)$ is a bounded function, it is shown that the parameter estimation error is guaranteed to decay exponentially as

$$||\tilde{W}|| \leq \alpha_4 e^{-\lambda_4(t-t_0)} + \frac{|\mu| + L_1 C_s}{\sqrt{2kmc_3}} \tag{53}$$

Hence the parameter estimation error and the redefined state variables, η converge exponentially to an adjustable neighborhood of the origin.

By definition, convergence of η and $\tilde{W}$ to a neighborhood of the origin implies that $||e|| \leq ||\eta|| + ||\Upsilon(t)||||\tilde{W}||$. Substituting for $||\eta||, ||\Upsilon(t)||$ and $\tilde{W}$, we obtain

$$||e|| \leq \alpha_p e^{-\lambda(t-t_0)} + \beta_p \tag{54}$$

where α_p and β_p are positive constants.

The convergence of the error vector, e, implies that the convergence of the prediction error, e_S and the exponential convergence of the closed-loop system to an adjustable neighborhood of the unknown steady-state optimum. We can summarize the above analysis result as follows.

Theorem 3. Consider the model of the density cell and the substrate concentration (12) and (13) in closed-loop with the state prediction (28), the controller (41), the dither signal (42) and the adaptive learning law (49). Assume that

$$\int_t^{t+T} \Upsilon(\tau)^T \Upsilon(\tau) d\tau \geq k_N I_N \tag{55}$$

for positive constants $T > 0$ and k_N where $\Upsilon(t)$ is the solution of (48). Then

- the error dynamics (29) converge exponentially to a small neighborhood of the origin,
- the parameter estimation errors $\tilde{W}$ converge exponentially to small neighborhood of the origin,
- the tracking error from the unknown steady-state, z_S, converges exponentially to a small neighborhood of the origin.

4. SIMULATION RESULTS

We show in this section the simulation results to demonstrate the effectiveness of the proposed adaptive extremum seeking control. To this end we consider the bioreactor with Haldan kinetics,

$$\mu(S) = \left(\frac{\mu_m S}{K_S + S + K_1 S^2} \right)^{1.5} \tag{56}$$

The following parameters and initial states are used in the simulation experiment

$$D = 1, \quad Y = 0.4, \quad K_1 = 0.1, \quad S(0) = 0$$
$$\mu_m = 1, \gamma_w = 100, \quad k_d = k_S = 0.75$$
$$k_z = 0.505, \quad w_m = 1/2, k_4 = k_7 = 1$$
$$k_{S0} = k_{Z0} = \frac{1}{2}, \ \Gamma_2 = 0.1$$

$$d(0) = 1, \quad \Upsilon(0) = 1, \quad \tilde{W}(0) = 1$$

Simulation results are shown in figures 1-3. Figure 1 shows the value of the objective function and its optimum, and it shows the quick convergence of the production rate (objective function) to its optimum. Moreover the figures 2 and 3 shows the convergence of the estimation and prediction error to a small neighborhood of the origin. Finally it is clear that the required control action to steer the system to its optimum is satisfied.

5. CONCLUSION

We have solved the problem of extremum seeking, for a mass structured cell population balance model in a bioreactor. It has been shown when the lyapunov function and designs parameters are well chosen, such that a persistent of excitation condition is satisfied, the proposed adaptive extremum seeking control guarantees the exponential convergence to a neighborhood of its maximum cell density.

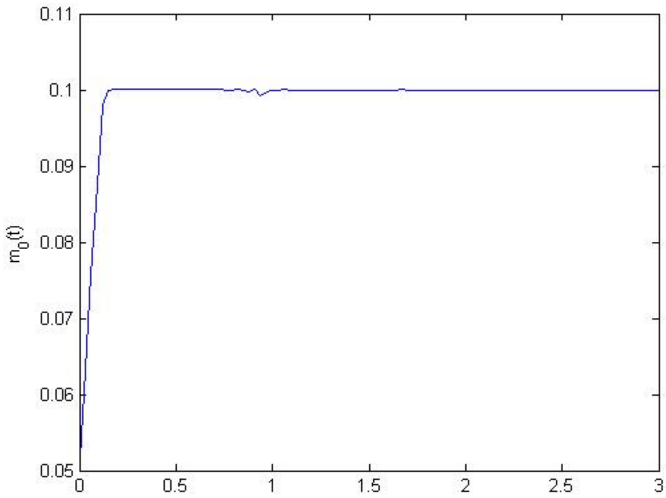

Fig. 1. objective function

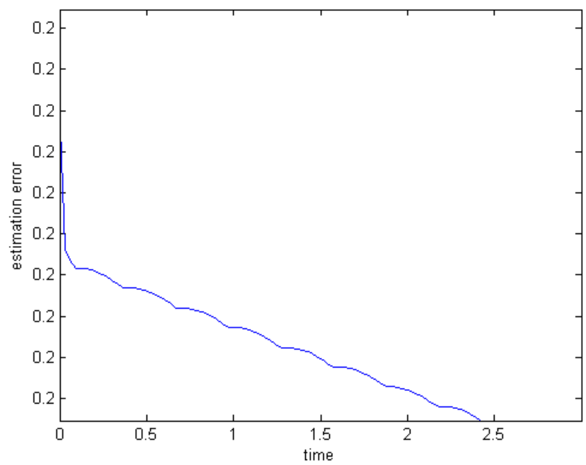

Fig. 2. estimation error

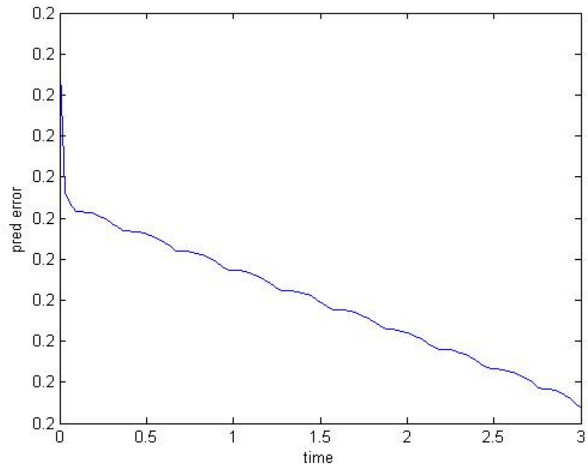

Fig. 3. prediction error

REFERENCES

Zhang,C., and Ordonez,R. (2012). Extremum-Seeking Control and Applications A Numerical Optimization-Based Approach. *Springer*.

Beniich N., Dochain D., (2009). Design and analysis of a nonlinear stabilizing controller for a mass structured cell population balance model with input constraints. *ECC'09, Budapest, Hungary*, August 23-26, pp.1884–1888.

Zhang,T., Guay,M. and Dochain,D. (2002) Adaptive extremum seeking control of continuous stirred tank bioreactors. *IFAC Proceedings*,35, Issue 1,449–454.

Hudon,N. Guay,M., Perrier, M. Dochain, D. (2008) Adaptive extremum-seeking control of convection-reaction distributed reactor with limited actuation. *Computers and Chemical Engineering*,32, 2994–3001.

Zhang,C., and Ordonez,R. (2007). Numerical optimization based extremum-seeking control with application to ABS design. *IEEE Transactions on Automatic Control*, 52, Issue 3,454–467.

Mantzaris N.V., Lio,J.J., Daoutidis,P., and Srienc,F. (1999). Numerical solution of a mass structured cell population balance in an environment of changing substrate concentration. *Journal of Biothechnology*, 71, 157–174.

Mantzaris N.V., Srienc,F., Daoutidis,P., Nonlinear productivity control using a multi-staged cell population balance model. *Chemical Engineering Science*, 57, 1–14.

Mantzaris N.V., Daoutidis,P. (2004). Cell population balance modeling and control in continuous bioreactors. *Journal of Process Control*,14, 775–784.