Maximum-likelihood extremum seeking control of microalgae cultures

Laurent Dewasme * **Alain Vande Wouwer** *
Christian Gabin Feudjio Letchindjio * **Afaq Ahmad** **
Sebastian Engell **

* *Systems, Estimation, Control and Optimization (SECO), University of Mons (UMONS), Belgium (e-mail: laurent.dewasme,alain.vandewouwer@umons.ac.be).*
** *Process Dynamics and Operations Group, Department of Biochemical and Chemical Engineering, TU Dortmund University, Germany (e-mail: afaq.ahmad,sebastian.engell@tu-dortmund.de)*

Abstract: This paper proposes a model-free extremum seeking control (ESC) approach to optimize the productivity of continuous cultures of microalgae, considering the dilution rate and the light intensity as manipulated variables, and the biomass concentration as single measurement. The resulting two-input single-output optimization problem is first solved using a recursive least-squares strategy based on the representation of the process by a Hammerstein block-oriented model. In order to face the presence of noise on the regressor variables (input and output signals), the problem is then reformulated as a maximum-likelihood estimation problem, which is solved on a moving horizon. Simulation results demonstrate the method performance.

Keywords: real-time optimization, optimal control, parameter estimation, least-squares, biotechnology

1. INTRODUCTION

Microalgae cultures in photobioreactors (PBRs) have received a vivid interest because of their numerous applications to the production of nutrients, pharmaceuticals, pigments, cosmetics and third-generation biofuels, as well as for the fixation of CO_2 or wastewater treatment. Process control and optimization often requires a process model. However, cultures of microalgae in PBRs have all the inherent difficulties of biological systems, i.e., their modeling is a difficult task resulting in structural and parametric uncertainties, and on-line measurements are limited. In this context, real-time optimization (RTO) appears as a well-suited framework, based on a minimal set of on-line measurements defining an objective function which can incorporate economical, safety or quality constraints (Darby et al., 2011). Furthermore, the consideration of possible model/plant mismatch can also be achieved either by considering robust and/or adaptive RTO techniques such as run-to-run methods (Srinivasan and Bonvin, 2002), or modifier-adaptation (Marchetti et al., 2009; Gao et al., 2016; Ahmad et al., 2019) which modifies the model-based objective function and constraint gradients to match with the true plant. Extremum seeking control (ESC) (Ariyur and Krstic, 2003), a direct input adaptation method transforming the RTO problem into a feedback control problem, presents the second advantage of driving the system to the extremum of the objective function, under a few assumptions on the problem convexity, without the need for a process model. We refer the reader to the following review papers for more details on ESC and its application to bioprocesses (Dewasme and Vande Wouwer, 2020; Tan et al., 2010).

Perturbation-based ESC is however particularly affected by the time-scale separation between the process dynamics, the perturbation frequency and the estimation/adaptation rate. When applied to a bioprocess with large time constants such as microalgae cultures, ESC converges extremely slowly, which constitutes a serious drawback. This was demonstrated in Dewasme et al. (2017) where ESC is applied to two specific microalgae strains using the classical estimation scheme based on the combination of a high-pass and low-pass filters. In order to overcome the time-scale separation, other estimation schemes have been proposed, for instance recursive least squares (Dewasme et al., 2009, 2011), which avoids using filters and the selection of cut-off frequencies. In Feudjio Letchindjio et al. (2019), recursive least squares estimation is combined with a Hammerstein representation of the process, where the static map is a quadratic function approximating the cost function. This method allows a significant acceleration of the convergence of the ESC. These results are validated experimentally in Feudjio Letchindjio et al. (2020).

In all these previous studies, irradiance is considered either as a fixed operating condition which is not optimized, or a possible step-wise varying disturbance. As stated in Bernard (2011), microalgal cells are photo-acclimating at a specific light intensity and their growth is varying as a convex Haldane function, describing activation and inhibition respectively at low and high light intensities, and therefore presenting an extremum. It is thus legitimate to manipulate the light intensity in laboratory PBRs in order to optimize the microalgae productivity. This work addresses the two-input-single-output optimization problem using a Hammerstein representation of the bioprocess and a parameter estimation approach to compute on-line the gradient of the cost function. In a first step, the estimation problem is formulated as a recursive least squares problem. However, the presence of measurement noise affects the regressor and leads to biased results. In a second step, the problem is therefore

solved using a maximum likelihood estimator on a moving horizon.

This paper is organized as follows. Section 2 describes the proposed multivariable extremum seeking strategy based on RLS or MLE. Section 3 presents the dynamic model of the microalgae cultures and the results of the application of the control strategy are discussed in section 4. Concluding remarks end this paper in section 5.

2. MULTIVARIABLE ESC

We consider an input-affine nonlinear dynamic system such as:

$$\dot{x} = f(x) + u\, g(x) \tag{1a}$$
$$y = Cx \tag{1b}$$
$$J = h(y(x), u) \tag{1c}$$

where $x \in \Re^n$ is the state variable vector, $u \in \Re^r$ the input vector, $y \in \Re^m$ the measured output vector, C the $m \times n$ measurement matrix representing the dynamics of the sensor, J the cost function to be maximized, and where the following necessary conditions of optimality (NCO), are fulfilled, considering nonlinear functions $f : \Re^n \to \Re^n$ and $h : \Re^{n\times r} \to \Re$.

***Assumption** 1. There exists a unique optimal input vector u^* such that $\nabla_u h(y(x_{ss}), u_{ss})_{x_{ss}=x^*, u_{ss}=u^*} = 0$ where x_{ss} and u_{ss} are steady-state values, that is $f(x_{ss}) + u_{ss} g(x_{ss}) = 0$, in a set $U = \{u = u_{ss} | u_{min} \leq u_{ss} \leq u_{max}\}$.*

***Assumption** 2. The steady-state objective function $J_{ss} = h(y(x_{ss}), u_{ss})$ is such that $\nabla_u^2 h(y(x_{ss}), u_{ss})$ is negative-definite at u^*.*

The first assumption relates to the existence of a unique couple of minimizers x^* and u^* under achievable steady-state conditions, that is, only for the input set U, while the second assumption states that the steady-state objective function is convex with a unique maximum. It must be noticed that, in the following, $J_{ss} = h(y(x_{ss}), u_{ss})$ is also assumed to be continuously differentiable.

In the following case study, a multi input single output system (MISO) is considered and the next assumption as well as upcoming developments therefore address the specific MISO case.

***Assumption** 3. The nonlinear system (1) can be approximated by a Hammerstein structure shown in Figure 1, separating the static relation $x(u)$ from the dynamics $y(x(u))$.*

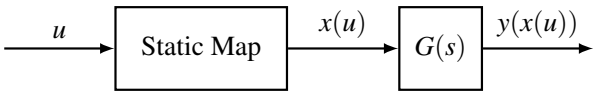

Fig. 1. Hammerstein representation of nonlinear system (1)

A first order static map is considered and reads:

$$x = b + m_1\, u_1 + m_2\, u_2 \tag{2}$$

The first-order dynamics are represented as:

$$G(s) = \frac{1}{1+\tau s} \tag{3}$$

where τ is the time constant and s stands for the Laplace variable. Since these dynamics are usually created by the use of a sensor, delivering discrete measurements at a specific sampling rate, it is legitimate to consider an equivalent discrete representation using the matched pole-zero method:

$$G(z) = \frac{K_1}{z-\alpha} \tag{4}$$

where $\alpha = e^{-\frac{T_s}{\tau}}$, T_s being the sampling period and $K_1 = 1-\alpha$.

The input-output map can therefore be written:

$$y(t) = K_1\, b + K_1\, m_1\, u_1(t-1) + K_1\, m_2\, u_2(t-1) + \alpha\, y(t-1) \tag{5}$$

and the gradient of J reads:

$$\begin{aligned}\nabla_u h(y,u) &= \left(y + u_1 \frac{\partial y}{\partial u_1}, u_1 \frac{\partial y}{\partial u_2}\right) \\ &= \left(y + u_1 \frac{\partial y}{\partial x}\frac{\partial x}{\partial u_1}, u_1 \frac{\partial y}{\partial x}\frac{\partial x}{\partial u_2}\right) \\ &= \left(y + u_1 \frac{\partial y}{\partial x}\, m_1, u_1\, \frac{\partial y}{\partial x}\, m_2\right)\end{aligned} \tag{6}$$

where an estimation of $\frac{\partial y}{\partial x}$ is proposed as:

$$\widehat{\frac{\partial y}{\partial x}} = \frac{y}{m_1 u_1 + m_2 u_2 + b} \tag{7}$$

In (Feudjio Letchindjio et al., 2018), the authors developed a recursive least-squares extremum seeking (RLS-ES) based on a Hammerstein representation of a single-input single-output system where the dilution rate is manipulated. The current study considers the extension of the method to the multivariable case, manipulating both the dilution rate and light irradiance. A RLS estimator with forgetting factor (Landau and Dugard, 1986) is first considered in the ESC loop in Figure 2:

$$e(t) = y(t) - \Phi(t-1)^T \theta(t-1) \tag{8a}$$
$$P(t) = \frac{1}{\lambda}\left[P(t-1) - \frac{P(t-1)\phi(t-1)\phi(t-1)^T P(t-1)}{\lambda + \phi(t-1)^T P(t-1)\phi(t-1)}\right] \tag{8b}$$
$$\theta(t) = \theta(t-1) + P(t)\phi(t-1)e(t) \tag{8c}$$

with

$$\Phi(t-1)^T = [1\ y(t-1)\ u_1(t-1)\ u_2(t-1)] \tag{9a}$$
$$\theta^T = [K_1 b\ \alpha\ K_1 m_1\ K_1 m_2] \tag{9b}$$

where e is the estimated output error, P is the covariance matrix of the estimation error and λ is the forgetting factor. The dither signal is designed as $d = [d_1, d_2]$, $d_1 = A_1 sin(\omega_1 t) + A_2 sin(\omega_2 t)$ and $d_2 = A_3 sin(\omega_3 t) + A_4 sin(\omega_4 t)$. Estimates of the parameters can therefore be obtained as follows:

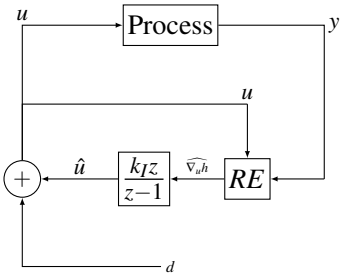

Fig. 2. Extremum seeking with a recursive estimator (RE).

$$\hat{\alpha} = \theta_2 \tag{10a}$$
$$\hat{K_1} = 1 - \theta_2 \tag{10b}$$
$$\hat{b} = \frac{\theta_1}{1-\theta_2} \tag{10c}$$
$$\hat{m_1} = \frac{\theta_3}{1-\theta_2} \tag{10d}$$
$$\hat{m_2} = \frac{\theta_4}{1-\theta_2} \tag{10e}$$

In order to avoid numerical issues due to the possible denominator cancellation of several elements of (10), an orthogonal projection, as suggested in Guay and Burns (2017), is used to force the parameters to remain in an uncertainty ball defined by the norm $\|\theta\| < L$. For more information, the reader may refer to Goodwin and Sin (1984). The inputs are assumed to belong to a set U defined by lower u_{min} and upper u_{max} values delimiting the optimum stable steady-state region of $J = h(y,u)$. However, since the current ES strategy is assumed to be model-free, the only way to force the calculated inputs to remain in U is (i) to apply a sufficiently high dither signal magnitude as suggested in Tan et al. (2009) and Bastin et al. (2009) and (ii) to include gradient estimation saturations ensuring that the dither signal is always able to keep the estimator, in average, in the stable region of the steady-state map optimum, such that:

$$\nabla_{min} < \widehat{\nabla_u h} < \nabla_{max} \tag{11}$$

A practical design of ∇_{min} and ∇_{max} is discussed further in the result sections.

Another difficulty stems from stochastic perturbations, which will corrupt the measurement signal $y(t)$ but also the regressor which uses past values of the measurements and the inputs. In this situation, where the regressor is not perfectly known, the parameter estimates provided by RLS are biased and in turn, the gradient estimation. It is therefore necessary to resort to maximum likelihood estimation (MLE), taking account of the presence of noise on the regressor. For linear models, a MLE algorithm has been proposed in a completely different context in (Bogaerts et al., 2003). The cost function to minimize can be formulated as:

$$L_{MLE} = \frac{1}{2}\sum_{t=1}^{M} \frac{e^2(t)}{\sigma^2(t) + \theta^T \Sigma(t) \theta} \tag{12a}$$
$$e(t) = y(t) - \Phi(t-1)^T \theta(t-1) \tag{12b}$$

where Σ is the covariance matrix of the perturbations acting on the regressor variables and σ is the variance of the measurement noise. This cost function is based on a set of M measurements and has to be minimized using a nonlinear programming solver. This is not an issue in the present context as the sampling process leaves plenty of time for the optimization. In practice, it is suggested to proceed with the optimization of (12a) over a moving horizon of M measurements at each sampling time T_s. To monitor the evolution of the numerical optimization, an approximation of the covariance matrix of the parameter estimation error is given by (Bogaerts et al., 2003):

$$P \approx \left(\sum_{t=1}^{M} \frac{\hat{x}_M(t) \hat{x}_M^T(t)}{\sigma^2(t) + \hat{\theta}_M^T \Sigma(t) \hat{\theta}_M} \right)^{-1} \tag{13a}$$
$$\hat{x}_M(t) = x(t) + \Sigma(t) \hat{\theta}_M \hat{\lambda}_M(t) \tag{13b}$$
$$\hat{\lambda}_M(t) = \frac{e(t)}{\sigma^2(t) + \hat{\theta}_M^T \Sigma(t) \hat{\theta}_M} \tag{13c}$$

where $\hat{x}_M$, $\hat{\lambda}_M$ and θ_M are respectively the state, Lagrange multiplier and parameter estimate vectors of the *MLE* optimization over a horizon M.

3. PROCESS ANALYSIS

3.1 Dynamic model

We consider the 4-state dynamic model proposed in (Bernard, 2011) and identified for the microalgae *Scenedesmus obliquus* in (Deschênes and Vande Wouwer, 2016), accounting for photo-inhibition and photo-acclimation:

$$\begin{aligned} \dot{X} &= \mu X - DX - RX \\ \dot{S} &= -\rho X + D(S_{in} - S) \\ \dot{Q} &= \rho - \mu Q \\ \dot{I}^* &= \delta\mu(\bar{I} - I^*) \end{aligned} \tag{14}$$

where X, S and Q are respectively the biomass, substrate (nitrate) and internal quota (representing the nutriment storage inside the cell). I^* is a conceptual variable representing the light at which the cells are photo-acclimated. S_{in} is the inlet substrate concentration. D, the dilution rate and I, the incident light intensity, are considered as the two process inputs.

The complex kinetics are defined by:

$$\begin{aligned} \gamma(I^*) &= \gamma_{max} \frac{k_{I^*}}{k_{I^*} + I^*} \\ Chl &= \gamma(I^*) X Q = \theta X \\ \lambda &= (aChl + bX + c)L \\ \bar{I} &= I \frac{K_{att}}{K_{att} + \lambda} \\ \bar{\bar{\mu}} &= \mu_{max} \left[\frac{\bar{I}}{\bar{I} + \frac{K_{sI^*}}{\theta} + \bar{I}^2 \frac{exp(Chl\frac{L}{2})}{K_{il}}} \right] \\ \mu &= \bar{\bar{\mu}} \left(1 - \frac{Q_0}{Q} \right) \\ \rho &= \rho_{max} \frac{S}{K_S + S} \left(1 - \frac{Q}{Q_1} \right) \end{aligned} \tag{15}$$

Table 1. Parameter values of model (14-15) for *Scenedesmus obliquus* (Deschênes and Vande Wouwer, 2016)

Parameters	*Values*
μ_{max}	1.47 d^{-1}
ρ_{max}	0.7 gN gC^{-1} d^{-1}
γ_{max}	1.1 gChl gN^{-1}
k_{I^*}	1970 μE m^{-2} s^{-1}
a	17348 m^2 $gChl^{-1}$
b	327 m^{-1}
c	0.14
K_{att}	1.22 μE m^{-2} s^{-1}
K_{sI^*}	0.22 μE m^{-2} s^{-1}
K_{iI}	700 μE m^{-2} s^{-1}
Q_0	0.011 gN gC^{-1}
Q_1	0.099 gN gC^{-1}
K_S	0.09 gN m^{-3}
I	60 μE m^{-2} s^{-1}
δ	1.8
R	0.028 d^{-1}
L	0.2 m^{-1}
S_{in}	0.12 gN m^{-3}

where *Chl* is the chlorophyll concentration and all the remaining parameter values are presented in Table 1.

Biomass productivity is the optimization objective function to be maximized and defined as $J = D\,X$.

3.2 Steady-state map

A bifurcation analysis of a similar model was achieved in (Dewasme et al., 2017) for a constant light intensity level (i.e., the SISO case where I is fixed). This analysis is now extended to the TISO case. Referring to Figure 3, the steady-state map is a smooth and convex function of the dilution rate D and the light intensity I, which has a maximum, fulfilling assumptions 1 and 2.

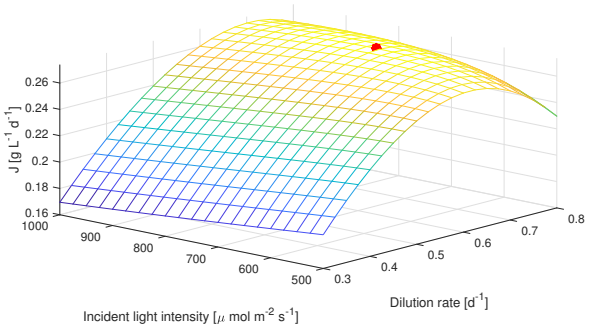

Fig. 3. Steady-state map showing the biomass productivity J as a function the inputs D and I. The red star indicates the optimum.

The optimum is located in $J = 0.274\ g\ L^{-1}\ d^{-1}$ and the input maximizers are $u^* = \left[0.676\ d^{-1}\ \ 732.491\ \mu mol\ m^{-2}\ s^{-1}\right]$. The following observations can be made:

- There exist two kinds of equilibria: the wash-out steady-state (where $X_{ss} = 0$ and $S_{ss} = S_{in}$) and a complex manifold, function of the steady-state input values, containing the optimum. In the following, we denote the corresponding regions respectively as wash-out and optimum stable steady-state regions;
- A numerical stability analysis can be achieved and leads to the results of Figure 4, where the eigenvalues of the Jacobian of $f(x)$, $Jac = \frac{\partial f}{\partial x}$, are represented by contour diagrams, functions of the steady-state input values.
- While the optimum is contained in the left stable region, it may be observed that system operation beyond $D = 1\ d^{-1}$, independently of I, can however lead to the wash-out region of attraction. Indeed, the first two eigenvalue diagrams, related to X and S, clearly shows a boundary (in red) separating both stable regions. This statement is supported by Figure 5 where the contours of the objective function J are indeed dropping to 0 (shown as "< 0.02") beyond the unstable boundary.

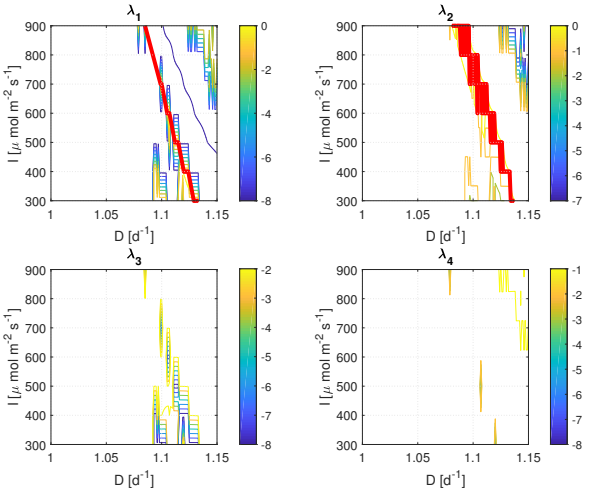

Fig. 4. Contours of the evolution of the eigenvalues of the Jacobian of $f(x)$: λ_1 to λ_4 are respectively related to X, S, Q and I^*. The red zones represent the positive contours (unstable regions), separating the λ_1 and λ_2 diagrams in two stable regions.

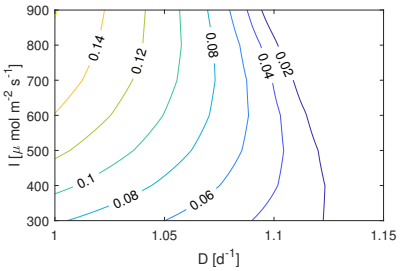

Fig. 5. Contours of the evolution of the objective J as a function of the inputs D and I.

4. MICROALGAE PRODUCTIVITY OPTIMIZATION

ESC with the RLS estimator is first applied in a noise-free ideal case with the parameters defined in Table 2.

Figures 6 and 7 show the performance of the strategy in 5 different simulation runs started with random input initial conditions (i.e., random initializations on the steady-state map). The algorithm converges within 10 days to the neighborhood of the objective function (J) maximum, which is a remarkable performance considering *SISO* results (Feudjio Letchindjio et al., 2018, 2019) converging within 10 to 20 days. The light intensity

Table 2. Discrete RLS-ES control strategy - parameter design

Parameters	*Values*
k_I	$[0.15\ 8\cdot10^4]$
λ	0.95
L	10
A_1	0.1
A_2	0.05
ω_1	2
ω_2	1
A_3	50
A_4	25
ω_3	3.5
ω_4	2.5
∇_{min}	$[-0.25\ \ -0.005]$
∇_{max}	$[0.1\ 0.005]$

may however require more time to reach the optimum due to the flatness (i.e., small gradient) of the map, reflected in the corresponding components of ∇_{min} and ∇_{max}. The latter are also designed such that the upper gradient limit related to D is set to an absolute smaller value (0.1) than the corresponding lower limit (-0.25) in order to ensure that the estimator remains in the optimum stable steady-state region. In this connection, the magnitudes of the dither signal components are taken sufficiently large, as recommended in Bastin et al. (2009), but also sufficiently small to not alter the convergence accuracy (see Chioua et al. (2007) for more details about the convergence of ESC algorithms in the particular case of Hammerstein systems).

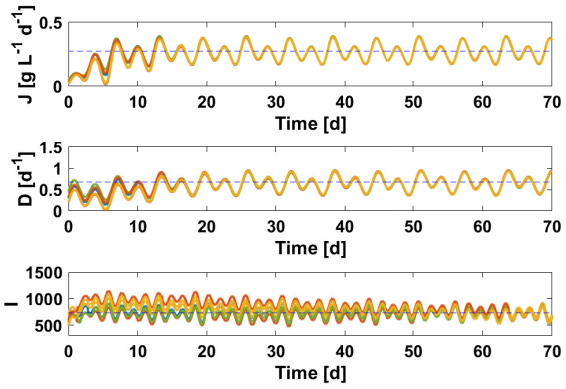

Fig. 6. RLS-ESC application: evolutions of the inputs and output. Optimal values are shown by the dashed lines.

A numerical validation of the proposed MLE Extremum Seeking ($ML-ES$) method is shown in Figures 8 and 9 for a relative standard deviation of the noise of 5 % acting on both the input and output signals (we consider in this way that the manipulation of the light or dilution rate could be subject to perturbations), a sampling time of 0.1 *day* and a moving-horizon of 5 samples (half a day).

Except for the dither magnitudes, which are halved, the other parameters selected in Table 2 are kept identical. The method very satisfactorily converges despite the effect of the noise. In a remarkable way, the amplitude of the dither signals could be decreased in such a way that the algorithm would be able to converge only thanks to the persistence of excitation provided by the natural perturbations (not shown in this paper). The evolution of the gradient components, shown in Figure 10, confirm that a close neighborhood of the optimum is attained

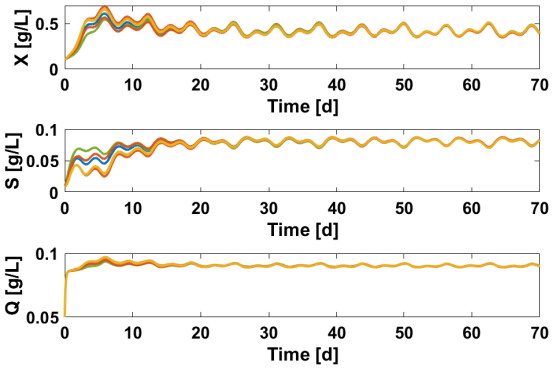

Fig. 7. RLS-ESC application: evolutions of the biomass, substrate and internal quota concentrations.

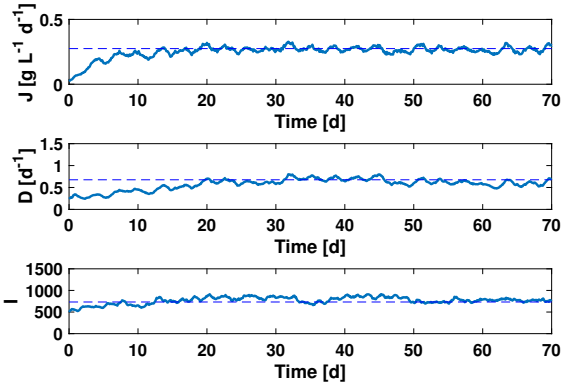

Fig. 8. ML-ESC application with noise corrupting the input/output signals: time evolution of the inputs and output. Optimal values are shown by the dashed lines.

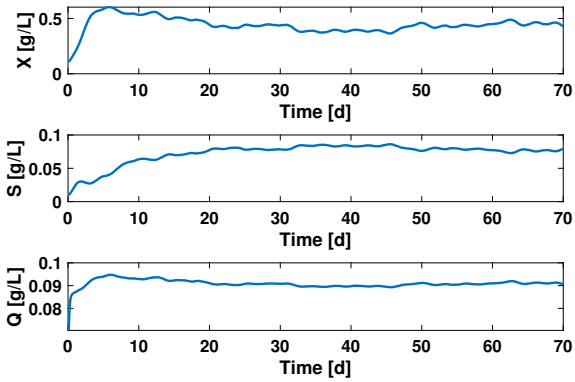

Fig. 9. ML-ESC application with noise corrupting the input/output signals: time evolution of the biomass, substrate and internal quota.

and maintained despite the absence of gradient bounds in the algorithm implementation.

5. CONCLUSION

This study investigates the use of the light irradiance as a second manipulated variable in the real-time optimization of continuous cultures of microalgae. A simple recursive least squares

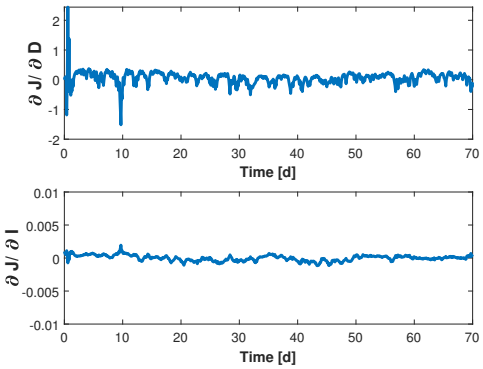

Fig. 10. ML-ES application with noise corrupting the input/output signals: evolution of the gradient components.

estimator based on a Hammerstein model allows developing an efficient extremum seeking algorithm, which however suffers from the effect of noise on the regressor variables. A maximum-likelihood receding horizon estimator is therefore used instead, which gives excellent convergence properties. Obviously, the dilution rate triggers faster dynamics than the light irradiance, which leads to photo-acclimation or photo-inhibition depending on the light intensity. Also, the relatively flat steady-state map with respect to light explains the slower convergence of the ESC scheme. Future research prospects include the consideration of a recursive version of the maximum likelihood estimator and experimental validation of the multivariable ESC with a laboratory-scale microalgae PBR.

ACKNOWLEDGEMENTS

This work was supported by the Fonds de la Recherche Scientifique – FNRS under Grant 2020/V 3/5/125 - 40001546 - JG/JN - 2217, allowing the sabbatical stay of Laurent Dewasme in the Process Dynamics and Operations Group of Prof. Sebastian Engell, Department of Biochemical and Chemical Engineering, TU Dortmund University, Germany.

REFERENCES

Ahmad, A., Gao, W., and Engell, S. (2019). A study of model adaptation in iterative real-time optimization of processes with uncertainties. *Computers and Chemical Engineering*, 122, 218–227.

Ariyur, K.B. and Krstic, M. (2003). *Real-time Optimization by Extremum-seeking Control*. John Wiley & Sons, INC, wiley-interscience edition.

Bastin, G., Nesic, D., Tan, Y., and Mareels, I. (2009). On extremum seeking in bioprocesses with multivalued cost functions. *Biotechnol Progress*, 25, 683–689.

Bernard, O. (2011). Hurdles and challenges for modelling and control of microalgae for co2 mitigation and biofuel production. *Journal of Process Control*, 21, 1378–1389.

Bogaerts, P., Delcoux, J., and Hanus, R. (2003). Maximum likelihood estimation of pseudo-stoichiometry in macroscopic biological reaction schemes. *Chemical Engineering Science*, 58, 1545–1563.

Chioua, M., Srinivasan, B., Guay, M., and Perrier, M. (2007). Dependence of the error in the optimal solution of perturbation-based extremum seeking methods on the excitation frequency. *The Canadian Journal of Chemical Engineering*, 85, 447–453.

Darby, M.L., Nikolaoub, M., Jones, J., and Nicholson, D. (2011). Rto: An overview and assessment of current practice. *Journal of Process Control*, 21, 874–884.

Deschênes, J.S. and Vande Wouwer, A. (2016). Parameter identification of a dynamic model of cultures of microalgae scenedesmus obliquus - an experimental study. *IFAC-PapersOnLine*, 49(7), 1050–1055.

Dewasme, L., Srinivasan, B., Perrier, M., and Vande Wouwer, A. (2011). Extremum-seeking algorithm design for fed-batch cultures of microorganisms with overflow metabolism. *J. Process Control*, 21(7), 1092–1104.

Dewasme, L. and Vande Wouwer, A. (2020). Model-free extremum seeking control of bioprocesses: A review with a worked example. *Processes*, 8(10), 1209.

Dewasme, L., Vande Wouwer, A., Srinivasan, B., and Perrier, M. (2009). Adaptive extremum-seeking control of fed-batch cultures of micro-organisms exhibiting overflow metabolism. In *Inproceedings of the ADCHEM conference in Istanbul (Turkey)*.

Dewasme, L., Letchindjio, C.G.F., Zuniga, I.T., and Wouwer, A.V. (2017). Micro-algae productivity optimization using extremum-seeking control. In *2017 25th Mediterranean Conference on Control and Automation (MED)*, 672–677. IEEE.

Feudjio Letchindjio, C.G., Deschenes, J.S., Dewasme, L., and Vande Wouwer, A. (2018). Extremum seeking based on a hammerstein-wiener representation. *IFAC-PapersOnLine*, 51(18), 744–749.

Feudjio Letchindjio, C.G., Dewasme, L., and Vande Wouwer, A. (2020). An experimental application of extremum seeking control to cultures of the microalgae scenedesmus obliquus in a continuous photobioreactor. *Int J Adapt Control Signal Process.*, 1–13. Https://doi.org/10.1002/acs.3196.

Feudjio Letchindjio, C.G., Dewasme, L., Deschênes, J.S., and Vande Wouwer, A. (2019). An extremum seeking strategy based on block-oriented models: Application to biomass productivity maximization in microalgae cultures. *Industrial and Engineering Chemistry Research*, 58(30), 13481–13494.

Gao, W., Wenzel, S., and Engell, S. (2016). A reliable modifier-adaptation strategy for real-time optimization. *Computers and Chemical Engineering*, 91, 318–328.

Goodwin, G. and Sin, K. (1984). *Adaptive filtering prediction and control*. Prentice Hall, New Jersey: Dover.

Guay, M. and Burns, D.J. (2017). A proportional integral extremum-seeking control approach for discrete-time nonlinear systems. *International Journal of Control*, 90(8), 1543–1554.

Landau, I.D. and Dugard, L. (1986). *Commande adaptative. Aspects pratiques et théoriques.* Masson, Paris.

Marchetti, A., Chachuat, B., and Bonvin, D. (2009). Modifier-adaptation methodology for real-time optimization. *Industrial & Engineering Chemistry Research*, 48(13), 6022–6033.

Srinivasan, B. and Bonvin, D. (2002). Interplay between identification and optimization in run-to-run optimization schemes. In *American Control Conference, Anchorage, AK*, 2174–2179.

Tan, Y., Moase, W., Manzie, C., Nesic, D., and Mareels, I. (2010). Extremum seeking from 1922 to 2010. In *Proceedings of the 29th Chinese Control Conference*, 14–26.

Tan, Y., Nesic, D., Mareels, I., and Astolfi, A. (2009). On global extremum seeking in the presence of local extrema. *Automatica*, 45, 245–251. Brief Paper.