Preprints of the 12th IFAC Symposium on Computer Applications in Biotechnology
The International Federation of Automatic Control
16-18, 2013, December. Mumbai, India

Design of Optimal Experiments for Parameter Estimation of Microalgae Growth Models ⋆

Rafael Muñoz-Tamayo * **Pierre Martinon** ** **Gaël Bougaran** *** **Francis Mairet** * **Olivier Bernard** *,****

* *BIOCORE-INRIA, BP93, 06902 Sophia-Antipolis Cedex, France (e-mail: {rafael.munoz_tamayo, francis.mairet, olivier.bernard}@inria.fr).*
** *Commands INRIA Saclay, Ecole Polytechnique, CMAP 91128 Palaiseau, France. (e-mail: pierre.martinon@inria.fr)*
*** *Ifremer, Laboratoire Physiologie et Biotechnologie des Algues, rue de l'île d'Yeu BP 21105 44311 Nantes cedex 3, France (e-mail: gael.bougaran@ifremer.fr)*
**** *LOV-UPMC-CNRS, UMR 7093, Station Zoologique, B.P. 28 06234, Villefranche-sur-mer, France*

Abstract: Mathematical models are expected to play a pivotal role for driving microalgal production towards a profitable process of renewable energy generation. To render models of microalgae growth useful tools for prediction and process optimization, reliable parameters need to be provided. This reliability implies a careful design of experiments that can be exploited for parameter estimation. In this paper, we provide guidelines for the design of experiments with high informative content that allows an accurate parameter estimation. We study a real experimental device devoted to evaluate the effect of temperature and light on microalgae growth. On the basis of a mathematical model of the experimental system, the optimal experiment design problem was solved as an optimal control problem. E-optimal experiments were obtained by using two discretization approaches namely sequential and simultaneous. The results showed that an adequate parameterization of the experimental inputs provided optimal solutions very close to those provided by the simultaneous discretization. Simulation results showed the relevance of determining optimal experimental inputs for achieving an accurate parameter estimation.

Keywords: biofuel, microalgae, model calibration, optimal control, optimal experiment design

1. INTRODUCTION

Microalgae have received a specific attention in the framework of renewable energy generation (Williams and Laurens, 2010). However, the assessment whether a microalgae species is a promising candidate for biofuel production in large scale cultivation is a difficult task since microalgae growth is driven by multiple factors including light intensity, temperature and pH. Mathematical modelling is thus required for quantifiying the effect of environmental factors on microalgae dynamics. To render mathematical models of microalgae growth useful tools to predict and optimize large scale systems, dedicated experiments are needed to provide data with high informative content for the model calibration stage. Providing accurate parameters is crucial since model-based optimality migth be sensitive to parameters values as shown in Muñoz-Tamayo et al. (2013).

In this paper, we address the problem of optimal experiment design (OED) for parameter estimation (see, *e.g.*, Walter and Pronzato (1997)) of microalgae models. The problem is formulated as an optimal control problem (see,*e.g.* Banga et al. (2002); Chianeh et al. (2011)) and solved numerically. The model under investigation describes the effect of temperature and light on microalgae growth. The model represents an experimental device for microalgae cultivation under batch mode. The apparatus consists of 18 photobioreactors located inside an incubator (Marchetti et al., 2012). This device named as the TIP allows to regulate in each photobioreactor the temperature, pH and light intensity (see Fig. 1). The simulation results presented in this paper are meant to provide guidelines for efficient experimental protocols in the TIP system.

⋆ This work benefited from the support of the Facteur 4 research project founded by the French National Research Agency (ANR).

2. MATHEMATICAL MODEL

Microalgae growth is strongly affected by temperature and light. Temperature has a homogeneous effect on uptake and growth rates (Geider, 1987), while light affects the rate of carbon assimilation during photosynthesis. In the model, the effects of light and temperature will be represented, respectively, by the factors ϕ_I, ϕ_T, described as

$$\phi_I = \frac{I}{I + K_{sI} + I^2/K_{iI}} \tag{1}$$

$$\phi_T = \begin{cases} 0, & T < T_{\min} \\ \dfrac{(T - T_{\max})(T - T_{\min})^2}{(T_{\text{opt}} - T_{\min})\left[(T_{\text{opt}} - T_{\min})(T - T_{\text{opt}}) - (T_{\text{opt}} - T_{\max})(T_{\text{opt}} + T_{\min} - 2T)\right]}, & T \in [T_{\min}, T_{\max}] \\ 0, & T > T_{\max}. \end{cases} \tag{2}$$

The effect of light (ϕ_I) is represented by a Haldane type kinetics that accounts for photoinhibition (Peeters and Eilers, 1978). The effect of temperature is described by the cardinal model developed for bacteria by Rosso et al. (1993) and validated for microalgae by Bernard and Remond (2012). Model parameters are defined in Table 1.

For microalgae organisms, the uptake of nutrients is uncoupled to cell growth. This mechanism is described by the cell quota model developed by Droop (1968), in which the growth rate is regulated by the concentration of a limiting nutrient. In our study, we consider the nitrogen to be such a nutrient.

Under the above assumptions, by applying mass balances for a batch system, we obtain the following equations (Bernard, 2011; Bernard and Remond, 2012)

$$\dot{s} = -\rho(\cdot)x, \tag{3}$$

$$\dot{q_n} = \rho(\cdot) - \mu(\cdot)q_n, \tag{4}$$

$$\dot{x} = \mu(\cdot)x, \tag{5}$$

where s (mg N/L) is the extracellular nitrogen concentration and x (mg C/L) is the concentration of carbon biomass. The term q_n (g N / g C) denotes the internal nitrogen quota, that is the concentration of substrate per biomass unit.

The nitrogen uptake rate (ρ) is modeled by a Michaelis-Menten kinetics including the effect of temperature and a regulation term by the internal quota.

$$\rho(\cdot) = \bar{\rho}\frac{s}{s + K_s}\left(1 - \frac{q_n}{Q_l}\right)\phi_T. \tag{6}$$

If the experiment is carried out at low cellular concentration, it is plausible to assume that light is homogeneous along the depth of the photobioreactor. Following the Droop model (Droop, 1968), the growth rate is described by

$$\mu(\cdot) = \tilde{\mu}\left(1 - \frac{Q_0}{q_n}\right)\phi_I\phi_T, \tag{7}$$

with $\tilde{\mu}$ is the theoretical maximal growth rate and Q_0 is the minimal quota.

It must be noticed that an experimental protocol can be designed under conditions of non-limiting nutrients to allow the cells to grow in exponential phase with a maximal nitrogen quota. In this case, the model represented by equations (3)-(5) can be simplified to

$$\dot{x} = f(x, \boldsymbol{\theta}, t) = \mu_{\max} x \phi_I \phi_T, \; x(0) = x_0, \tag{8}$$

with $\boldsymbol{\theta}$ the parameter vector defined by

$$\boldsymbol{\theta} = [\mu_{\max},\ K_{sI},\ K_{iI},\ T_{\min},\ T_{\max},\ T_{\text{opt}}].$$

In (8), $\mu_{\max}$ is the maximal growth rate defined as (Mairet et al., 2011)

$$\mu_{\max} = \tilde{\mu}\left(1 - \frac{Q_0}{Q_m}\right), \tag{9}$$

with Q_m the maximal quota.

As a first approach, we will use the reduced model described in (8) to tackle the optimal experiment design problem. Table 1 shows the model parameters. They correspond to the microalgae *Isochrysis* aff. *galbana*. Parameter values were mainly taken from Mairet et al. (2011) and Muñoz-Tamayo et al. (2013). The values of the model parameters are necessary for solving the OED problem locally as will be explained below.

Table 1. Model parameters.

Parameter	Definition	Value
$\tilde{\mu}$	Theoretical maximal growth rate	2.11 d^{-1}
$\mu_{\max}$	Maximal growth rate	1.18 d^{-1}
$\bar{\rho}$	Maximal uptake rate	0.10 g N (g C d)$^{-1}$
K_s	Nitrogen saturation constant	0.018 g N m^{-3}
K_{sI}	Light saturation constant	150 μE $m^{-2}s^{-1}$
K_{iI}	Light inhibition constant	2000 μE $m^{-2}s^{-1}$
Q_0	Minimal nitrogen cell quota	0.05 g N (g C)$^{-1}$
$T_{\min}$	Lower temperature for microalgae growth	-0.20 °C
$T_{\max}$	Upper temperature for microalgae growth	33.30 °C
T_{opt}	Temperature at which growth rate is maximal	26.70 °C

3. OED PROBLEM FOR PARAMETER ESTIMATION

The problem of OED for parameter estimation consists in designing an experimental protocol that provides data with high informative content to allow an accurate identification of the model parameters. Classical approaches of OED for parameter estimation rely on the optimization of a scalar function of the Fisher information matrix (FIM), since this matrix is the core for the calculation of the confidence intervals of the parameter estimates. In this paper, we use as criterion of optimality the smallest eigenvalue

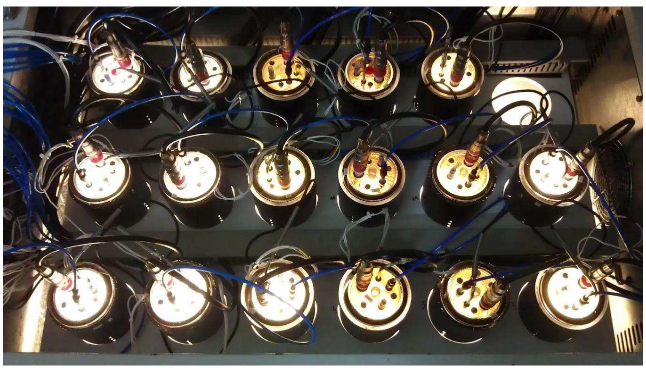

Fig. 1. The TIP system. The device has 18 batch photobioreactors for microalgae cultivation.

($\lambda_{\min}$) of the FIM. Maximizing $\lambda_{\min}$ implies to minimizing the length of the largest axis of the confidence ellipsoids for the parameters (Walter and Pronzato, 1997). The resulting solution of the optimization is called E-optimal.

We consider here a local design approach. Our aim is to design optimal experiments on the basis of a nominal paramater vector $\widehat{\boldsymbol{\theta}}$.

In our case study, the observations correspond to the concentration of biomass. We assume that the vector of measurements collected at time t_i can be modelled as:

$$y(t_i) = y_{\mathrm{m}}(t_i, \boldsymbol{\theta}^*) + \varepsilon, \tag{10}$$

where $y_{\mathrm{m}}(t_i, \boldsymbol{\theta}^*)$ is the deterministic output of the model ($y_{\mathrm{m}}(t_i, \boldsymbol{\theta}^*) = x$) and $\boldsymbol{\theta}^*$ the true value of the parameter vector. The measurement error ε is assumed to follow a normal distribution $\varepsilon \sim \mathbf{N}(0, \sigma^2)$.

For the nominal vector $\widehat{\boldsymbol{\theta}}$, The FIM is computed as

$$\mathbf{F}(\widehat{\boldsymbol{\theta}}) = \frac{1}{\sigma^2} \int_0^{t_{\mathrm{f}}} \left[\frac{\partial y_{\mathrm{m}}}{\partial \boldsymbol{\theta}}\right]^{\mathrm{T}}_{(t_i, \widehat{\boldsymbol{\theta}})} \left[\frac{\partial y_{\mathrm{m}}}{\partial \boldsymbol{\theta}}\right]_{(t_i, \widehat{\boldsymbol{\theta}})} dt. \tag{11}$$

Once the FIM is calculated, the covariance matrix of the estimator can be approximated to

$$\widehat{\mathbf{P}} = \mathbf{F}^{-1}(\widehat{\boldsymbol{\theta}}). \tag{12}$$

The square root η_j of the jth diagonal element of $\widehat{\mathbf{P}}$ is an estimate of the standard deviation of $\widehat{\theta}_j$.

The term in brakets in (11) contains the sensitivity of the output w.r.t. the parameter vector $\boldsymbol{\theta}$. Let $s_j = \frac{\partial y_{\mathrm{m}}}{\partial \theta_j}$ denote the sensitivity of the model output to the parameter θ_j. The dynamics of s_j follows

$$\dot{s}_j = \left[\frac{\partial f}{\partial x}\right]_{(x, \boldsymbol{\theta}, t)} s_j + \left[\frac{\partial f}{\partial \theta_j}\right]_{(x, \boldsymbol{\theta}, t)}, \; s_j(0) = 0. \tag{13}$$

The sensitivity functions were computed automatically with the Matlab Toolbox IDEAS (Muñoz-Tamayo et al., 2009). The toolbox is devoted to estimate parameters of ODE models. It uses symbolic differentitation to calculate the sensitivity functions that are used for the evaluation of the FIM.

The matrix $\mathbf{F}$ is a square matrix of dimension 6×6. Our strategy for solving the OED problem was that of partitioning the full problem into subproblems dedicated to improve the accuracy of the estimation of a couple of parameters, while the other parameters were assumed to be known. In this case, for each subproblem, $\mathbf{F}$ is a square matrix of dimension 2×2. This strategy, also adpoted for estimating cardinal temperatures in *E. coli* (Van Derlinden et al., 2008), aims at reducing the complexity of the optimization problem.

Each subproblem is devoted to the assessment of the effect of temperature or light on microalgae growth. This means that we do not consider a couple determined by one parameter of ϕ_I and one parameter of ϕ_T. Therefore, for the subproblems associated to the temperature parameters, the light was set to $I = 547$ μE m$^{-2}s^{-1}$. For the subproblems describing ϕ_I, the temperature was set to $T = 26.7$ °C. The constant values for I and T correspond to the optimal values for growth.

For each subproblem, the OED problem was formulated as an optimal control problem

$$\begin{aligned} \min_{T(t), I(t)} \quad & -\log(\lambda_{\min}) \\ \text{s.t.} \quad & \\ & T_{\mathrm{L}} = 12 \leq T(t) \leq T_{\mathrm{U}} = 33.2°\mathrm{C} \\ & I_{\mathrm{L}} = 20 \leq I(t) \leq I_{\mathrm{U}} = 1200\ \mu\mathrm{E\ m^{-2}s^{-1}} \\ & \dot{x} = \mu_{\max} x \phi_I \phi_T,\ x(0) = x_0. \end{aligned} \tag{14}$$

A total number of nine subproblems is obtained. Table 2 shows the combination of parameters and the experimental input (T or I) for each subproblem. In practice, the nine solutions will be implemented in duplicates in the TIP. The time of the experiment was set to $t_f = 4$ d.

The optimal problems were solved following two strategies of discretization, namely simultaneous and sequential. The simultaneous method was applied with the open source toolbox Bocop (Bonnans et al., 2012)(`http://bocop.org`). Bocop uses the Ipopt method for performing the optimization (Wächter and Biegler, 2006).The sequential approach, also called control vector parameterization (CVP), was implemented by using the Matlab toolbox SSmGo (`http://www.iim.csic.es/ gingproc/ssmGO.html`). SSmGo performs global optimization by using a scatter search method (Rodríguez-Fernández et al., 2006; Egea et al., 2007). For the CVP approach, the parameterization depicted in Fig. 2 was used.

The experimental inputs are thus defined by four parameters, namely u_1, u_2, t_1, t_2. For the case of the temperature,

Table 2. Subproblems of the OED strategy.

Experiment	couple of parameters	Experimental input
1	$(\mu_{\max}, K_{sI})$	I
2	$(\mu_{\max}, K_{iI})$	I
3	(K_{sI}, K_{iI})	I
4	$(\mu_{\max}, T_{\min})$	T
5	$(\mu_{\max}, T_{\max})$	T
6	$(\mu_{\max}, T_{\mathrm{opt}})$	T
7	$(T_{\min}, T_{\max})$	T
8	$(T_{\min}, T_{\mathrm{opt}})$	T
9	$(T_{\max}, T_{\mathrm{opt}})$	T

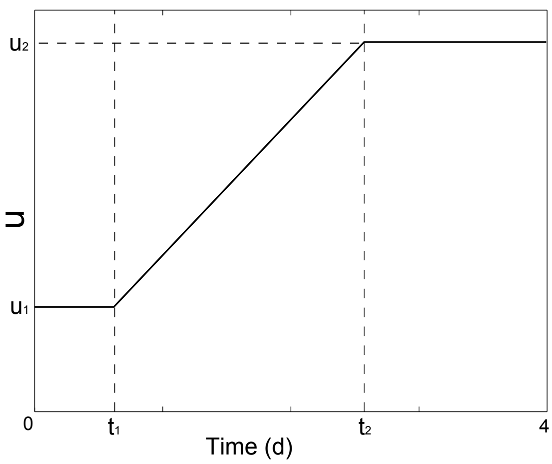

Fig. 2. Parameterization of the experimental inputs u (T, I) for the CVP approach.

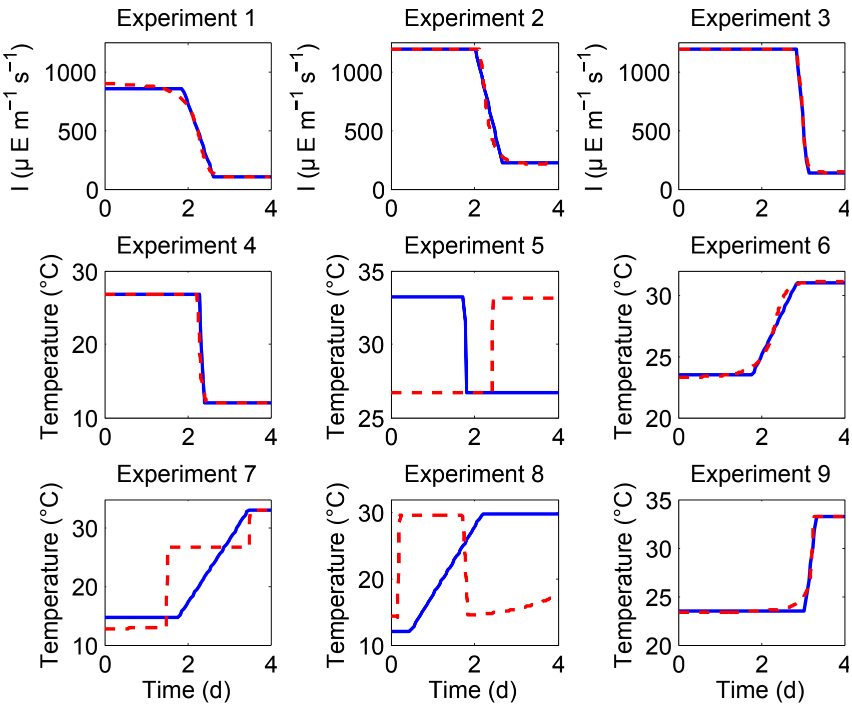

Fig. 3. Optimal experimental inputs given by the CVP approach (solid lines) and the sequential approach (dashed lines).

the rate of change $((u_2 - u_1)/(t_2 - t_1))$ is determined by the thermal dynamics of the equipment. Hence, the rate of temperature change was bounded to $[-5, 15]$ °C h^{-1}. These boundaries, together to those in (14), correspond to the physical boundaries of the TIP system. No boundaries were imposed to the rate of change of light, since it can be changed instantaneously.

4. RESULTS AND DISCUSSION

Figure 3 shows the optimal trajectories of light and temperature obtained with the simultaneous and the CVP approaches. The initial concentration of biomass was set to $x_0 = 10$ mg/L. For the simultaneaous approach, we used a uniform Gauss II (4th order) discretization with 100 time steps. The state and control variables were intialiazed with constant values, and the tolerance for the Ipopt solver was set to 10^{-8}. The controls found with the simultaneous approach are quite close in shape to piecewise linear functions. Overall, the CVP and the simultaneous methods find very similar solutions with the exception of the experiments 7 and 8.

Table 3 compares the optimality cost functions provided by the simultaneous and the CVP methods. For all the experiments, the simultaneaous approach converges to better solutions than the CVP ones. However, the CVP approach provides optimality cost functions very close to those obtained with the sequential approach as shown in Table 3. Only for experiments 5 and 7, the simultaneous solutions outperform substantially the CVP solutions.

It is clear that for the model structure described here, the CVP strategy is a good approach for designing high informative experiments for microalgae growth models.

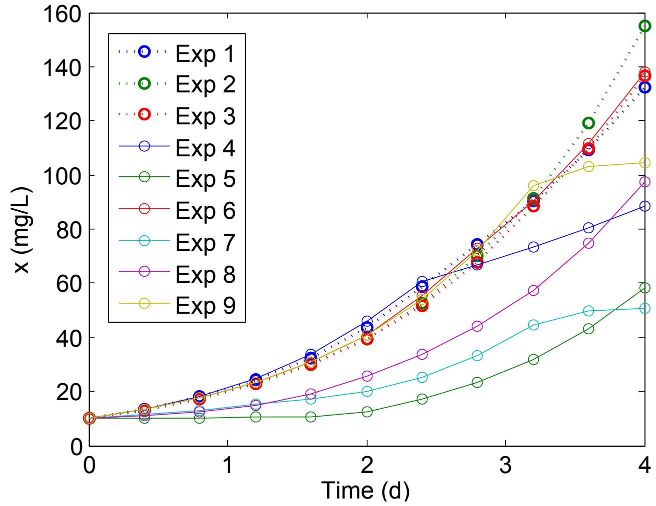

Fig. 4. Dynamics of biomass concentrations for the E-optimal experiments obtained with the CVP approach.

The simulation of the nine E-optimal experiments with the CVP controls is displayed in Fig 4. Note that in the experiments 5,7,9, the biomass concentration exhibits, for a certain time interval, a behaviour close to the steady state. This is due to the fact that the temperature reaches a very close value to $T_{\max}$ and thus the growth rate becomes close zero. When performing the experiments, caution should be made for the selection of the maximal operational temperature. Indeed, an erroneous *a priori* on $T_{\max}$ with a higher value than the real maximal temperature would lead to cell inactivation (Bernaerts et al., 2005).

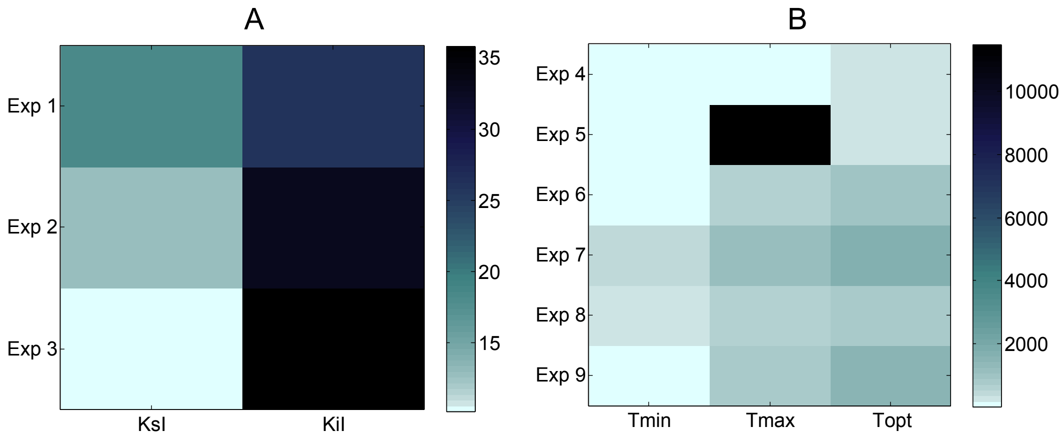

Fig. 5. Overall sensitivity of the biomass concentration to the parameters for the E-optimal experiments. A. Experiments with light variation. B. Experimentes with temperature variation.

Table 3. Comparison of E-optimal strategies.

Experiment	$-\log(\lambda_{\min})$		
	Simultaneous (J_{Sim})	CVP (J_{cvp})	$J_{\text{cvp}}/J_{\text{Sim}}$
1	5.2237	5.2320	1.0016
2	10.9787	10.9851	1.0006
3	8.6528	8.6868	1.0039
4	0.3685	0.3687	1.0005
5	-5.3981	-4.1850	0.7753
6	-2.9686	-2.9592	0.9968
7	-0.3008	-0.1402	0.4661
8	-1.3744	-1.2710	0.9248
9	-3.8131	-3.8053	0.9980

Table 4. Relevance of optimal experiment design on the accuracy of parameter estimation.

	Standard deviation of the parameters	
	Non optimal trajectories	Optimal trajectories
Experiment 3		
K_{sI}	12.005	14.098
K_{iI}	446.950	85.830
Experiment 8 (values in Kelvin units)		
$T_{\min}$	3.091	0.617
T_{opt}	1.400	0.453

A sensitivity analysis was performed by gathering the information of the sensitivities of the nine experiments. It was observed that for the experiments subjected to light variation, the parameter $\mu_{\max}$ was the most influential parameter. For the temperature experiments, the parameters of the cardinal model were all more influential than $\mu_{\max}$.

Figure 5 shows an overall representation of the sensitivity of the biomass to the parameters for the nine experiments. The parameter $\mu_{\max}$ was not included in the graphical representation to highlight the effects of temperature and light on the dynamics of the microalgae biomass. The overall picture reflects the consistency of the optimal solutions considering the whole nine subproblems. For instance, the highest sensitivity K_{sI} is obtained in experiment 1, while the highest sensitivity of K_{iI} is obtained in experiment 3. The importance of photoinhibition is cleary displayed in Fig. 5A. Concerning the experiments with temperature variation (Fig. 5B), it is concluded that the parameter $T_{\max}$ is the most influential parameter.

To assess the relevance of optimal experiment design for estimating accurate parameters, we evaluated the standard deviation of the parameter estimates for non-optimal and optimal inputs for the experiments 3 and 8. According to Fig. 2, the non-optimal inputs were defined with the following parameters: for the temperature $T_1 = 15°\text{C}, T_2 = 28°\text{C}, t_1 = 2.0\text{ d}, t_2 = 2.24\text{ d}$. For the light, $I_1 = 200\ \mu\text{E m}^{-2}\text{s}^{-1}, I_2 = 500\ \mu\text{E m}^{-2}\text{s}^{-1}, t_1 = 2.0\text{ d}, t_2 = 2.08\text{ d}$.

Ten equidistant sampling times were used for the calculation of the standard deviation of the estimates based on the Fisher information matrix. The results are given in Table 4. For the experiment 3, the standard deviation of the parameter K_{sI} provided by optimal solution has the same order of magnitude than that obtained with of the non-optimal solution. However, the accuracy of the estimation of the parameter K_{iI} obtained with the optimal input is by far better than the accuracy obtained with the non-optimal solution. For the experiment 8, the standard deviations obtained with the optimal solution are almost one third of the standard deviations given by the non-optimal solution. These results highlight the importance of a careful design of experiments for minimizing the uncertainty associated to the parameter estimation. It should be remarked, however, that even with the optimal input, the accuracy of the estimation of K_{sI} is not excellent. This is due to the known practical identifiability problems associated to this type of models (Dochain and Vanrolleghem, 2001). A parameterization of the Haldane equation as proposed by Bernard and Remond (2012) might be a solution to improve the accuracy of the estimation.

To conclude, a preliminar study on OED for parameter estimation of microalgae models has been performed providing guidelines to design informative experiments. A further study includes robust estimation methods (Körkel et al., 2004) to handle uncertainty on the nominal values of the parameters. In terms of model structure, improvements are needed to enlarge the predictions capabilities of the model. The mathematical model presented here assumes that temperature and light affect instantenously microalgae growth. However, microalgae can exhibit the phenomenon of acclimation, *i.e.* microalgae can adapt its photosynthetic system to changes of light and temperature (Geider, 1987). Moreover, radical changes in the temperature can produce a stress to the microalgal cells and affect the exponential behaviour. Experimental data are needed to assess those aspects.

In the near future, experiments will be performed by following the protocol of experimental inputs determined in this study. These experiments will be instrumental to identify accurate parameters and also to investigate the dynamics of acclimation.

REFERENCES

Banga, J.R., Versyck, K.J., and Impe, J.F.V. (2002). Computation of optimal identification experiments for nonlinear dynamic process models: a stochastic global optimization approach. *Ind. Eng. Chem. Res.*, 41, 2425–2430.

Bernaerts, K., Gysemans, K.P.M., Nhan Minh, T., and Van Impe, J.F. (2005). Optimal experiment design for cardinal values estimation: guidelines for data collection. *Int J Food Microbiol*, 100, 153–165.

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.

Bernard, O. and Remond, B. (2012). Validation of a simple model accounting for light and temperature effect on microalgal growth. *Bioresour Technol*, 123, 520–527.

Bonnans, Frédéric, J., Martinon, P., and Grélard, V. (2012). Bocop - a collection of examples. Technical report, INRIA. URL http://hal.inria.fr/hal-00726992. RR-8053.

Chianeh, H., Stigter, J.D., and Keesman, K.J. (2011). Optimal input design for parameter estimation in a single and double tank system through direct control of parametric output sensitivities. *Journal of Process Control*, 21, 111–118.

Dochain, D. and Vanrolleghem, P. (2001). *Dynamical Modelling and Estimation in Wastewater Treatment Processes*. IWA Publishing, London.

Droop, M.R. (1968). Vitamin B12 and marine ecology. iv. the kinetics of uptake, growth and inhibition in M*onochrysis lutheri*. *J. Mar. Biol. Ass. U. K.*, 48, 689–733.

Egea, J.A., Rodríguez-Fernández, M., Banga, J.R., R., and Martí (2007). Scatter search for chemical and bioprocess optimization. *Journal of Global Optimization*, 37, 481–503.

Geider, R.J. (1987). Light and temperature dependence of the carbon to chlorophyll a ratio in microalgae and cyanobacteria: implications for physiology and growth of phytoplankton. *New Phytologist*, 106, 1–34.

Körkel, S., Kostina, E., Bock, H.G., and Schlöder, J.P. (2004). Numerical methods for optimal control problems in design of robust optimal experiments for nonlinear dynamic processes. *Optimization Methods and Software*, 19, 327–338.

Mairet, F., Bernard, O., Masci, P., Lacour, T., and Sciandra, A. (2011). Modelling neutral lipid production by the microalga *Isochrysis aff. galbana* under nitrogen limitation. *Bioresour Technol*, 102, 142–149.

Marchetti, J., Bougaran, G., Dean, L.L., Mégrier, C., Lukomska, E., Kaas, R., Olivo, E., Baron, R., Robert, R., and Cadoret, J.P. (2012). Optimizing conditions for the continuous culture of *Isochrysis* affinis *galbana* relevant to commercial hatcheries. *Aquaculture*, 326-329, 106–115.

Muñoz-Tamayo, R., Laroche, B., Leclerc, M., and Walter, E. (2009). IDEAS: a parameter identification toolbox with symbolic analysis of uncertainty and its application to biological modelling. In *Prepints of the 15th IFAC Symposium on System Identification, Saint-Malo, France*, 1271–1276. URL http://www.inra.fr/miaj/public/logiciels/ideas/index.html.

Muñoz-Tamayo, R., Mairet, F., and Bernard, O. (2013). Optimizing microalgal production in raceway systems. *Biotechnol Prog*, 29, 543–552.

Peeters, J.C.H. and Eilers, P. (1978). The relationship between light intensity and photosynthesis—a simple mathematical model. *Hydrobiological Bulletin*, 12, 134–136.

Rodríguez-Fernández, M., Egea, J.A., and Banga, J.R. (2006). Novel metaheuristic for parameter estimation in nonlinear dynamic biological systems. *BMC Bioinformatics*, 7, 483.

Rosso, L., Lobry, J.R., and Flandrois, J.P. (1993). An unexpected correlation between cardinal temperatures of microbial growth highlighted by a new model. *J Theor Biol*, 162(4), 447–463.

Van Derlinden, E., Bernaerts, K., and Van Impe, J.F. (2008). Accurate estimation of cardinal growth temperatures of escherichia coli from optimal dynamic experiments. *Int J Food Microbiol*, 128, 89–100.

Walter, E. and Pronzato, L. (1997). *Identification of Parametric Models from Experimental Data*. Springer, London.

Wächter, A. and Biegler, T. (2006). On the implementation of an interior-point filter line-search algorithm for large-scale nonlinear programming. *Mathematical Programming*, 106, 25–57.

Williams, P.J.B. and Laurens, L.M.L. (2010). Microalgae as biodiesel & biomass feedstocks: Review & analysis of the biochemistry, energetics & economics. *Energy and Environ. Sci.*, 3, 554–590.