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Identification of a cell population model for algae growth processes ⋆

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Abstract: The growth process of a *Chlamydomonas reinhardtii* cell population is modelled with experimental data obtained in a batch reactor. To describe the growth process of this culture, the Droop model, extended by cell population balance model, is considered. On the basis of available measurements and the mathematical model, an optimization problem is defined in order to determine the kinetic parameter values for the growth functions of the Droop model and the cell division parameters of the cell population balance model.

Keywords: Cell population balance model, cell distribution, Droop model, partial integro-differential equations, system identification.

1. INTRODUCTION

Microalgae are a group of prokaryotic and eukaryotic photosynthetic microorganisms that grow rapidly due to their simple structure. After nitrogen starvation, the biomass can reach a very high lipid content (more than 60% of dry weight under certain stress conditions [Metting (1996)]). These possibilities have led some authors to consider microalgae to be employed to produce biofuels in an economically effective and environmentally sustainable manner, as one of the main biofuel sources for the future [Chisti (2007), Concas et al. (2014)]. Additionally, autotrophic microalgae and cyanobacteria use photons as energy source to fix carbon dioxide (CO_2), they could be used to consume inorganic nitrogen and phosphorus in urban or industrial effluents or to generate useful chemicals. Indeed, some green algae, *e.g. Chlamydomonas reinhardtii*, have shown the ability to produce significant amounts of hydrogen gas during sulfur deprivation, [Hemschemeier et al. (2008)]. For these reasons the production of these biofuels can be coupled with flue gas CO_2 mitigation, wastewater treatment, and the production of high-value chemicals.

A model able to describe the cell growth phenomenon can be a key tool to optimize the operating conditions for bioreactors and improve control system performance [Becker (1994)]. In the literature, there are numerous models that describe microalgae growth as a function of the environmental variables, such as nutrients and light [Flynn (2001)]. In the current work, one of the earliest models is considered, the Droop model [Droop (1973)]. This model describes the ability of microalgae to store nutrients by an intracellular quota and distinguishes between substrate uptake and biomass growth.

The cellular biomass consists of a population of individual cells. Each cell goes through the so-called cell cycle, including growth and division: after a certain point, it divides and splits its cellular mass into two daughter cells, each of which undertakes its own cell cycle. For this reason, at any point in time, the cells of the population exist at different stages of the cell cycle and they contain different quantities of proteins, lipids, DNA and other cell properties. Consequently, since properties are really distributed among the cells of the population, a cell population is a heterogeneous system. This directly motivates to enhance process models by considering the cell distribution.

The mathematical models for describing the distributed nature of cell growth processes are the so-called cell population balance models, which have been presented in the literature [Fredrickson et al. (1967), Tsuchiya et al. (1966)]. These models naturally allow the integration of information about cell division and partitioning of cellular material. Furthermore, contrary to unsegregated models, which can predict only average population properties, cell population balance models are able to predict cell properties over the entire distribution. However, since such models typically consist of first-order, partial integro-differential equations coupled with nonlinear ordinary differential equations, their solution poses a serious challenge because they are characterized by considerable mathematical complexity.

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In this work, the Droop model has been extended by the population model to analyze the growth and the cell distribution phenomena in a *Chlamydomonas reinhardtii* culture with the aim of identifying the parameter values that characterize the functions within the model.

The paper is structured as follows. In Section 2 the model used to describe the growth process and the discretization method for the numerical analysis are presented. In Section 3 the optimization problem is expressed and described. In Section 4 the operating conditions and the experimental features are reported. In Section 5 the experimental results are shown and comparisons between the measurement data and the model predictions are made.

2. MODEL FORMULATION

2.1 Droop Model

In order to describe the cell growth process, the biological mass model employed by M.R. Droop is considered [Droop (1973)]. This model is able to analyse the growth phenomenon of algae cells with nutrient limitation. The idea introduced by Droop is to consider, separately, the external substrate concentration S and the internal substrate S_{ic}, *i.e.* the concentration of substrate absorbed by the algae cells [Lemesle and Mailleret (2008)]. Considering b as the biomass concentration the cell quota q is defined as

$$q = \frac{S_{ic}}{b}. \tag{1}$$

According to the Droop model, the growth process is ruled by two kinetic phenomena: the external substrate uptake and the biological conversion of the internal substrate into biomass. Cell quota time derivative can be calculated considering that the uptake rate for S is equal to the generation rate for S_{ic}, due to mass conservation. With this consideration, deriving (1), the relation between $\dot{q}$ and the system's state variables can be computed [Packer (2014)]. Let $\rho(S)$ and $\mu(q)$ be the specific functions that describe the substrate uptake rate and the biomass growth rate (per biomass unit), respectively. Considering perfect mixing within the batch reactor, the Droop model equations are defined as

$$\dot{b} = \mu(q)b - \frac{\dot{V}}{V}b \tag{2.1}$$

$$\dot{S} = -\rho(S)b - \frac{\dot{V}}{V}S \tag{2.2}$$

$$\dot{q} = \rho(S) - \mu(q)q \tag{2.3}$$

$$\dot{V} = h \tag{2.4}$$

$$b(0) = b_0 \quad S(0) = S_0, \quad q(0) = q_0, \quad V(0) = V_0, \tag{2.5}$$

where V is the reactor volume. Note that (2) is obtained by a mass balance performed across a variable *control volume*, whose change in time is modeled by a function $h : \mathbb{R}_+ \to \mathbb{R}$.

2.2 Population Model

The Droop model belongs to a class of biological models useful to describe the cellular growth process considering the biomass inside the system. Therefore, this model is not able to analyse a crucial aspect of biological system: due to the division process, cell properties (*e.g.* cellular mass) are distributed among the cell population and, for this reason, at any moment, the system is characterized by a cell distribution over the mass domain [Mantzaris et al. (2001)]. In order to develop a mathematical model able to describe this phenomenon, the class of population models proposed in [Mantzaris and Daoutidis (2004)] is considered. This analysis introduces a new physical quantity, $n(m,t)$, that represents the cell mass distribution and $n(m,t)dm$ is the number of cells with mass $\in [m, m+dm]$, at time t, per unit volume.

These models are composed of a system of partial integro-differential equations which describes the biological phenomenon of cell growth and the temporal dynamics of the cell distribution

$$\begin{aligned}\partial_t n(m,t) = &- \partial_m[r_g(m,q)n(m,t)] \\ &- \Gamma(m,S,q)n(m,t) - \frac{\dot{V}}{V}n(m,t) \\ &+ 2\int_m^1 \Gamma(\eta,S,q)n(\eta,t)P(\eta,m)d\eta \end{aligned} \tag{3.1}$$

$$\dot{S} = -\int_0^1 r_u(m,S)n(m,t)dm - \frac{\dot{V}}{V}S \tag{3.2}$$

$$\dot{q} = \frac{\int_0^1 (r_u(m,S) - qr_g(m,q))n(m,t)dm}{\int_0^1 mn(m,t)dm} \tag{3.3}$$

$$n(1,t) = 0 \qquad \forall\, t > 0 \tag{3.4}$$

$$n(m,0) = n_0(m) \qquad m \in [0,1] \tag{3.5}$$

$$S(0) = S_0, \qquad q(0) = q_0. \tag{3.6}$$

The cell distribution balance equation (3.1) consists of five terms. The left-hand side is represented by the accumulation term that accounts for the time dynamics of the cell distribution. The right-hand side is composed of the growth term (the first one), that describes the variation of the cell mass during the growth process, the division term (the second one), that describes the loss of cells of mass m due to their division into cells of smaller mass and the birth term (the last one) that is due to the production of cells of mass m from the division of greater mass cells [Fredrickson et al. (1967)]. In addition, the differential equation (3.1) accounts for the variation of volume in time through the third term on the right-hand side.

In (3), t is the time, m is the dimensionless mass $\in [0,1]$, $n(m,t)$ is the cell distribution density function, $\Gamma(m,S,q)$ is the cell division rate, and r_g and r_u are the growth rate and uptake rate functions, for the single cell. The probability division function $P(\eta,m)$ accounts for stochastic effects during division: $P(\eta,m)dm$ is the probability that a cell of mass η is divided in a cell of mass m. The function that describes the time dynamics of the volume is identical to the corresponding equation of the Droop model (2.4).

It is possible to express r_g and r_u through the specific rate functions, $\rho(S)$ and $\mu(q)$, when these are referred to the biomass unit by a linear dependency on the mass m [Mantzaris and Daoutidis (2004)]

$$r_u(m,S) = \rho(S)m \tag{4}$$
$$r_g(m,q) = \mu(q)m, \tag{5}$$

as well as there is a direct proportionality between cell division rate and growing cell rate function

$$\Gamma(m,S,q) = r_g(m,q)\gamma(m,S). \tag{6}$$

In virtue of mass conservation, and, considering the hypothesis that a mother cell splits into two daughter cells [Fredrickson et al. (1967)], $P(\eta,m)$ has the following properties

$$P(\eta,m) = 0 \qquad \forall\ \eta \leq m \tag{7.1}$$
$$P(\eta,m) = P(\eta,\eta-m). \tag{7.2}$$

Due to (7.2), if the mass interval $[0,\eta]$ is considered, the probability division function must be symmetric with respect to the mother half mass, $\eta/2$. Thus, the function chosen to model the probabilistic nature of the division phenomenon must have its statistical mean and median equal to the symmetrical point, $\eta/2$. This can be modelled by a probability density function of a particular Beta probability distribution [Mantzaris and Daoutidis (2004)], defined as

$$P(\eta,m) = \frac{1}{B(p)}\frac{1}{\eta}(m/\eta)^{p-1}(1-m/\eta)^{p-1}, \tag{8}$$

where the two parameters of Beta distribution are both equal to the value p and $B(p)$ represents the Euler Gamma function [Anderson and Qiu (1997)].

The specific uptake rate $\rho(S)$ and the specific growth rate $\mu(q)$ used are the functions that are typically considered in the Droop model [Lemesle and Mailleret (2008)],

$$\rho(S) = \frac{\rho_{max}S}{K_s+S} \tag{9.1}$$
$$\mu(q) = \bar{\mu}(1-\frac{q_0}{q}), \tag{9.2}$$

where ρ_{max} and $\bar{\mu}$ are the maximum values of specific uptake and growth rate, respectively. The half saturation constant is denoted by K_s and represents the external substrate value such that $\rho(S)$ is equal to $\rho_{max}/2$ and q_0 is the minimum allowed value for internal cell quota.

2.3 First Moment

Due to the definition of n, the cell distribution first moment is equal to the biomass concentration, b

$$b = \int_0^1 mn(m,t)dm. \tag{10}$$

On the basis of (10) and considering (3.1), the time derivative of b can be expressed as [Mantzaris and Daoutidis (2004), Schaum and Jerono (2019)]

$$\begin{aligned}\dot{b} = \int_0^1 m\partial_t n(m,t)dm = \\ = -\int_0^1 m\left\{\partial_m[r_g(m,q)n(m,t)]\right\}dm + \\ -\int_0^1 m\Gamma(m,S,q)n(m,t)dm + \\ +\int_0^1 2m\int_m^1 \Gamma(\eta,S,q)n(\eta,t)P(\eta,m)d\eta\ dm \\ -\frac{\dot{V}}{V}\int_0^1 mn(m,t)dm.\end{aligned}$$

Due to mass conservation, it holds that the mass obtained through cell birth must be equal to the mass lost by cell division (3.1). Besides, considering (3.4) and using integration by parts, it holds that

$$-\mu(q)\int_0^1 m\partial_m[n(m,t)m]dm = \mu(q)\int_0^1 n(m,t)mdm.$$

In view of these considerations, using (10), it is possible to demonstrate that the first moment of (3.1) is equal to (2.1). This analytical feature is essential for the experimental analysis because it allows the application of the population model or the Droop model, depending on the specific analysis that is being conducted. To analyse the biomass growth process and to identify the kinetic parameters of (4) and (5), the biomass and substrate measurements are needed. Once the kinetic parameters are obtained, their values can be used in the population model to identify the cell division parameters of $P(\eta,m)$ (8) and $\gamma(m,S)$ (6).

2.4 Discretization Methods

For implementation, the PDE equation (3.1) is discretized in the mass domain. To perform the discretization, the trapezoidal rule and the backwards finite differences are used. Moreover, the mass domain is normalized on $[0,1]$. Note that this domain can be changed by linear transformation [Mantzaris and Daoutidis (2004)]. The numerical approximation of (3.1) is developed as

$$\begin{aligned}\dot{n}_i(t) = -\frac{(r_g(m_i,q)n(m_i,t)) - (r_g(m_{i-1},q)n(m_{i-1},t))}{\Delta m} \\ -\Gamma(m_i,S,q)n(m_i,t) - \frac{\dot{V}}{V}n(m_i,t) \\ +2\Delta m\sum_{j=i+1}^{N_m-1}\Gamma(m_j,S,q)n(m_j,t)P(m_j,m_i),\end{aligned}$$

where $n_i(t)$ is the cell distribution with mass m_i at time t, N_m is the number of discretization points in the mass domain that is discretized with a constant step size Δm. In the numerical development of the birth term (devised through trapezoidal rule) the first and the last term of the discrete integral are not included. They are equal to 0, due to equations (7.1) and (3.4), respectively.

3. IDENTIFICATION STRUCTURE

The first step in the identification problem is to obtain the kinetic parameters of (9.1) and (9.2), namely $\boldsymbol{p}_k = [\rho_{max}, K_s, \bar{\mu}, q_0]$. Considering the state vector $\boldsymbol{x} = [b,S,q,V]^T$, the optimization problem is given by

$$\min_{p_k} J_k(\boldsymbol{y}, \hat{\boldsymbol{y}}, \boldsymbol{p}_k) = \left\| \sum_{i=1}^{N_t} (\hat{\boldsymbol{y}}(t_i) - \boldsymbol{y}(t_i))^2 \right\|_1$$
$$\dot{\hat{\boldsymbol{x}}} = \boldsymbol{f}(\hat{\boldsymbol{x}}, t) \qquad \hat{\boldsymbol{x}}(0) = \hat{\boldsymbol{x}}_0, \quad t \geq 0$$
$$\hat{\boldsymbol{y}} = C\hat{\boldsymbol{x}}$$
$$C = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \end{bmatrix}$$
$$\boldsymbol{x} \geq 0 \qquad \boldsymbol{p}_k \geq 0,$$

where C takes into account the available measurements b and S, $\boldsymbol{f}(\boldsymbol{x}, t)$ is the right-hand side of the Droop model (2), N_t is the number of measurements over time, $\hat{\boldsymbol{x}}$ represents the model prediction, $\boldsymbol{y}$ is the measurement vector, $\hat{\boldsymbol{y}}$ is the model prediction of measurements and $\hat{\boldsymbol{x}}_0$ is the initial states vector whose values are given by the initial states measurements $b(0)$, $S(0)$ and $V(0)$, whereas $q(0)$ is supposed equal to the parameter value q_0. In the second step, the population balance model (3) is considered to estimate the parameters that characterize the division rate function $\Gamma(m, S, q)$ and the probability density function $P(\eta, m)$. Let $\boldsymbol{p}_d$ be the parameter vector and $\boldsymbol{x_d} = [n_1, ..., n_{N_m}, S, q, V]^T$ the state vector, the optimization problem is defined as follows

$$\min_{p_d} J_d(\boldsymbol{y}_d, \hat{\boldsymbol{y}}_d, \boldsymbol{p}_k, \boldsymbol{p}_d) = \left\| \sum_{i=1}^{N_t} (\hat{\boldsymbol{y}}_d(t_i) - \boldsymbol{y}_d(t_i))^2 \right\|_1$$
$$\dot{\hat{\boldsymbol{x}}}_d = \boldsymbol{f_d}(\hat{\boldsymbol{x}}_d, t) \qquad \hat{\boldsymbol{x}}_d(0) = \hat{\boldsymbol{x}}_{d0}, \quad t \geq 0$$
$$\hat{\boldsymbol{y}}_d = C_d \hat{\boldsymbol{x}}_d$$
$$C_d = \begin{bmatrix} 1 & 0 & \dots & 0 & 0 & 0 & 0 \\ 0 & 1 & \dots & 0 & 0 & 0 & 0 \\ \vdots & \vdots & \ddots & 0 & 0 & 0 & 0 \\ 0 & 0 & \dots & 1 & 0 & 0 & 0 \end{bmatrix}$$
$$\boldsymbol{x}_d \geq 0, \qquad \boldsymbol{p}_d \geq 0,$$

where C_d is a rectangular matrix with N_m rows that takes into account the cell distribution measurement $n(m, t)$ is used, $\boldsymbol{f_d}(\hat{\boldsymbol{x}}_d, t)$ is the right-hand side of population balance model (3) and $\hat{\boldsymbol{x}}_{d0}$ is the initial states vector whose values are given by the initial states measurements. Note that this minimization problem is solved with respect to $\boldsymbol{p}_d$ because $\boldsymbol{p}_k$ has been determined by minimizing J_k. To implement numerical algorithms for the optimization problems, the function *fmincon* in MATLAB is used and the SQP method is chosen to investigate the parameters domain.

4. EXPERIMENTAL SETUP

The experimental data have been obtained through a lab-scale reactor initially filled with a solution composed by 250 ml of demineralized water and media, and 5 ml of microalgae cells. It was characterized by an air flow feed of 0.05 $l\ min^{-1}$, useful to maintain perfect mixing and by a light intensity (photon flux) of 40 $\mu mol\ s^{-1}\ m^{-2}$.

By taking samples at daily rate, the biomass and the substrate concentration were measured. Through an optical density measurement, the absorbance of the sample was obtained and it was converted into concentration using an empirical relation between b and OD. Considering Lambert-Beer's equation, a linear relation between OD and concentration can be supposed, if the latter is low, which was ensured by samples dilution. Biomass dry weight measurements have been performed by passing defined volume through GF/C filters and the resulting OD was measured.

From the same probe for the OD measurement, a sample of solution was extracted and analyzed to estimate the cell distribution. This measurement was realized by the Casy cell counter and analyzer of Omni Life Science (OLS) that determines how many cells of a specific size were presented in a defined sample volume. Once obtained these data, using the biomass concentration measurements, the cell density has been estimated, *i.e.* the mass per unit of cellular volume. With this information and considering that $n(m, t)dm$ is the cell number with $m \in [m, m + dm]$ per unit volume, the cell distribution data was computed by discretizing the integral of cell distribution over mass domain by the trapezoidal rule. To evaluate h (2.4), the solution volume was measured and the function that described this variation was established, by a linear fitting.

The media components [1] are shown in Table 1.

Table 1. Media components

COMPONENT	$mg\ l^{-1}$
KNO_3	252.775
$NaH_2PO_4 \cdot H_2O$	310.5
$Na_2HPO_4 \cdot 2H_2O$	44.5
$MgSO_4 \cdot 7H_2O$	123.25
$CaCl_2 \cdot 2H_2O$	7.35
$FeSO_4 \cdot 7H_2O$	6.95
H_3BO_3	61.0
$CuSO_4 \cdot H_2O$	2.5
$MnSO_4 \cdot 7H_2O$	61.0
$ZnSO_4 \cdot 5H_2O$	2.5
$(NO_4)_6Mo_7O_{24} \cdot 4H_2O$	12.5

5. RESULTS

In Fig. 1 is shown the comparison between experimental data of b and S and the Droop model prediction whose parameters were obtained with the first optimization step.

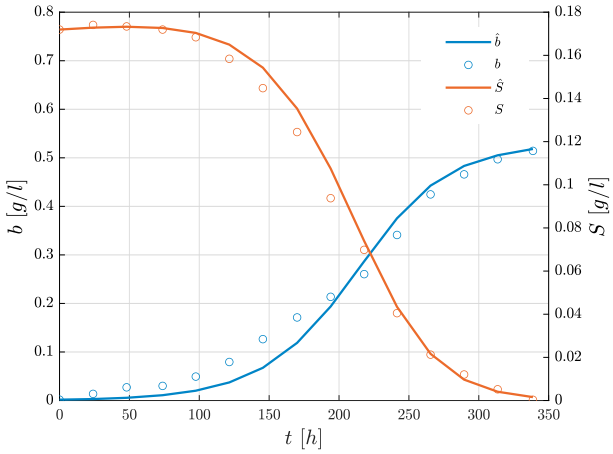

Fig. 1. Biomass and substrate concentration: comparison between experimental data and model prediction.

[1] Modified version of Medium for Unicellular Green Algae (www.uni-goettingen.de).

The Droop model (2) manages to approximate the experimental data of b and S except for the initial biomass values where the model prediction is characterized by an offset higher with respect to the other time instance.

Once the kinetic parameters of Droop model are obtained, the cell division parameters can be identified.

The distribution function γ, associated to the cell division, is usually based on the hypothesis that the division distribution is dependent only on cell mass

$$\gamma(m) = \frac{\Phi_{[m_0,\sigma]}}{1 - \int_0^m \Phi_{[m_0,\sigma]} dm}. \tag{11}$$

Where $\Phi_{[m_0,\sigma]}$ is a Gaussian truncated distribution with a support $\in [0, 1]$, a mean m_0 and a deviation σ.

As shown in [Mantzaris and Daoutidis (2004)]. Using (11), the cell distribution model prediction, $\hat{n}(m, t)$, is characterized by the statistical mode that remains, at any moment, on the same mass value. The reason of this feature is that, for the whole process, the same proportion between growth and division rate is kept. Considering (6), if (11) is used, the ratio between the cell division rate and the cell growth rate does not change with respect to the time, it remains equal to $\gamma(m)$.

However, the data obtained with the experiments do not show this trend. It is observed that the mode of the cell distribution changes its mass coordinate with respect to the time. As shown in Fig. 2, the maximum of $n(m, t)$ moves to higher values of mass and this has to be the consequence of the fact that the division rate and the growth rate do not keep the same ratio during the process. Specifically, the division rate is getting lower with respect to the time and this decrease leads to a shift in the distribution towards bigger cells. For this reason, it was needed to examine this behavior to understand its causes and try to adapt the model. Experimental data with $m \in [0, 0.5]$ are considered to show more clearly the mode shift.

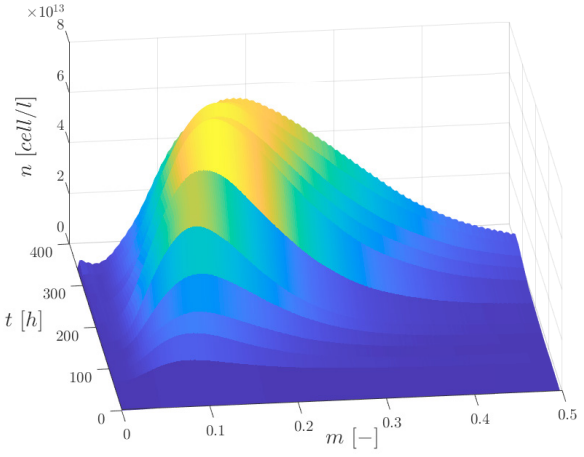

Fig. 2. Cell population distribution: experimental data.

The idea to describe this phenomenon is that the cell division process depends on the external substrate concentration; while the metabolic uptake decreases its rate because S is close to zero, also cell division can be inhibited by nutrient stress. To consider this effect, the function γ has been adapted by adding a linear dependency on S. In order to modulate this dependency, the amplitude parameter α has been considered

$$\gamma(m, S) = \frac{\Phi_{[m_0,\sigma]}}{1 - \int_0^m \Phi_{[m_0,\sigma]}} \left(\frac{S}{\alpha}\right). \tag{12}$$

The result of the model prediction can be seen in Fig. 3 and Fig. 4. In Fig. 3 it can be observed that the model manages to follow the trend of cell distribution data and it is able to describe the mode variation of the distribution. In Fig. 4, the direct comparison between model prediction and experimental data is shown.

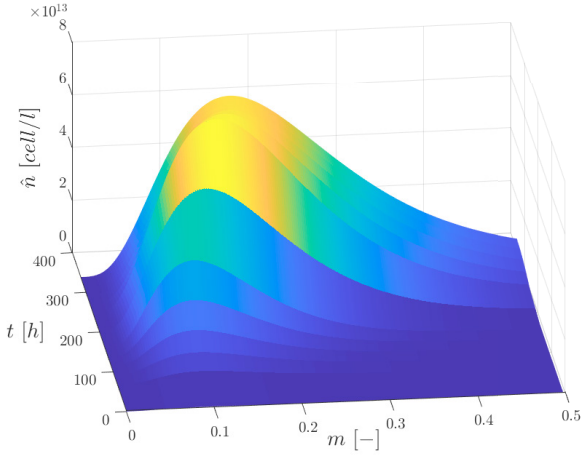

Fig. 3. Cell population distribution: model prediction.

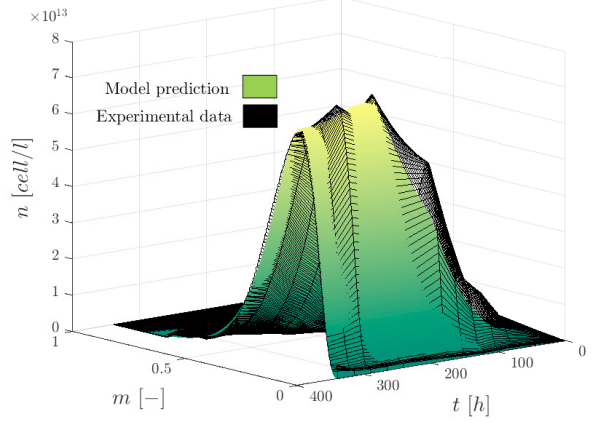

Fig. 4. Cell distribution: comparison between model prediction and experimental data.

With the purpose of evaluating the model performances, it is crucial to estimate the adjusted coefficient of determination $\bar{R}^2$ [Neter et al. (1996)], and the relative error E. These calculations are performed for every time sample (t_k) using (13) and (14)

$$\bar{R}^2(t_k) = \frac{(N_m - 1)R^2 - (k_p - 1)}{N_m - k_p} \tag{13}$$

$$E(t_k) = \frac{\int_0^1 |n(m,t_k) - \hat{n}(m,t_k)|\, dm}{\int_0^1 n(m,t_k) dm}, \qquad (14)$$

where R^2 is the coefficient of determination, k_p is the number of explanatory variables (parameters to identify) and N_m is the sample size, *i.e.* the discretization points in the mass domain [Neter et al. (1996)]; $\hat{n}(m,t_k)$ is the model prediction and $n(m,t_k)$ is the measurement. The results related to this calculation are shown in Fig. 5 where the relative error of the biomass concentration estimation E_b is also presented (15).

$$E_b = \frac{\left| b(t_k) - \hat{b}(t_k) \right|}{b(t_k)} \qquad (15)$$

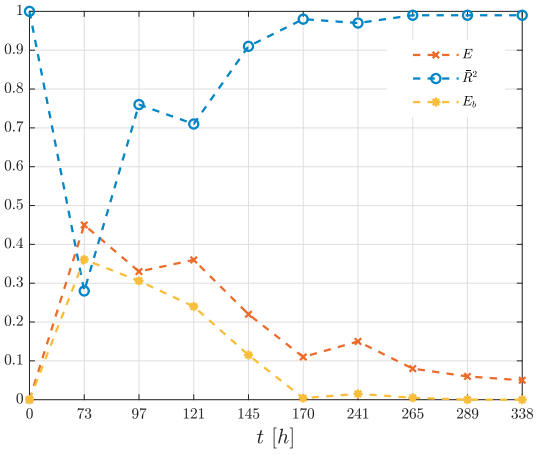

Fig. 5. Error analysis and statistical evaluation.

In Fig. 5 is shown that the prediction quality increases with the time and this is due to the fact that the biomass concentration relative error is getting lower. Indeed when the model is not characterized by high performances (lower $\bar{R}^2$ and higher E), the relative biomass concentration error (E_b) is high. This confirms the close dependency between the first optimization step and the modeling of the cell distribution, but this allows to conclude that an accurate estimation of the kinetic parameters ($\boldsymbol{p}_k$) is needed to evaluate a model for the description of the cell distribution phenomenon.

The parameters obtained are shown in Table 2.

Table 2. Model parameters

ρ_{max} $[h^{-1}]$	K_s $[g\ l^{-1}]$	$\bar{\mu}$ $[h^{-1}]$	q_0 $[-]$
0.0587	0.8	0.2786	0.3759
m_0 $[-]$	σ $[-]$	α $[g\ l^{-1}]$	p $[-]$
0.0943	0.1754	0.1057	30.0012

6. CONCLUSIONS

The growth process of *Chlamydomonas reinhardtii*, a green microalga species, has been studied by performing an identification analysis based on experimental data. This phenomenon has been analyzed through the Droop model extended by cell population model to consider that the cell properties are distributed with respect to the mass. The experimental features and the numerical approximations are presented with the proposal of a certain distribution function γ, useful to describe the trend of measurements. An optimization problem has been formulated in order to identify the parameter values of the model. Through an optimization algorithm implemented on MATLAB, the parameter values have been determined and the prediction performance is evaluated by using the normalized error and the adjusted coefficient of determination $\bar{R}^2$.

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