PBL Methodology Applied for the Development of a Software for Optimizing Bioprocesses Scaling

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Abstract

Nowadays, less than 40% of experimental developments in bioprocesses are taken to industrial scale, because of the lack of computational tools that facilitate the calculation of the dimensions and operating parameters of an industrial scale bioreactor. Known existing tools for making this kind of estimations are rare and their license prices are near USD 6000. These computational tools are based on approximations of mathematical models. Using the PBL methodology, learned in the basic science courses of engineering, it was decided to solve a differential equations challenge. The problem was taken from differential equations subject. From this challenge, arose the idea to optimize bioprocesses scaling, by the use of a computational tool. In the research group CIBIOT, which belongs to the engineering school of the Pontificia Bolivariana University, was raised the challenge to develop a software that was accessible to a large group of people, easy to handle, as accurate as possible, so it could obtain the most exact parameters for taking a laboratory scale bioreactor to an industrial scale bioreactor. The accuracy of the software was achieved by using an analytical study of the volumetric oxygen transfer coefficient K_La by the use of the differential equations. It was proposed an analytical solution based on the oxygen balance equation in an aerobic bioreactor, for modeling the volumetric oxygen transfer coefficient K_La. The solution was parametrically adjusted using experimental data of a microalgae growth. After all these steps were finished, it was developed a software capable of carrying out with agility and precision the needed calculations for making successfully the scaling of bioprocesses. The software was developed using Visual Basic ®.

Keywords: Volumetric coefficient, bioreactor, bioprocesses scaling.

1 Introduction

The existing interest of bioprocesses scaling incorporate low weight molecules, as the ethanol, organic acids, and similar, which embrace a global market that generates an income above USD 1 billion, only in the pharmaceutical area (Becker, 2013).

The transition from laboratory scale to pilot scale, and from pilot scale to industrial scale are points where the economic and business creating viability is evaluated. This is why the development of tools that allow the estimation of scaling parameters is of great importance, not only in the academic sector, but in the industrial area (Doran, 2013).

Bioprocesses scaling is accomplished through the use of heuristic approximations of a real behaviour, using scale similitude methods. Most used criteria include geometrical similitude, hydrodynamic similitude of mixing parameters and volumetric oxygen transfer coefficient K_La similitude (Doran, 2013).

Nevertheless, very few studies approach the analysis of diffusion coefficients from an analytical viewpoint using differential equations.

Taking advantage of this need, it was decided to optimize the scaling of bioprocesses by using the PBL methodology, trying to learn not only from chemical engineering but also from differential equations and basic programming skills. This resulted on the combination of different areas of knowledge, which gave the opportunity to develop a computational tool based on a differential equation that came from an experimental study model.

In this paper is proposed an equation for the calculation of the K_La based on the solution of differential equations. Also is proposed the development of a computational tool based on the mentioned equation for bioprocesses scaling.

2 Methodology

For developing a computational tool for bioprocesses scaling, it was proposed an analytical solution based on the oxygen balance equation in an aerobic bioreactor for modelling the volumetric oxygen transfer coefficient K_La. The solution was parametrically adjusted with experimental data, using a microalgae growth model.

After all this steps were accomplished, it was generated a computational tool for the determination of the scale dimensions of a bioreactor, generating an application using the Visual Basic ® Software. The details of each step are shown up next.

2.1 Modelling the volumetric oxygen transfer coefficient K_La

For modelling the K_La coefficient it was set the oxygen balance for an aerobic batch bioreactor, as shown in Equation 1.

$$(dC/dt)=OTR-OUR, \quad (1)$$

where dC/dt is the oxygen accumulation rate in the liquid phase, OTR is the oxygen transfer rate from gas to liquid, and OUR is the microalgae oxygen uptake rate.

It was employed the dynamic method for estimating the K_La in Equation 1, and using the recommendations given by Doran (2013) it was obtained the expression shown in Equation 2.

$$(dC_L/dt)= K_La(C_L^*-C_L)-N_A, \quad (2)$$

where C_L, C_L^*, N_A and t are respectively the oxygen concentration in the liquid (ppm), the saturation concentration of the oxygen (ppm), the oxygen desorption rate for cellular demand (ppm/s) and the time.

For solving Equation 2, which is an ordinary differential equation, it was used the Laplace transform method.

2.2 Experimental data collection for K_La calculation.

The K_La value was obtained experimentally in a direct way. For making it possible, it was employed a one litre Applikon ADI 1030 bioreactor, which was provided with an oxygen sensor. A fermentation of microalgae cells was carried out in this process. It was measured the oxygen concentration in the time, dissolved in the fermentation. Two phases where used to achieve this goal: deoxygenation, suspending the oxygen intake in the bioreactor, and oxygenation, bubbling 0.8 L/min of air, at a velocity of agitation of 250 rpm, as shown in Figure 1.

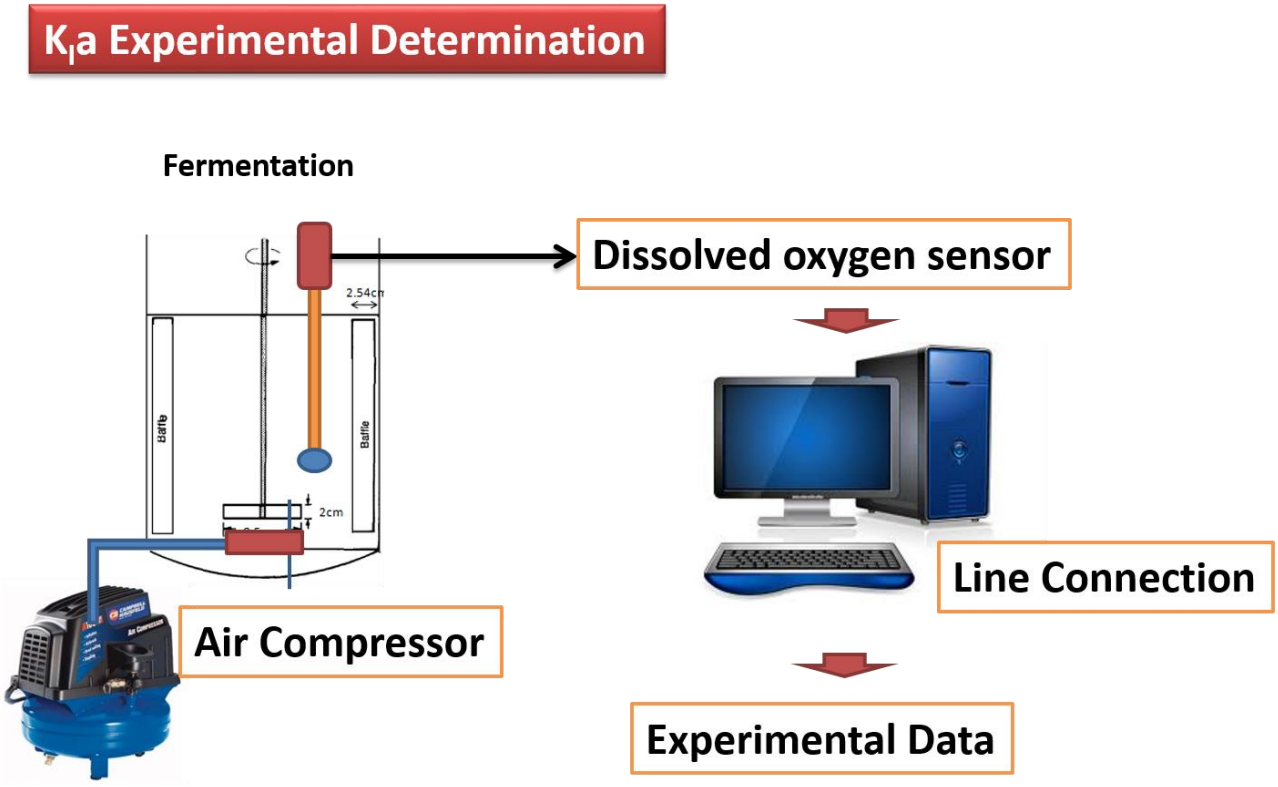

Figure 1. Experimental assembly for oxygen concentration data collection in a laboratory scale bioreactor.

2.3 Bioprocess scale up application development

It was developed an application in Visual Basic ® for collecting online experimental data of the oxygenation of the system. The application also calculates K_La using Equation 3, validates the experimental behaviour and calculates the dimensions of a scale bioreactor.

For this process, it was established a calculation routine that allows estimating the K_La using Equation 3, employing the least squares method and, after that, calculates the dimensions of a scale bioreactor based on the calculated K_La using shape factors of geometrical similitude, following the recommendations given by Doran (Doran, 2013).

3 Results analysis

The determination of the K_La in bioreactors is essential for establishing the efficiency of the aeration, and also for quantifying the variable effects that operate in the dissolved oxygen intake (Khoo, 2011; Radmann, 2008; Putt, 2011; Zeng, 2011; Otzuki, 2001; Garcia, 2009).

The oxygen has to pass through a series of transport resistors to be metabolized by the microorganisms. These resistors depend of the bubble hydrodynamics, temperature, cellular activity and density, solution constitution and other factors. In Figure 2 are shown the resistors involved in the oxygen transfer from the interior of the air bubble to the interior of the cell. (Montoya, 2003).

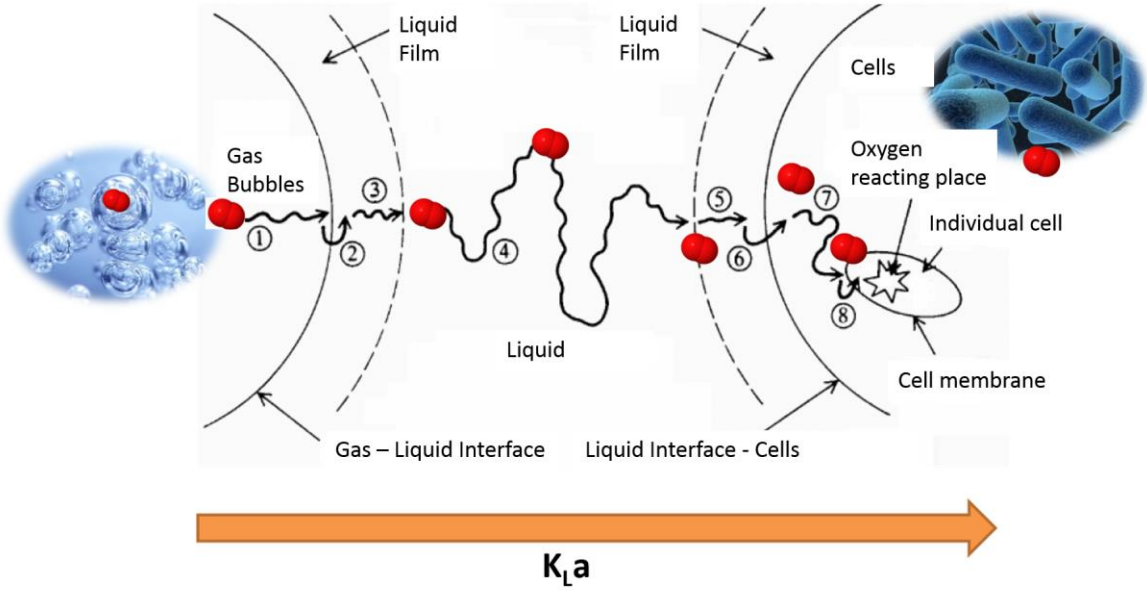

Figure 2. Oxygen transfer resistors.

The dynamic method is based on the measurement of the dissolved oxygen concentration in the medium in the absorption and desorption stages. After a change of the concentration in the inlet gas, it was analysed the change in the dissolved oxygen concentration dynamics. (Garcia, 2009).

This method consists in supplying air until reaching the oxygen saturation concentration in the liquid. (Garcia, 2009).

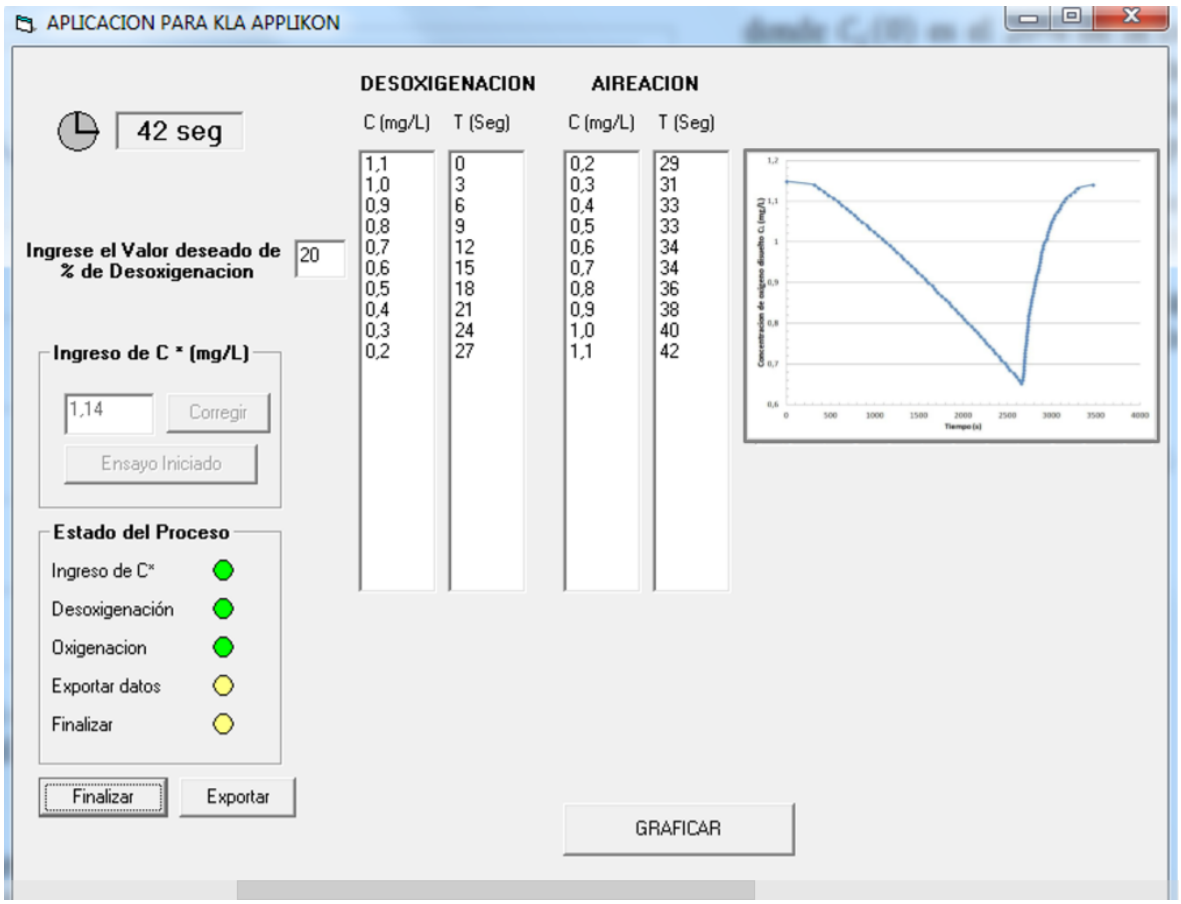

Figure 3. Layout of the computational tool interface.

The experimental data obtained for the deoxygenation and oxygenation are shown in Figure 4.

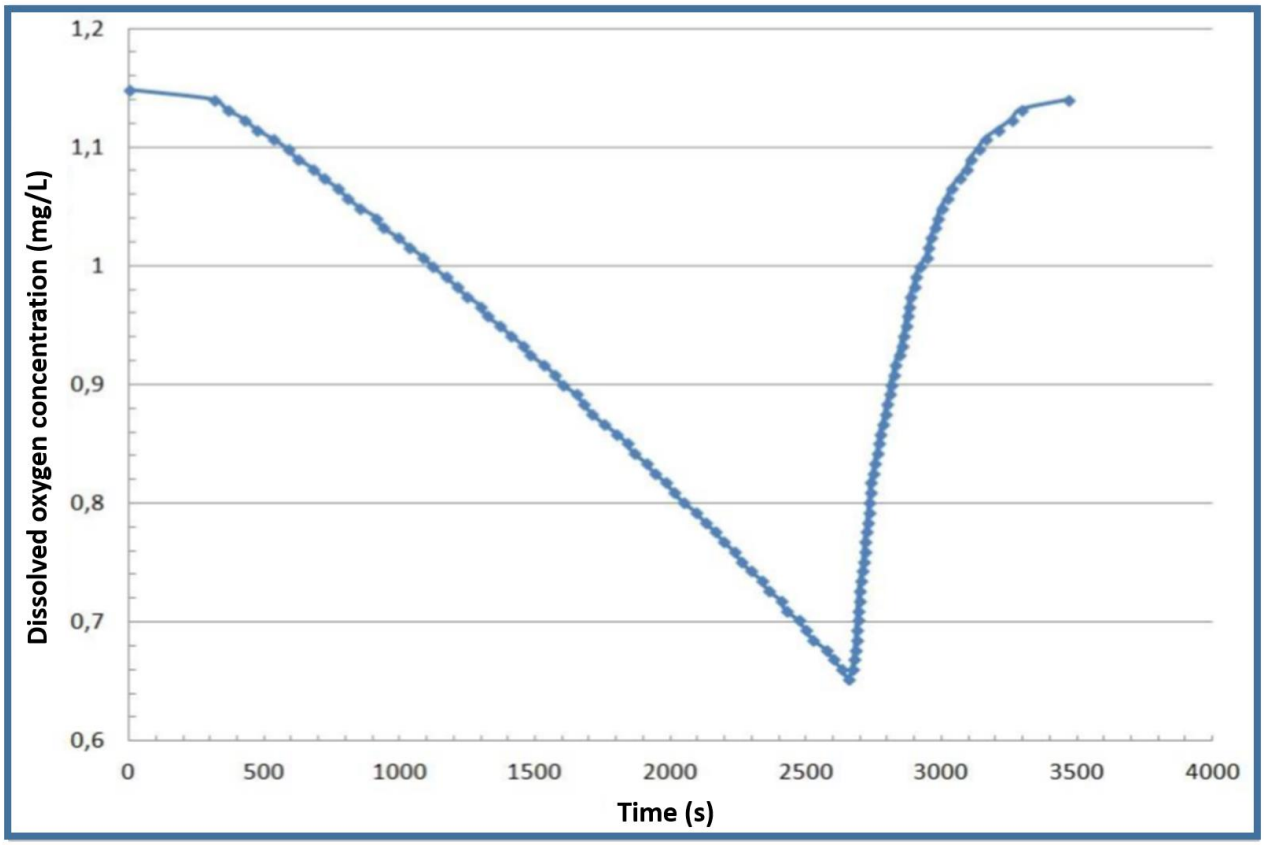

Figure 4. Experimental data for K_La calculation.

After applying the Laplace solution method in Equation 2, it was obtained a model for the calculation of the K_La. The mentioned model is shown in Equation 3.

$$C_L(t) = \frac{K_L a\, C_L^{*} - N_A}{K_L a}\left(1 - e^{-K_L a\, t}\right) + C_L(0)\, e^{-K_L a\, t}, \quad (3)$$

where $C_L(0)$ is 20% of the oxygen saturation concentration (ppm). Mentioned percentage results to be a recommended value for avoiding cellular stress (Doran).

From Figure 4, it was found an oxygen desorption rate value by cellular demand, N_A of 2x10-4 ppm/s, and a C_L* of 1.14 ppm.

With the data obtained in Figure 4, and employing the solution of Equation 3, it was found a K_La value of 3,85 x10-3 s-1. The complete model is shown in Equation 4.

$$C_L(t) = 1{,}14 - \frac{2x10^{-4}}{K_L a}\left(1 - e^{-K_L a\, t}\right) + 0{,}661 e^{-K_L a\, t}, \quad (4)$$

The correlation coefficient for this model was 0.998, which shows an adequate model adjustment to the real process. The model adjustment to experimental data is shown in Figure 5.

Using the proposed methodology, it can be established a calculation routine oriented to facilitate the scaling of bioprocesses, since the K_La estimation results to be the decisive stage in the geometrical calculation of an industrial scale bioreactor.

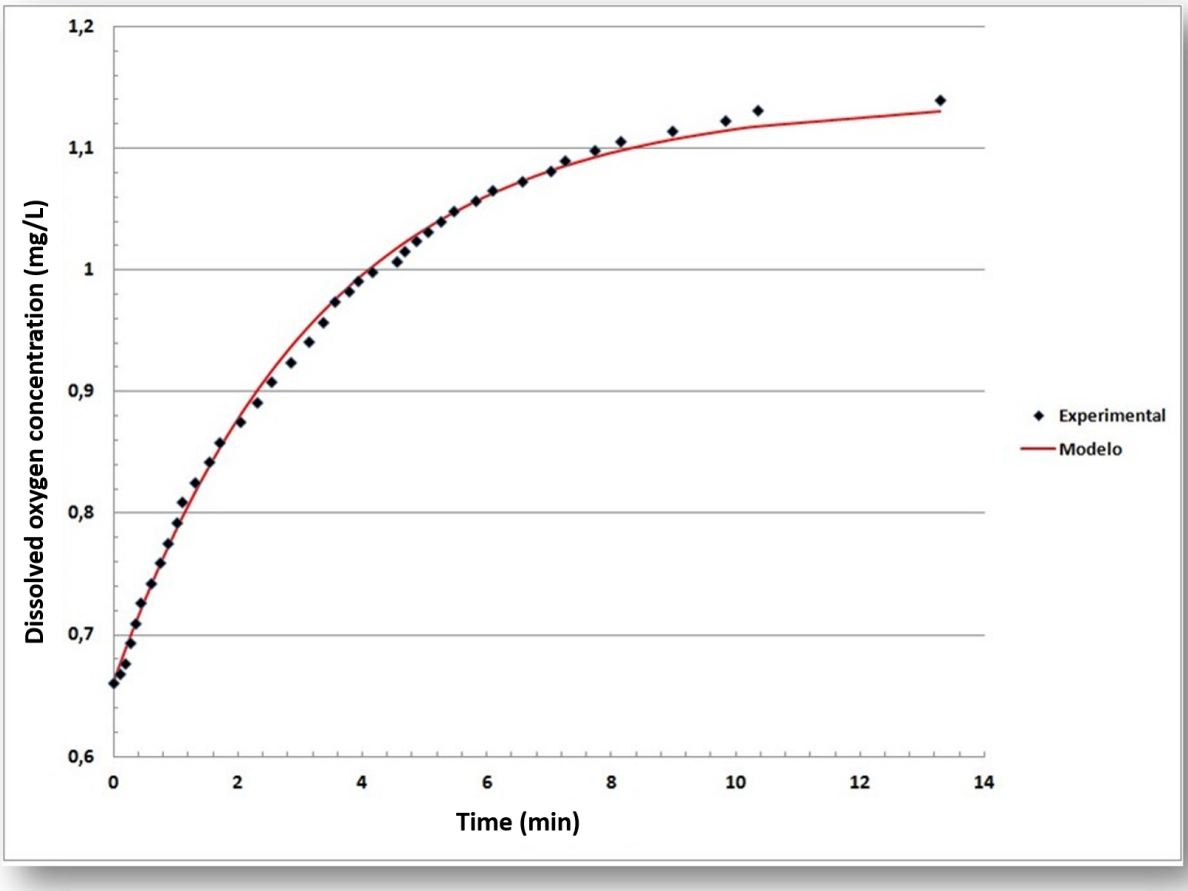

Figure 5. Real data and model comparison.

4 Conclusions

It was developed a differential equation based on the oxygen mass balance in a bioprocess, and from this equation, it was found an expression for estimating de volumetric oxygen transfer coefficient K_La starting from experimental data.

Using the method shown in Equations 3-4, it was found a K_La value of 3,85 x10-3 s-1 for the bioreactor, comparable with other research works in laboratory scale bioprocesses.

PBL methodology is of great importance for engineering learning. It guides students and researchers to take a problem solution to the ultimate boundaries, making every problem an opportunity to learn and develop new solutions.

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