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Modeling and simulation of tanks-in-series airlift bioreactors for production of lactic acid by fermentation

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Abstract−A tanks-in-series model was applied for mathematical modeling of the unsteady state performance of 70 and 100 liters airlift bioreactor for the production of lactic acid by fermentation. A set of first-order differential equations for the material balances of micro-organism, substrate, product, and dissolved oxygen around hypothetically well mixed stages was solved simultaneously utilizing computer program in MATLAB. The kinetic model utilized considered the effect of two substrates (glucose and dissolved oxygen) on the growth rate. The effect of air velocity on the lactic acid production was investigated. Results of this model have been validated with experimental data.

Key words: Airlift Bioreactor, Lactic Acid, Dissolved Oxygen, Modeling, Bioreactors

INTRODUCTION

Most industrial bioreactors are still conventional stirred tanks. As an alternative, recently, airlift bioreactor (ALB) designs have received increased attention. Due to their simple construction and less shear stress imposed up on shear sensitive cells compared with stirred tanks, they have potential applications in biotechnology industries [1]. Airlift bioreactors are comprised of four distinct zones, each with its own particular flow pattern. The first zone, in which the gas is sparged, is known as the riser, through which the gas-liquid dispersion travels upward cocurrently. This section has a higher fractional gas hold up and is where most of the gas-liquid mass transfer takes place. The liquid leaving the top of the riser enters a gas disengagement zone, the gas-liquid separator, where, depending on its specific design, some or most of the dispersed gas is removed. The gas-free liquid (or a dispersion of lesser gas hold up) then flows into the downcomer and travels to the base of the device, through the bottom, where it re-enters the riser. Thus, the liquid phase circulates continuously around the loop. The airlift bioreactor is commonly used in aerobic fermentation processes [2]. One of its industrial applications is fermentation of lactic Acid. Lactic acid is used mainly as the feedstock for production of biodegradable polylactic acid. It is also widely used in the food processing and pharmaceutical industries [3]. However, an accurate description of the performance of airlift bioreactors is still difficult [1,2]. Mixing in airlift bioreactors is usually imperfect and mathematical models for such reactors may not be described by either perfect mixing (continuous stirred tank reactors: CSTR) or plug flow (plug flow reactors: PFR). The mixing model used in most investigations dealing with airlift bioreactors is an axial dispersion model (ADM) [4-7]. It should be noted that the ADM could satisfactorily describe only mixing, which slightly deviates from the plug flow. On the other hand, a tanks-in-series model is applicable to the whole mixing extent ranging from perfect to plug flow mixing. Moreover, the tanks-in-series model provides a set of first-order differential equations, which may be solved using rather simple numerical techniques.

In spite of the applicability and flexibility of the tanks-in-series model, only few mathematical modeling investigations have been published for simulation of fermentation systems including imperfect mixing in an airlift bioreactor. Tanks-in-series is more realistic and advantageous compared to the ADM. Moreover, little work has been done on unsteady state performance of airlift bioreactors [8-10].

In this study, a mathematical model based up on a tanks-in series model without back flow has been developed to simulate the fermentation of Lactic acid in airlift bioreactors under unsteady state conditions and validated with available experimental data.

METHODS

1. Mathematical Modeling

The airlift bioreactor is composed of a column divided into regions containing the riser and downcomer. These reactors are usually classified into internal and external loop bioreactors according to the type of liquid recirculation.

In the tanks-in-series model, the flow in the airlift bioreactor is considered as flow through a series of equal sized, well-mixed stirred stages or tanks and the parameter describing non-ideal flow is the number of stages. The model is represented schematically in Fig. 1.

Following assumptions were made while deriving equations of the present mathematical model:

1. There are no radial gradients in liquid and gas phase
2. Isothermal condition holds in the reactor thus no energy balance is needed

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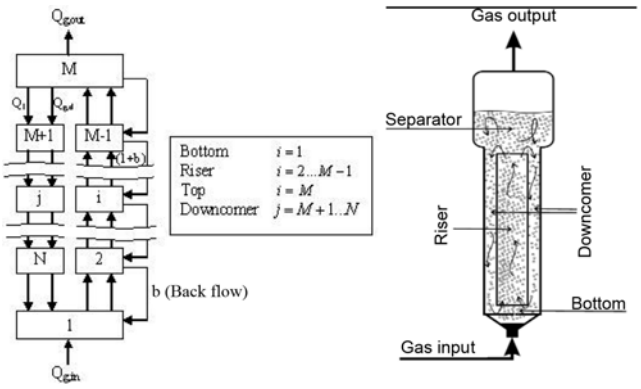

Fig. 1. Schematic diagram of the tank-in-series model for the air-lift bioreactor.

3. Reaction occurs just in the liquid phase

4. The gas holdup in the top and bottom sections is equal to the gas holdup in the riser.

5. The gas hold-up and mass transfer coefficients are almost constant along the riser and downcomer

6. Ideal gas behavior is assumed to be applicable to the gas phase under operating conditions.

7. The oxygen concentration in the gas phase is assumed to be uniform [11]. According to low oxygen consumption rate compared to oxygen transfer rate, the value of equilibrium dissolved oxygen concentration, C_l^*, was taken to be constant throughout the fermentor and during the fermentation and set equal to 0.00651 g dm^{-3}, which is., $C_l(t=0)$ [11]. This is justified by considering high turbulence in the airlift reactor that keeps oxygen concentration of the gas phase almost constant.

2. Material Balances in Different Sections of the ALB

The tanks-in-series model provides simultaneous first order ordinary differential equations, which are material balances of the microorganism, substrate, product, and dissolved oxygen for hypothetical well-mixed tanks or stages [12]. The unsteady state material balances of these components can be written as follows:

2-1. Bottom Section (i=1)

For the microorganism, substrate, and product (C=X, S, and P)

$$\frac{dX_1}{dt}=\frac{Q_l}{V_1}(X_2-X_1)tr_{X_1} \tag{1}$$

$$\frac{dS_1}{dt}=\frac{Q_l}{V_1}(S_2-S_1)tr_{S_1} \tag{2}$$

$$\frac{dP_1}{dt}=\frac{Q_l}{V_1}(Co_2-Co_1)+r_{co_1}+K_{la}(Co^*-Co_1) \tag{3}$$

2-2. Intermediate Tanks (i=2, …, n−1)

For the microorganism, substrate, and product (C=X, S, and P)

$$\frac{dX_1}{dt}=\frac{Q_l}{V_1}[X_{i-1}-2X_i+X_{i+1}]+r_{X_i} \tag{4}$$

$$\frac{dS_1}{dt}=\frac{Q_l}{V_1}[S_{i-1}-2S_i+S_{i+1}]+r_{S_i} \tag{5}$$

$$\frac{dP_1}{dt}=\frac{Q_l}{V_1}[P_{i-1}-2P_i+P_{i+1}]+r_{P_i} \tag{6}$$

For the dissolved oxygen (C_1)

$$\frac{dCo_i}{dt}=\frac{Q_l}{V_i}[Co_{i-1}-2Co_i+Co_{i+1}]+r_{Coi}+K_{la}(Co^*-Co_i) \tag{7}$$

2-3. Top Section (i=N)

For the microorganism, substrate, and product (C=X, S, and P)

$$\frac{dX_n}{dt}=\frac{Q_l}{V_n}[X_{n-1}-X_n]+r_{X_n} \tag{8}$$

$$\frac{dS_n}{dt}=\frac{Q_l}{V_n}[S_{n-1}-S_n]+r_{S_n} \tag{9}$$

$$\frac{dP_n}{dt}=\frac{Q_l}{V_n}[P_{n-1}-P_n]+r_{P_n} \tag{10}$$

For the dissolved oxygen (C_1)

$$\frac{dCo_n}{dt}=\frac{Q_l}{V_n}[Co_{n-1}-Co_n]+r_{con}+K_{la}(Co^*-Co_n) \tag{11}$$

3. Kinetic Model

The kinetic model will be used in this simulation to describe the lactic acid fermentation. The model is given by the following equations:

$$r_{X_i}=\mu_i X_i=\frac{dX_i}{dt} \tag{12}$$

$$r_{S_i}=-\gamma\frac{dS_i}{dt}-\lambda X_i \tag{13}$$

$$r_{P_i}=\alpha\frac{dX_i}{dt}+\beta X_i \tag{14}$$

$$r_{Co_i}=-\delta\frac{dX_i}{dt}-Q_{X_i} \tag{15}$$

i=1→N, where the specific growth rate (μi) is described by Contois model,

$$\mu_i=\mu_m\frac{S_i}{K_S X_i}\times\frac{C_{1,i}}{K_O X_i+C_{1,i}} \tag{16}$$

$$\gamma=\left(\frac{1}{y_{XS}}+\frac{\alpha}{y_{PS}}\right) \tag{17}$$

$$\lambda=\left(\frac{\beta}{y_{PS}}+m_S\right) \tag{18}$$

$$\delta=\left(\frac{1}{y_{XO}}+\frac{\alpha}{y_{PO}}\right) \tag{19}$$

Table 1. Kinetic parameters estimated

Parameter	Adjusted values
μ_m	7.06×10^{-5}
α	14.59
β	1.76×10^{-4}
γ	38.4058
λ	7.75×10^{-9}
δ	0.6569
ζ	7.47×10^{-6}
k_S	34.586
k_O	0.0003

$$\sigma=\left(\frac{\beta}{y_{PO}}+m_O\right) \tag{20}$$

The initial conditions of afore-mentioned ordinary differential equations are $X=X_o$, $P=P_o$, $S=S_o$, $C=C_{1o}$, $t=0$.

The kinetic parameters estimated from experiments in 70 and 100 liter stirred tank reactors [13] have been used in the present simulation for predicting the lactic acid fermentation in airlift bioreactor. Adjustment of these kinetic parameters by experimental data was necessary to get a better agreement between experimental and theoretical results [14]. The set of the adjusted kinetic parameters used in the present simulations is summarized in Table 1.

4. Hydrodynamic and Mass Transfer Correlations

The overall gas holdup was determined through the following equation [15]:

$$\varepsilon_g=5.10\times10^{-3}\left(\frac{p_G}{V_l}\right)^{0.499} \tag{21}$$

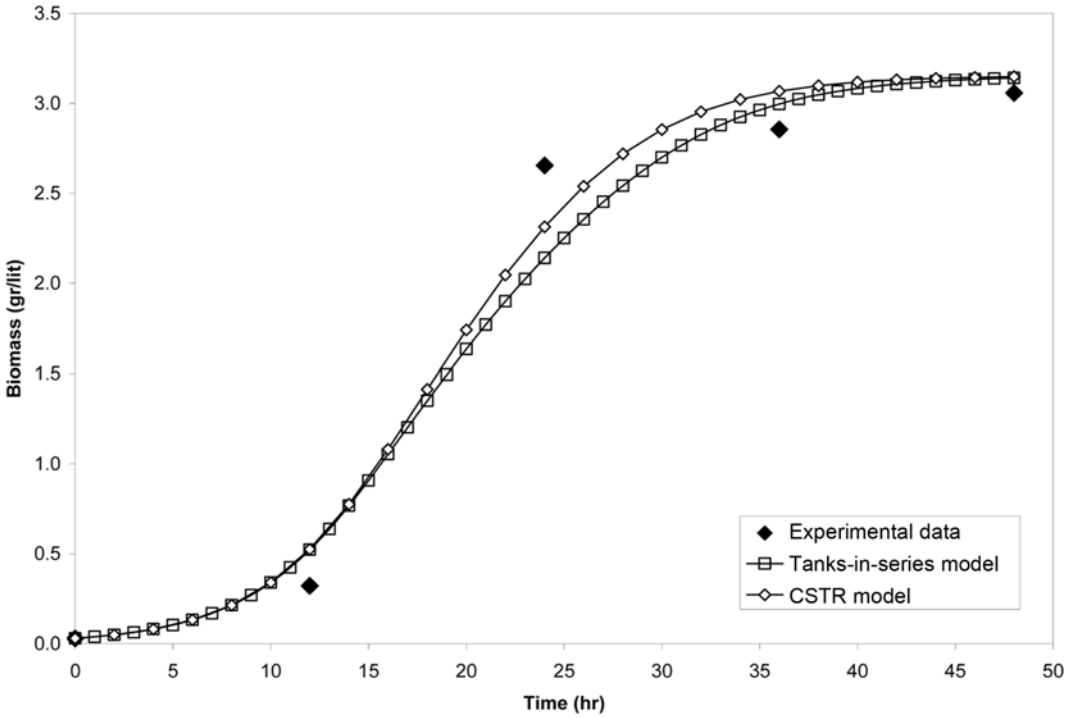

Fig. 2. Comparison of simulated (this study) and experimental profile ([13]) of microorganism in a 70 liter ALB (%r.m.d: 5.81).

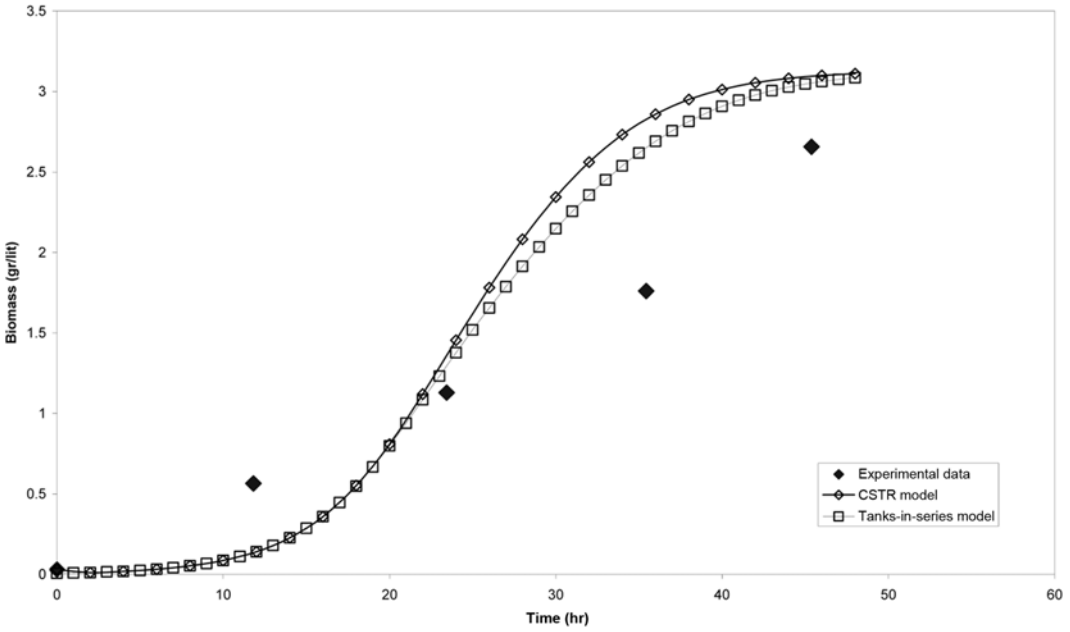

Fig. 3. Comparison of simulated (this study) and experimental profile ([13]) of microorganism in a 100 liter ALB (%r.m.d: 18.21).

For the axial dispersion coefficient of the liquid phase Towell and Ackermann [7,11] found:

$$D_{ax} = 2.61 D_r^{1.5} U_{gr}^{0.5} \quad (22)$$

The overall oxygen transfer coefficient was calculated by the following equation [12],

$$K_{la} = 1.76 \times 10^{-4} \left(\frac{P_G}{V_l}\right)^{0.925} \quad (23)$$

Where

$$\left(\frac{P_G}{V_l}\right) = V_g P_{1g} \quad (24)$$

5. Method of Solution

The mathematical model supplies a set of N first-order differential equations and for five components (biomass, Lactic acid, substrate, dissolved oxygen, and mole fraction of oxygen in the gas phase), the total number of equations will be 5×N 1st ODEs; these equations are to be solved simultaneously by Euler method in MATLAB. However, for computer simulation, further correlations and parameters are required, including geometrical parameters, kinetic model,

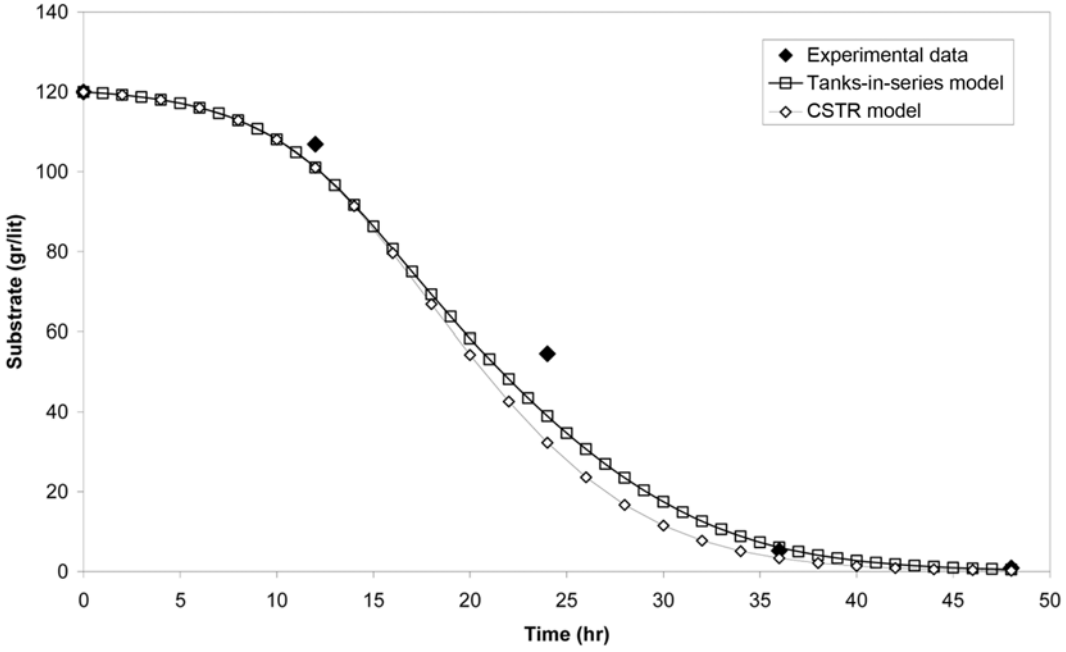

Fig. 4. Comparison of simulated (this study) and experimental profile ([13]) of substrate in a 70 liter ALB (%r.m.d: 2.74).

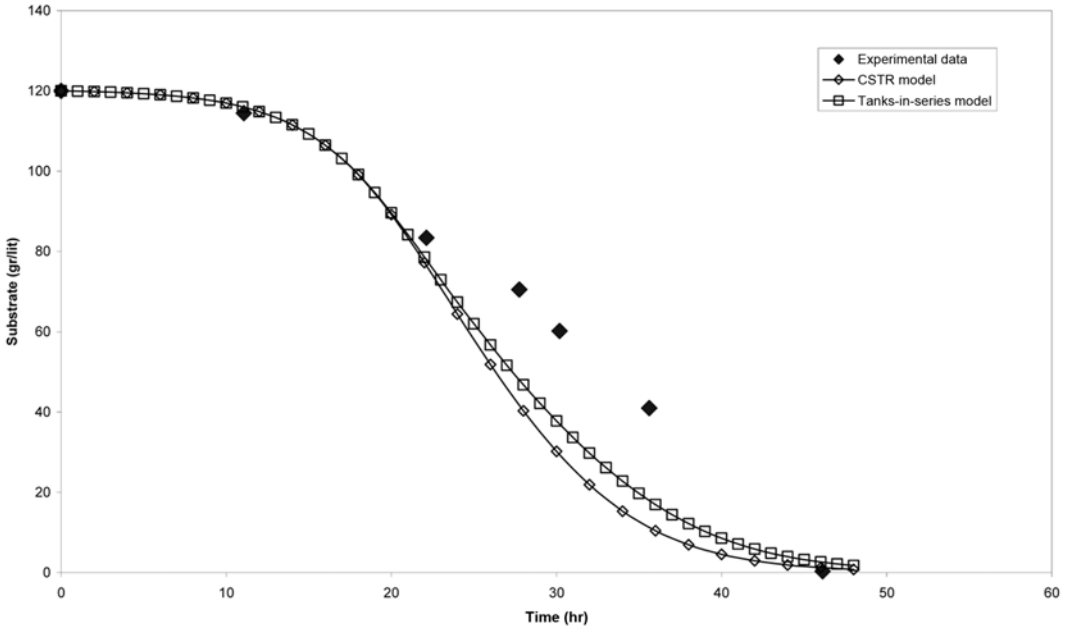

Fig. 5. Comparison of simulated (this study) and experimental profile ([13]) of substrate in a 100 liter ALB (%r.m.d: 10.52).

mass transfer and hydrodynamic parameters. These values have been evaluated using suitable relations in section 2.4.

It is noteworthy that the experimental data utilized in this work are those of Miura et al. performed in 70 and 100 liter ALB. The mutant strain *Rhizopus* sp. MK-96-1196 microorganism was used in that study [13].

RESULTS AND DISCUSSION

1. Simulation of Lactic Acid Production

Figs. 2-9, show typical time profiles of the biomass, lactic acid, substrate, and dissolved oxygen, respectively, in a 70 and 100 liter internal loop airlift bioreactor. In these figures the obtained profiles from the present work are compared with simulation results of a simple mixed reactor (CSTR) as well as experimental data. The results for the CSTR model are obtained by applying a single mixed reactor equation to the whole airlift bioreactor.

The percent mean relative deviation is used for discussion of the accuracy of the model and is presented in each figure between tank-in-series simulation results and experimental values and defined as follows:

$$\%\text{m.r.d} = \frac{100}{\text{n}}\left|\frac{\text{M}_i^{exp} - \text{M}_i^{calc}}{\text{M}_i^{exp}}\right|$$

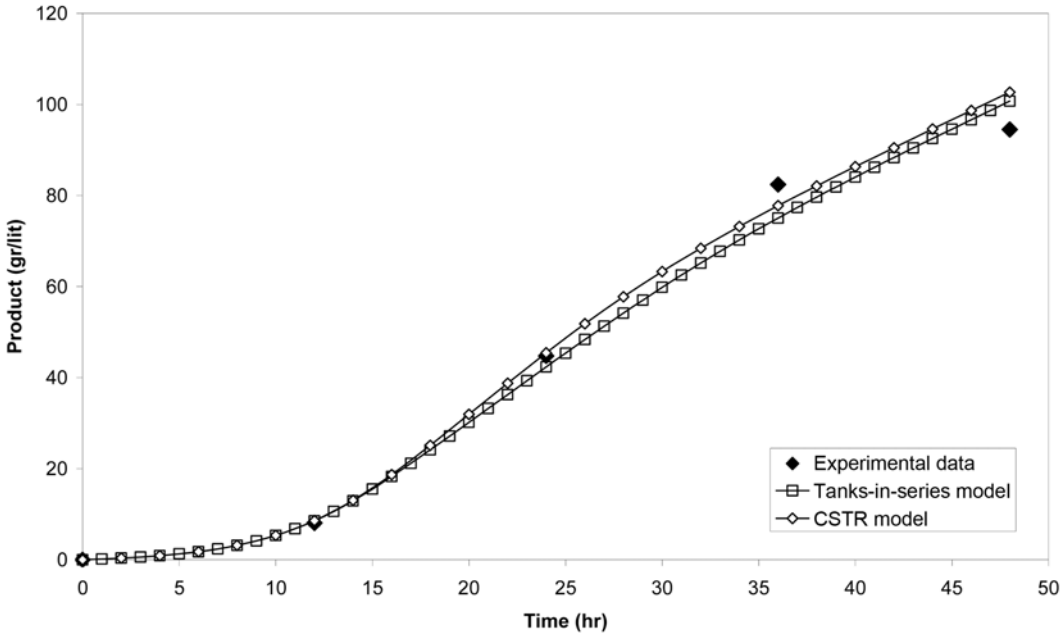

Fig. 6. Comparison of simulated (this study) and experimental profile ([13]) of LA in a 70 liter ALB (%r.m.d: 5.59).

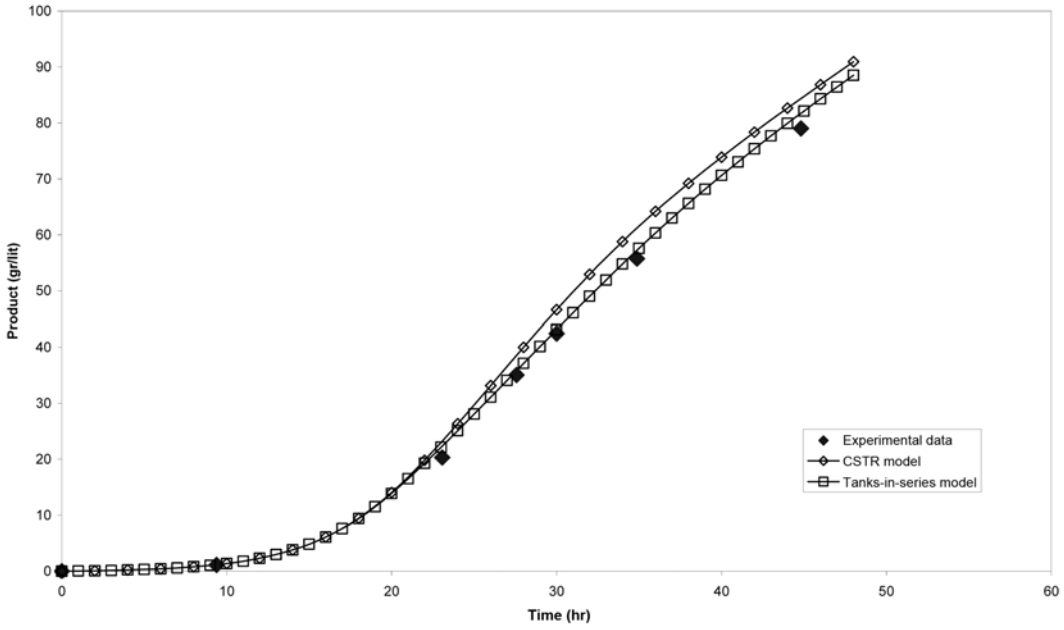

Fig. 7. Comparison of simulated (this study) and experimental profile ([13]) of LA in a 100 liter ALB (%r.m.d: 5.02).

Where M is a generic property and n is the number of experimental data considered.

Through Figs. 2 and 3 it is seen that during the exponential growth phase, the biomass concentration exponentially increases with cultivation time and the corresponding substrate concentration rapidly approaches zero. Growth rate decelerates due to depletion of the substrate and dissolved oxygen near the end of the exponential growth phase.

Furthermore, comparison of the simulated and experimental profiles for the biomass, lactic acid substrate, and dissolved oxygen is shown in Figs. 4-9. The prediction of the model is quite satisfactory and it may well describe the lactic acid fermentation in an airlift bioreactor.

2. Effect of Air Velocity on the Cell Growth

Figs. 10-13 show the effect of air velocity (air flow rate) on the biomass growth and LA, keeping 48 h as a fixed time for the duration of fermentation. The biomass growth increased with increased air velocity. Therefore, the production of biomass and LA is enhanced with air velocity.

Beyond 5 mm s^{-1} the effect of air velocity on the biomass growth and LA produced was not significant. This can be attributed to the fact that high airflow rates can lead to high gas holdups, enhanced

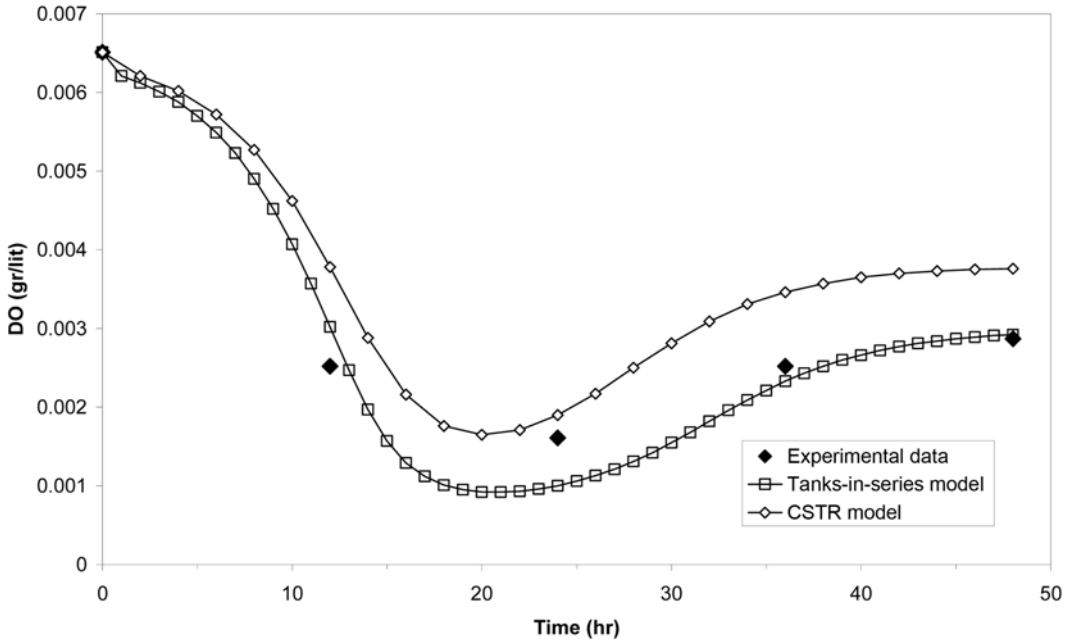

Fig. 8. Comparison of simulated (this study) and experimental profile ([13]) of DO conc. in a 70 liter ALB (%r.m.d: 14.75).

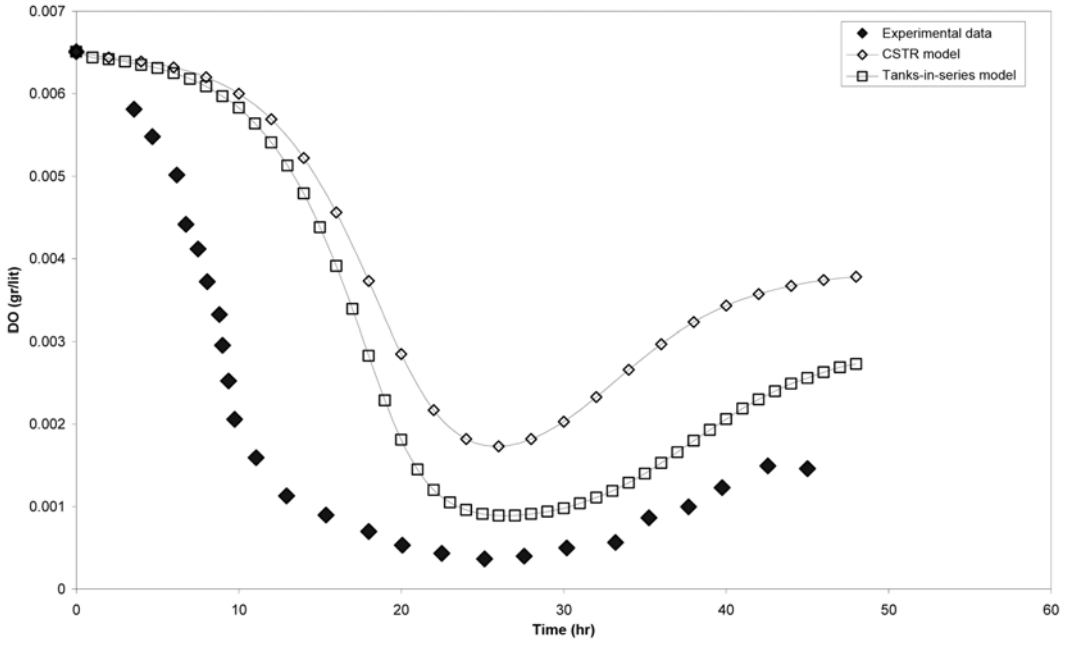

Fig. 9. Comparison of simulated (this study) and experimental profile ([13]) of DO conc. in a 100 liter ALB (%r.m.d: 18.59).

Fig. 10. Effect of air velocity on the microorganism at 48 h of fermentation.

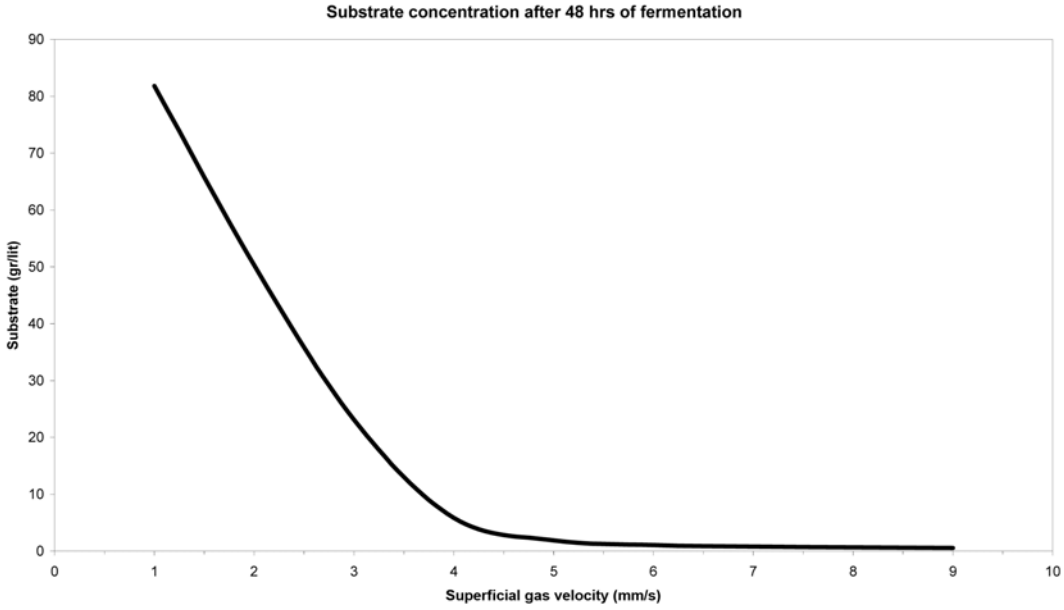

Fig. 11. Effect of air velocity on the substrate at 48 h of fermentation.

bulk mixing and improved DO and mass transfer, which promotes the biomass growth and consequently the lactic acid. When the airflow rate exceeded 5 mm s^{-1}, the increase in the biomass growth with airflow rate was reduced. The reason for this was that high airflow rate produced a high shear stress, which could potentially lead to cellular damage, consequently reducing the ability of cells to produce lactic acid. Another reason could be that higher airflow rates resulted in higher respiration rates, potentially leading to a significant decrease in glucose source (substrate) availability for any purpose, including lactic acid synthesis. The results show that there was an optimum range of air velocity from 1 to 5 mm s^{-1} for lactic acid fermentation in a 100 liter airlift bioreactor. This would have an additional process benefit of minimizing the costs of compressed air, a major contributor to the cost of running a large-scale airlift bioreactor [15].

CONCLUSION

A mathematical model using tanks-in-series under unsteady state conditions was developed to describe the production of Lactic acid in an airlift bioreactor. The model has been tested and the values were compared with experimental data. The model is suitable to predict the effect of air velocity on the process. For lactic acid fermentation an optimum range of air velocity (1-5 mm s^{-1}) is suitable in a 100 liter airlift bioreactor beyond which the process will not be economical.

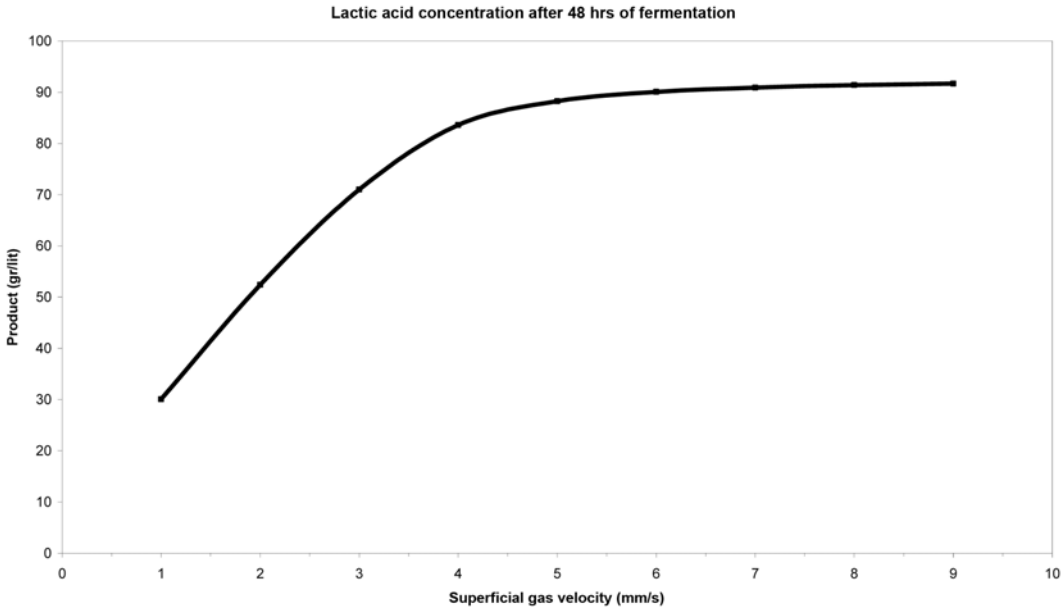

Fig. 12. Effect of air velocity on Lactic acid at 48 h of fermentation.

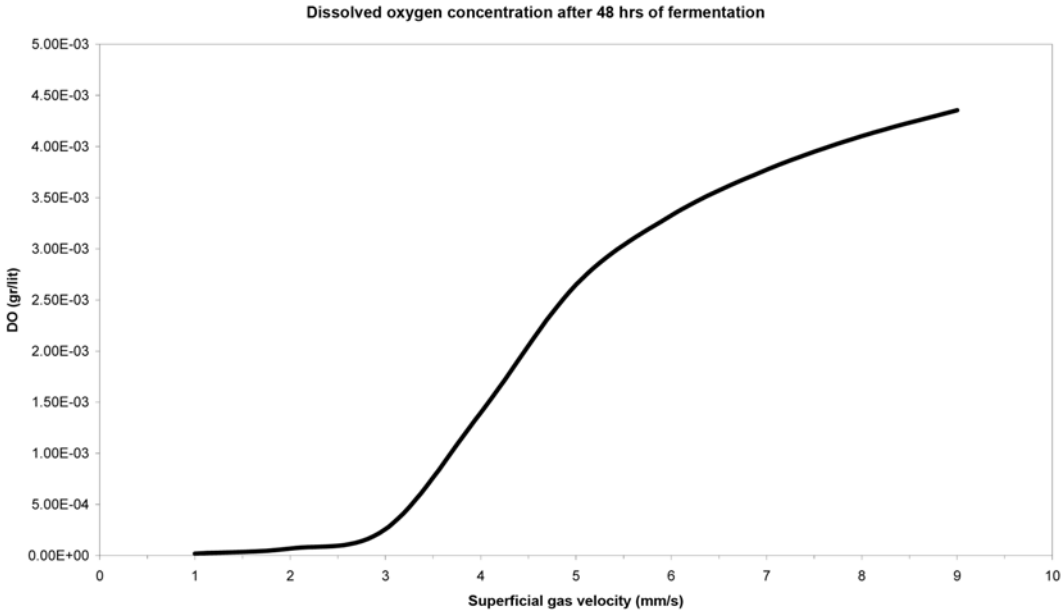

Fig. 13. Effect of air velocity on dissolved oxygen at 48 h of fermentation.

NOMENCLATURE

ALB : airlift bioreactor
C_l : dissolved oxygen concentration [g dm^{-3}]
C_l^* : equilibrium dissolved oxygen concentration [g dm^{-3}]
D_{ax} : axial dispersion coefficient [m^2 s^{-1}]
k_la : overall oxygen mass transfer coefficient [h^{-1}]
K_O : contois oxygen limitation constant
K_S : contois saturation constant
m_O : maintenance coefficient g substrate (g cells h)$^{-1}$
m_S : maintenance coefficient g substrate (g cells h)$^{-1}$
N : number of stages in the bioreactor
P : product concentration [g dm^{-3}]
Q_l : liquid flow rate [dm^3 min^{-1}]
Q_G : gas flow rate [dm^3 min^{-1}]
S : substrate concentration [g dm^{-3}]
t : time [h]
U_{gr} : superficial liquid velocity in the downcomer [m s^{-1}]
U_{lr} : superficial liquid velocity in the riser [m s^{-1}]
V_L : working volume of the reactor [dm^3]
X : biomass concentration [g dm^{-3}]
Y_{PO} : yield constant [g product/g oxygen]
Y_{PS} : yield constant [g product/g glucose]
Y_{XO} : yield constant [g biomass/g oxygen]
Y_{XS} : yield constant [g biomass/g glucose]
α : growth-associated product formation coefficient

β : non-growth-associated product formation coefficient [h^{-1}]
γ : growth associated parameter in the Luedeking-Pirt-like equation for substrate uptake [g substrate/g biomass]
δ : parameter in the Luedeking-Pirt-like equation for oxygen uptake [g oxygen/g biomass]
λ : non-growth associated parameter in the Luedeking-Pirt-like equation for substrate uptake [g substrate/g biomass h]
μ : specific growth rate [h^{-1}]
μ_m : maximum specific growth rate [h^{-1}]
ε_g : gas hold up

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