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Application of the Theory of the Structure of the Stream Flow for Modeling of Stirred Tank Bioreactors

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Summary: In this paper, investigations of the structure of the stream-flow in a lab scale stirred tank bioreactor are developed with the relevant research methods. The chouse on the following statistical criteria: Fisher function, correlation coefficient, and relative error is developed. The best results at low impeller speed are received at a model with stagnancy zone. The obtained results are used for modeling of a stirred tank bioreactor.

Keywords: Theory of the Structure the Stream Flow, Computing Fluid Dynamic, Mass Transfer, Stirred Tank Bioreactors.

1. INTRODUCTION

Bioreactors are increasingly used to make a variety of products across several industries. For example, they are used in the manufacture of antibiotics such as penicillin. About 70% of ingredients for the food industry are made through fermentation [2].

The effectiveness of the bioreactors to big degree is defined from the conditions of relation between the growing populations of the microorganisms with the environment. At using of the method of cultivation of the microorganisms the development of the cell population is connected with the transport of the foodstuffs from the cultural middle to the cell surface and the leading of the metabolite product [1, 16].

Mathematical tools and computational capacity allow at the moment a more fundamental approach in bioreactor. Computational Fluid Dynamics (CFD) has already been used in many studies to predict flow patterns and local gas volume fractions in the stirred gas-liquid vessels [2-5, 7, 8, 12, 15]. The CFD as connected to the reaction kinetic, heat and mass transfer models has become an interesting tool for the scale-up and the design of gas-liquid stirred tank reactors and other gas-liquid contacting devices. These computational tools include many modelling options, assumptions and a set of parameters. Therefore, their validation against experiments is needed [17].

The investigation of the structure of the stream flow allows the numeral values of the characteristics of distribution of the cells on time stay to be valued. For description of the structure of the stream-flow mathematical models interpreting on a appointed image the character of moving of the liquid in the apparatus are used and they are used in capacity of a separate block of the full mathematical model of the process. The complexity of the constructive formed of the bioreactors also and the physical-chemical specialties of the fermentation middle do not allow immediately the equations of the hydrodynamic to be used for analysis and modeling of the processes in the bioreactor. At these conditions it is effective models that reflect in a compact form the basic regularity of the hydrodynamic situation in the apparatus to be used [6, 10, 11, 13].

In this paper the structure of the stream-flow in a stirred tank bioreactor is used for modeling of the hydrodynamic and choice of a bioreactor model.

2. MATERIALS AND METHODS

For modeling of the structure of the stream-flow at relation between the height and the diameter that does not exceed (H/D) ≤ 2, the model of *perfect mixing* is used also and the follow combined models: *model with standstill zone*; *model with bypass and model with bypass and standstill zone* [6].

1. Model for perfect mixing. The function of the response (*F-curve*) is defined with the dependence:

$$F(t) = 1 - \exp\left(-\frac{t}{\bar{t}}\right) \qquad (1)$$

where: $\bar{t} = \frac{V}{v}$; V – bioreactor volume taken from liquid, m^3; v – volume rate of liquid phase, m$^3\cdot$s^{-1}.

The model of perfect mixing is the simplest and the most convenient for practical calculating. Its application is restricted for bioreactors with small volume and intensive mixing.

When the apparatus diameter is raised in more cases reaching to ideal mixing on all apparatus volume does not succeed, therefore for description of the structure of stream flows the combined models are used.

2. Combined models. In the base of the combined models is the idea for the possibility for presenting of the working bioreactor volume with different zones whose character of the moving of the liquid is equal the volume of zone. In this way if on the through apparatus volume ideal mixing is not reach then it can reached in the definite zone.

2.1. Model with standstill zone. The *F-curve* is defined with the dependence:

$$F(t) = 1 - \exp\left(-\frac{1}{(1-d)}\frac{t}{\bar{t}}\right) \tag{2}$$

The volume of the zone with perfect mixing is determined from the empiric dependence [6]:

$$\frac{V_m}{V} = 0.98\left(\frac{P_L}{V}\right)^{0.028} \tag{3}$$

where: P_L is the stirring power, W.

The stirring power is determined by the dependence [9]:

$$P_L = 179.5\,\rho n^3 d^5 \,\mathrm{Re}^{-0.4}.$$

This model is applied at little impeller speed in apparatus with large volume and wall up elements intro the apparatus.

2.3. Model with bypass. The *F-curve* is defined with the dependence:

$$F(t) = 1 - k \exp\left(-k \frac{t}{\bar{t}}\right) \tag{4}$$

This model is applied at mixing with low impeller speed and situated near to input and output.

2.4. Model with bypass and standstill zone. The *F-curve* is defined with the dependence:

$$F(t) = 1 - k \exp\left(-\frac{k}{(1-d)} \frac{t}{\bar{t}}\right) \tag{5}$$

The character of the moving of the liquid is defined simple by the geometrical parameters of the systems, the physical conditions and the characteristic of the middle and the boundary conditions of the system.

3. INVESTIGATION OF THE STREAM FLOW

In this paper the method of the impulse induction of the tracer in the stream flow is used. The *F-curve* is worked with statistical methods, i.e. it is calculated with the mean value and dispersion [6].

The experiments are leaded in a small scale stirred tank bioreactor 2L-M. It is included to a System for Automation Control ABR 201. It allows controlling the follows general parameters of the fermentation process: stirrer speed – n, min^{-1}; partial pressure of oxygen in the middle – pO_2, %; temperature – T, ^0C; concentration of hydrogen ions – pH and level of the foam in the bioreactor.

The scheme of the experimental treatment is shown in [9]. The conditions for leading of the investigations and general constructive sizes are shown in Table 1.

Table 1. General tools of the bioreactor

Volume of bioreactor,	V	1.7 l
High of liquid in the bioreactor,	H	150 mm
Impeller speed,	n	400 min^{-1}
Relation,	H/D	1.5
Temperature,	T	35^0C
Number of baffles assembly,	z_O	3
Width of baffles assembly,	b	12.0 mm
Number of impeller,	z_S	1
Slope angle of paddle impeller,	α	90^0
Eccentricity of impeller,	δ	0.0 mm
Height of paddle impeller,	h	12.0 mm
Width of paddle impeller,	l	14.0 mm
Distance of first impeller from the bottom,	h_1	58.0 mm
Inside diameter of tube of the cooler,	d_0	13 mm
Outside diameter of tube of the cooler,	d_1	15 mm
Submerge length of the cool in the liquid,	L	max. 175 mm

The obtained results at investigation of the structure of the stream-flow are shown in Fig. 1.

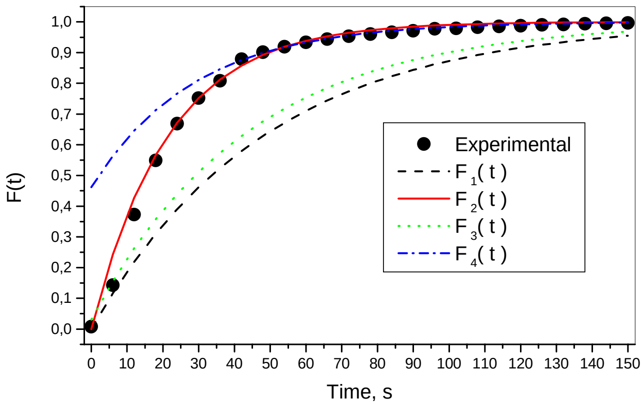

Fig. 1 Experimental curve of the response and simulated data on the model (at Re=21513, n=400 min^{-1})

The symbols in Fig. 1 are: $F_1(t)$ – model of perfect mixing; $F_2(t)$ – model with standstill zone; $F_3(t)$ – model with bypass and $F_4(t)$ – model with bypass and standstill zone.

The experimental data are normalized in the interval [0, 1] by the equation $F_E(i) = c(i)/c_{\max}$, where: c(i) is pO_2 and c_{max} is the maximal value of pO_2 at the investigations.

The obtained results after the parametric identification, experimental values of the statistical criteria: correlation coefficient – R^2, Fisher function – F_E, relative error – S_L and Sum of Squares of Weight Residuals (*SSWR*) criterion for the examined models of the structure of the stream-flows are shown in Table 2.

Table 2. Statistical information for investigated models

Model	*d*	*k*	*SSWR*
Perfect mixing	0.00	0.00	0.79
Model with standstill zone	0.33	0.00	0.02
Model with bypass	0.00	0.97	0.51
Model with bypass and standstill zone	0.34	0.54	0.50
Model	R^2	F_E	S_L
Perfect mixing	0.942	1.52	0.31
Model with standstill zone	0.997	1.84	0.25
Model with bypass	0.853	1.90	0.65
Model with bypass and standstill zone	0.898	1.91	12.27

The mean time stay is equal to $\bar{t} = 48.47$ s. The dispersion has value: σ^2_t=1585.37 and σ^2_θ=339.4. The theoretical value of Fisher Function is $F_T(25,1)$=4.24. The theoretical correlation coefficient has value $R^2_T(24)$=0.381.

The developed experimental investigations and obtained results (Fig. 1 and Table 2) show the best statistical indexes the models with standstill zone has and perfect mixing have. The experimental Fisher Function is less than the theoretical value, despite that the comparison of the correlation coefficients shows that all models are adequate.

4. MODEL OF STIRRED TANK BIOREACTORS

The developed investigations of the structure of the stream flow for a lab scale stirred tank bioreactor 2L-M show the models for gas-phase (GF), liquid-phase (LF) and the bio-phase (BF) should be constructed on base of the model with perfect mixing and the model *standstill zone*.

For perfect mixing model and fed-batch fermentation process the systems equation for three main phases in bioreactor have the following types:

Gas-phase:

$$\begin{aligned}
\frac{dC_G^{O_2}}{dt} &= -K_G a^{O_2}\left(\frac{RT}{\varepsilon_G}\right)\left(p\frac{C_G^{O_2}}{m_{O_2}} - C_L^{O_2}\right) \\
\frac{dC_G^{CO_2}}{dt} &= -K_G a^{CO_2}\left(\frac{RT}{\varepsilon_G}\right)\left(C_L^{CO_2} - p\frac{C_G^{O_2}}{m_{CO_2}}\right)
\end{aligned} \tag{6}$$

Bio-phase:

$$\begin{aligned}
\frac{dX}{dt} &= \mu X - \frac{F}{V}(X - X_0) \\
\frac{dS}{dt} &= \frac{F}{V}(S_0 - S) - \alpha^S \mu X \\
\frac{dC_L^{O_2}}{dt} &= K_L a^{O_2}\left(p\frac{C_G^{O_2}}{m_{O_2}} - C_L^{O_2}\right) - \alpha^{O_2}\mu X - \frac{F}{V}C_L^{O_2} \\
\frac{dC_L^{CO_2}}{dt} &= K_L a^{CO_2}\left(C_L^{CO_2} - p\frac{C_G^{O_2}}{m_{CO_2}}\right) + \alpha^{CO_2}\mu X - \frac{F}{V}C_L^{CO_2}
\end{aligned} \tag{7}$$

where: X – concentration of biomass in LP, kg·m^{-3};
S – concentration of substrate in LP, kg·m^{-3};
$C_G^{O_2}$ – concentrations of O_2 in GP, %;
$C_G^{CO_2}$ – concentrations of CO_2 in GP, %;

$C_L^{O_2}$ – concentrations of O_2 in LP, %;
$C_L^{CO_2}$ – concentrations of CO_2 in LP, %;
$K_G a$ – volumetric mass transfer coefficient for GP, h^{-1};
$K_L a$ – volumetric mass transfer coefficient for LP, h^{-1};
ε_G – gas hold-up, %;
m – Henry's law constant, $Pa \cdot .m^3 \cdot kg^{-1}$;
p – input pressure of aeration gas, Pa;
Q_G – gas flow rate, $m^3 \cdot s^{-1}$;
R – universal gas constant, R=8.3143, $J \cdot mol^{-1} \cdot K^{-1}$;
T – temperature, K.

The specific growth rate depends on the kinetic process parameters and physic-chemical characteristics of the middle: $\mu = \mu(X, S, C_L, C_G, pH, T \; and \; etc.)$. It is define for each concrete process.

The system equation for the batch process is received from (7) at $F = 0$.

5. CONCLUSIONS

1. The developed investigations of the structure of the stream-flows in a stirred tank bioreactor show at low frequencies of stirrer standstill zones gives the best results. Then the most suitable is the model of the structure of the stream-flows with standstill zone. It is appropriate also at big density and viscosity of the middle.
2. A model for stirred tank bioreactor is offered on base of the investigated structure of the stream flow at bath and fed-batch cultivation for the three base phases: gas-phase, liquid-phase and bio-phase.
3. The future investigations for the examined bioreactor works will be continued with using of computing fluid dynamic (CFD) modeling. In this way, the hydrodynamic situation and accurately location of the standstill zones will be fuller described.

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