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Estimating the Limiting Rate of Dilution in Technology for Lactic Acid Production by Continuous Fermentation

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Abstract—The estimation of the dilution rate in a fermenter is associated with biotechnological features. The time of residence of the stream of substrates in the fermenter should ensure the growth of the microbial population. In other words, if the dilution rate D is higher or equal to the limiting value D_{lim}, synthesis has no time to take place and, as a consequence, no product (specifically lactic acid) is formed. In this study, as a result of mathematical modeling, the technological parameter $D < D_{\text{lim}}$ has been calculated, which ensures real conditions for the practical implementation of the continuous process of lactic acid production.

Keywords: biotechnology, lactic acid production, continuous process, fermenter, biomass, substrate, mathematical modeling, limiting dilution rate

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INTRODUCTION

The estimation of the dilution rate D in a fermenter is associated with biotechnological features. The residence time of the stream of substrates in the fermenter should ensure the growth of the microbial population; i.e., if the dilution rate D is higher than or equal to the limiting value D_{lim}, synthesis has no time to take place and, as a consequence, a product, namely, lactic acid, is not formed. The estimation of the limiting value D_{lim} is only possible using mathematical models.

A large number of studies are devoted to the mathematical modeling of the lactic acid production, and the main publications are considered in reviews [1, 2]. It should be noted that the majority of publications are of a particular character; i.e., they study particular strains with particular sources of raw materials for particular conditions (pH, temperature, etc.).

However, an analysis of these publications makes it possible to formulate the relationships of the generalized mathematical model, which includes equations for growth in the population of microorganisms; the formation of the main product, namely, lactic acid; the formation of by-products; the consumption of a substrate; and the formation of an additional amount of the main substrate from certain components of raw materials.

The objective of this study is to calculate the technological parameter $D < D_{\text{lim}}$, which ensures real conditions for the practical implementation of the continuous process of lactic acid production.

MATHEMATICAL MODELING

The equation of the mathematical model for the formation of biomass has the generalized form

$$DX - \mu X = 0. \tag{1}$$

Equations for lactic acid and byproducts (in aggregate) are written in the following unified form, since they are metabolism products

$$(\alpha\mu + \beta)X - DP = 0 \tag{2}$$

and

$$(\alpha_B\mu + \beta_B)X - DB = 0. \tag{3}$$

An equation for the substrate contains two components: the consumption of the substrate by growing microorganisms and the formation of an additional amount of the substrate due to the degradation of individual components of raw materials. Thus, the equation can be written as

$$D(S_0 - S) - \frac{1}{Y_{X/S}}\mu X + k_M M = 0. \tag{4}$$

An equation for the formation of an additional amount of the substrate has the following form:

$$D(M_0 - M) - k_M M = 0. \tag{5}$$

An equation for the specific growth rate in the generalized form is written as

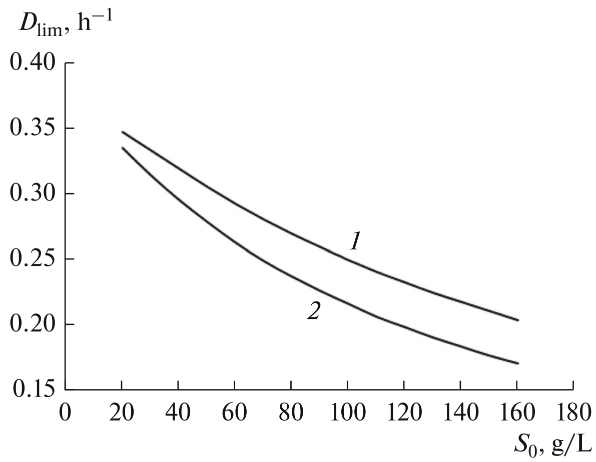

Fig. 1. Dependence of D_{lim} on S_0: (1) $M_0 = 0$ and (2) $M_0 = 0.5S_0$.

$$\mu = \mu_{max}\frac{K_iS}{K_mK_i + K_iS + S^2} \times\left(1-\frac{X}{X_{max}}\right)^{n_1}\left(1-\frac{P}{P_{max}}\right)^{n_2}. \quad (6)$$

Equation (6) takes into account the possibility of inhibition by the substrate (K_i), biomass (X_{max}, n_1), and product (P_{max}, n_2).

The limiting value of the dilution rate $D = D_{lim}$ is determined by the following conditions: the entering substrate with the concentration S_0 and the formed substrate with the concentration M are completely washed out at $D = D_{lim}$ without forming biomass and, as a consequence, without forming a product. Thus, at the outlet of the apparatus, we have $X = 0$ and $P = 0$.

The concentration of the substrate formed from the component of raw materials M at $D = D_{lim}$ is calculated by the following formula:

$$M(D_{lim}) = \frac{D_{lim}M_0}{D_{lim} + k_M}. \quad (7)$$

Using Eq. (1) and relationship (6), in which $X = 0$ and $P = 0$, and substituting $S = S_0 + \frac{D_{lim}M_0}{D_{lim} + k_M}$, we derive a nonlinear algebraic equation for calculating the value of D_{lim} in the following form:

$$\begin{aligned} &D_{lim}(D_{lim} + k_M)^2 K_mK_i \\ &+ K_i(D_{lim} + k_M)(D_{lim} - \mu_{max}) \\ &\times[S_0(D_{lim} + k_M) + D_{lim}M_0] \\ &+ D_{lim}[S_0(D_{lim} + k_M) + D_{lim}M_0]^2 = 0. \end{aligned} \quad (8)$$

To choose the initial approximation in the solution to nonlinear equation (8), we calculate the difference between D^0_{lim} and D_{lim}, where D^0_{lim} is written under the condition $M_0 = 0$; i.e., when there is no additional substrate feed, i.e.,

$$D^0_{lim} = \mu_{max}\frac{K_iS_0}{K_mK_i + K_iS_0 + S_0^2}. \quad (9)$$

To calculate D_{lim}, we use the following designation:

$$S' = S_0 + M = S_0 + \frac{D_{lim}M_0}{D_{lim} + k_M}. \quad (10)$$

In this case, D_{lim} can be written as

$$D_{lim} = \mu_{max}\frac{K_iS'}{K_mK_i + K_iS' + (S')^2}. \quad (11)$$

We derive the difference

$$D^0_{lim} - D_{lim} = \frac{\mu_{max}K_iS_0\left(K_mK_i + K_iS' + (S')^2\right) - \mu_{max}K_iS'\left(K_mK_i + K_iS_0 + S_0^2\right)}{\left(K_mK_i + K_iS_0 + S_0^2\right)\left(K_mK_i + K_iS' + (S')^2\right)}. \quad (12)$$

Expanding the numerator, we write conditions for estimating the sign of difference (12). This condition has the following form:

$$S_0S' - K_mK_i > 0. \quad (13)$$

Difference (12) is higher than zero if $K_mK_i < S_0S'$.

Thus, we have $S_0(S_0 + M) - K_mK_i > 0$.

By setting $S_0 \geq K_mK_i$, we have D^0_{lim} always higher than D_{lim}, which makes it possible to choose the initial value of D_{lim} in (8) using D^0_{lim}.

It is possible to calculate the maximum value of D^0_{lim}. The condition of the maximum is as follows:

$$\frac{dD^0_{lim}}{dS_0} = 0;$$

i.e., the value of S_0 for max D^0_{lim} can be written as

$$S_0 = (K_mK_i)^{1/2}. \quad (14)$$

After substituting S_0 according to (14) into the relationship for D^0_{lim}, we derive the maximum value of D^0_{lim}, which is a benchmark for choosing the initial value of D_{lim}.

Substitution yields the following relationship:

$$\max D_{\text{lim}}^{0} = \frac{\mu_{\max}}{2\left(\frac{K_{\text{m}}}{K_{\text{i}}}\right)^{1/2} + 1}. \quad (15)$$

The results of estimations for D_{lim} are presented in Fig. 1. Line *1* corresponds to the condition $M_0 = 0$; i.e., there is no substrate feed due to the degradation of the component of raw materials. Line *2* corresponds to the condition $M_0 \neq 0$; in this case, we have $M_0 = 0.5S_0$ in all calculations.

Thus, the values of D_{lim} (line *1*) were calculated by formula (9). The value of D_{lim} (line *2*) was calculated using the solution to nonlinear equation (8).

The numerical values of constants in calculating D_{lim} were as follows: $K_{\text{m}} = 0.79$ g/L, $K_{\text{i}} = 164$ g/L, $\mu_{\max} = 0.403$ h^{-1} [3], and $k_M = 0.035$ h^{-1} [4].

The initial value for solving Eq. (8) was determined as follows. The maximum value $\max D_{\text{lim}}^{0}$ was calculated by formula (15), and it was 0.354 h^{-1} for the adopted values of constants. Thus, $D_{\text{lim}}^{\text{ini}}$ was chosen from the following range:

$$0 < D_{\text{lim}}^{\text{ini}} < 0.354.$$

In all calculations, we specified $D_{\text{lim}}^{\text{ini}} = 0.1$.

CONCLUSIONS

In this study, as a result of mathematical modeling, the technological parameter $D < D_{\text{lim}}$ has been calculated, which ensures real conditions for the practical implementation of the continuous process of lactic acid production.

NOTATION

B	concentration of the by-product, g/L
$D = Q/V$	dilution rate, h^{-1}
D_{lim}	limiting value of the dilution rate, h^{-1}
K_{i}	inhibition constant, g/L
K_{m}	substrate saturation constant, g/L
k_M	rate constant for substrate formation from the component of raw materials, h^{-1}
M, M_0	concentrations of the component of raw materials from which an additional substrate is formed in the inlet stream and the fermenter, respectively, g/L
P	concentration of the product, g/L
$P_{\max}$	maximum concentration of the product, g/L
Q	volumetric flow rate through the fermenter, m^3/h
S	concentration of the substrate, g/L
S_0	concentration of the substrate in the inlet stream, g/L
V	filled volume of the fermenter, m^3
X	concentration of biomass, g/L
$X_{\max}$	maximum concentration of biomass, g/L
$Y_{X/S}$	stoichiometric coefficient, g/g
α	constant in the kinetic relationship for the main product (lactic acid), g/g
β	constant in the kinetic relationship for the main product (lactic acid), h^{-1}
α_B	constant in the kinetic relationship for the by-product, g/g
β_B	constant in the kinetic relationship for the by-product, h^{-1}
μ	specific growth rate, h^{-1}
$\mu_{\max}$	maximum specific growth rate, h^{-1}

SUBSCRIPTS AND SUPERSCRIPTS

B	byproduct
ini	initial value
M	component of raw materials from which an additional substrate is formed
P	product
S	substrate
X	biomass

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