

# Design and Mathematical Description of Differential Contactors Used in Extractive Fermentations

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The performance of differential contactors for use in extractive fermentation is complicated by the effects of product formation in the contactor. When product formation is significant, approximate analytical solutions are presented for the performance of the contactor for two limiting cases: high and low substrate concentrations. When products are formed at a constant rate, there is a minimum raffinate solute concentration that can be obtained, in contrast to the behavior of a column in the absence of product formation. General equations describing the behavior of the system for product formation with backmixing in both phases are presented. The case of a stripping factor not equal to unity is considered.

## INTRODUCTION

Many important industrial fermentations are adversely affected by the accumulation of toxic metabolites in the broth during fermentation. Most strains of *Saccharomyces* yeast, for example, are completely inhibited by ethanol concentrations above 110 g/L.<sup>1</sup> In the acetone-butanol fermentation, a butanol concentration of only 10–15 g/L totally inhibits product production and cell growth of *Clostridium acetobutylicum*.<sup>2,3,4</sup> Product inhibition decreases fermentor productivity, limits final product concentrations and requires the use of dilute substrates in the fermentor. Large fermentors are thus required and product separation and stillage handling costs are high.

The effects of product inhibition can be reduced by removing toxic metabolites from the broth during fermentation. One versatile method of *in situ* product removal is extractive fermentation. Here, an organic solvent is contacted with the broth during fermentation; toxic products are extracted into the solvent and product inhibition is reduced. The production of acetone and butanol by extractive fermentation has recently been demonstrated in laboratory scale fermentors.<sup>5–7</sup> Fermentor productivity was increased, concentrated substrates could be used, and final butanol concentration in the extraction solvent was higher than can be obtained in regular batch fermentation.

Extractive fermentation can be carried out in two basically different ways: extraction solvent can be added directly to the fermentor or whole broth can be cycled to an external vessel where solvent is contacted with the broth. In both

methods of extractive fermentation, the design of the process is complicated by the continual formation of products during extraction. Fournier<sup>8</sup> and Kollerup and Daugulis<sup>9</sup> have presented models describing extractive fermentation processes in which the extraction solvent is added directly to the fermentor. In production-scale fermentors, however, high agitation is required to disperse the extraction solvent in the broth. The high shear rate generated at the impeller can create stable emulsions of solvent in the broth<sup>6</sup> leading to difficult separation of solvent and broth in later unit operations. It may thus be preferable to contact the solvent and broth in an external extraction vessel. In many types of differential extraction devices, such as reciprocating-plate or pulsed columns, shear rate is relatively uniform over the cross-sectional area of the column. Agitation in the column can be adjusted to provide good mass-transfer while preventing the formation of stable emulsions.

In this article, approximate analytical solutions describing performance of differential contactors in extractive fermentation are derived. The influence of different operating variables on extractor performance is discussed and a simple method of determining the significance of product formation by the cells in the extractor is described.

## MODEL DEVELOPMENT

Figure 1 shows a schematic diagram of an extractive fermentation process. Whole broth, containing viable cells, is cycled from the fermentor to a differential contactor in which extraction solvent and broth are contacted in countercurrent flow. Inhibitory products in the broth are extracted into the solvent so that product inhibition is reduced. Extracted broth is recycled to the fermentor while the products contained in the solvent are recovered by suitable means such as distillation or back-extraction.

Mass balances over a differential section of a contactor with two phases passing countercurrently in one-dimensional steady state flow and product production taking place in the continuous phase yield the following equations:

$$E_x \frac{d^2 c_x}{dz^2} - U_x \frac{dc_x}{dz} - k_{0x} \alpha (c_x - c_x^*) + \tau_{\text{Prod}} = 0 \quad (1)$$

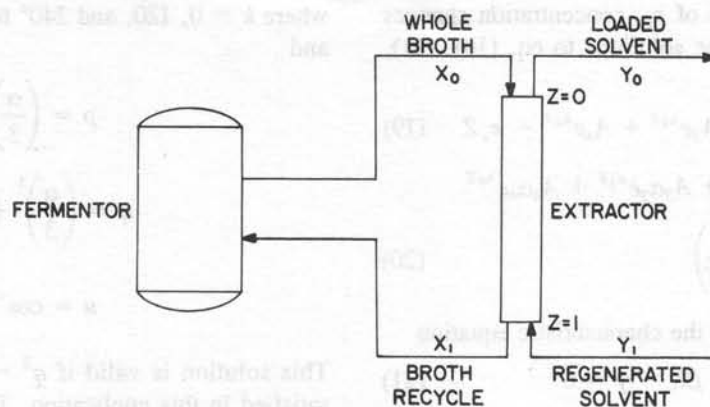


Figure 1. Schematic of an extractive fermentation process.

$$E_y \frac{d^2 c_y}{dz^2} + U_y \frac{dc_y}{dz} + k_{0x} \alpha (c_x - c_x^*) = 0 \quad (2)$$

where  $E_x, E_y$  are effective turbulent diffusion coefficients and  $\tau_{\text{Prod}}$  is the rate of product formation in the continuous phase.

In order to solve eqs. (1) and (2) the kinetics of product formation must be known. Assuming that Monod kinetics describe cell growth and that sugar is the limiting substrate, the specific growth rate  $\mu$  is given by

$$\mu = \frac{\mu_m c_s}{K_s + c_s} \quad (3)$$

For constant yields of cell mass and product, the volumetric rate of product formation can be represented by

$$\tau_{\text{Prod}} = \frac{Y_{p/s} \mu_m c_s c_m}{Y_{x/s} (K_s + c_s)} \quad (4)$$

Two useful solutions to eqs. (1) and (2) can be obtained by considering limiting cases of this kinetic expression. When the substrate is in excess ( $c_s \gg K_s$ ), the rate of product formation is given by

$$\tau_{\text{Prod}} = \frac{Y_{p/s} \mu_m c_m}{Y_{x/s}} \quad (5)$$

Assuming that the concentration of cell mass is constant throughout the extraction column, the rate of product formation can be expressed as a zero-order reaction

$$\tau_{\text{Prod}} = v_x \quad (6)$$

where

$$v_x = \frac{Y_{p/s} \mu_m c_m}{Y_{x/s}} = \text{const.} \quad (7)$$

The second limiting case is for low substrate concentrations ( $c_s \ll K_s$ ) where product production, again assuming a constant cell mass in the extractor, is proportional to substrate concentration

$$\tau_{\text{Prod}} = \frac{v_x}{K_s} c_s \quad (8)$$

Equations (1) and (2) can be solved for the two limiting cases represented by eqs. (6) and (8). The case of high substrate concentration will be considered first.

## LIMITING CASES

### Case I: High substrate concentrations

When the concentration of substrate is high ( $c_s \gg K_s$ ), the rate of product formation in the extraction column is constant and is given by eq. (6). Assuming a linear equilibrium relationship represented by

$$c_x^* = m c_y \quad (9)$$

eqs. (1) and (2) can be expressed in dimensionless form.<sup>10</sup>

$$\frac{d^2 X}{dZ^2} - P_x B \frac{dX}{dZ} - N_{0x} P_x B (X - Y) + \frac{v_x L^2}{E_x (c_x^0 - m c_y^1)} = 0 \quad (10)$$

$$\frac{d^2 Y}{dZ^2} + P_y B \frac{dY}{dZ} + F N_{0x} P_y B (X - Y) = 0 \quad (11)$$

where the dimensionless concentrations are given by

$$X = \frac{c_x - c_x^1}{c_x^0 - c_x^1} = \frac{c_x - m c_y^1}{c_x^0 - m c_y^1} \quad (12)$$

$$Y = \frac{c_y - c_y^1}{c_y^0 - c_y^1} = \frac{m(c_y - c_y^2)}{c_x^0 - m c_y^1} \quad (13)$$

Elimination of  $Y$  between eqs. (10) and (11) gives

$$\frac{d^4 X}{dZ^4} - \alpha \frac{d^3 X}{dZ^3} - \beta \frac{d^2 X}{dZ^2} - \gamma \frac{dX}{dZ} - \delta = 0 \quad (14)$$

where

$$\alpha = B(P_x - P_y) \quad (15)$$

$$\beta = N_{0x} B(P_x + F P_y) + P_x P_y B^2 \quad (16)$$

$$\gamma = N_{0x} P_x P_y B^2 (1 - F) \quad (17)$$

$$\delta = \frac{v_x L^2 F P_y B N_{0x}}{E_x (c_x^0 - m c_y^1)} \quad (18)$$

In eq. (18),  $\delta$  represents a dimensionless rate of product formation. The relative importance of product formation and mass transfer in the contactor is indicated by the magnitude of  $\epsilon_x = \delta/\gamma$ . At large value of  $\epsilon_x$ , concentration changes in the contactor are due primarily to product for-

mation while at small values of  $\varepsilon_x$ , concentration changes are due to mass transfer. The solutions to eq. (10), (11), and (14) are given by

$$X = A_1 + A_2 e^{\lambda_2 Z} + A_3 e^{\lambda_3 Z} + A_4 e^{\lambda_4 Z} - \varepsilon_x Z \quad (19)$$

$$Y = A_1 + A_2 \alpha_2 e^{\lambda_2 Z} + A_3 \alpha_3 e^{\lambda_3 Z} + A_4 \alpha_4 e^{\lambda_4 Z} - \varepsilon_x \left( Z + \frac{1}{N_{0x} F} \right) \quad (20)$$

where the  $\lambda_i$  are the roots of the characteristic equation

$$\lambda^3 - \alpha \lambda^2 - \beta \lambda - \gamma = 0 \quad (21)$$

and the  $\alpha_i$  are given by

$$\alpha_i = 1 + \frac{\lambda_i}{N_{0x}} - \frac{\lambda_i^2}{N_{0x} P_x B} \quad (22a)$$

or<sup>10</sup>

$$\alpha_i = \frac{F(1 - \lambda_i/P_x B)}{1 + \lambda_i/P_y B} \quad (22b)$$

The coefficients  $A_i$  are obtained from the boundary conditions given by Miyauchi and Vermeulen.<sup>11</sup> These boundary conditions assume step changes in the concentrations of the continuous and dispersed phase feeds as they enter the column due to backmixing, while the phases leaving the extractor exhibit no concentration "jumps". The coefficients  $A_i$  are given by

$$\sum_{i=2}^4 \lambda_i \alpha_i A_i = \varepsilon_x \quad (23)$$

$$\sum_{i=2}^4 \lambda_i e^{\lambda_i A_i} = \varepsilon_x \quad (24)$$

$$\sum_{i=1}^4 \left( 1 - \frac{\lambda_i}{P_x B} \right) A_i = 1 - \frac{v_x}{P_x B} \quad (25)$$

$$\sum_{i=1}^4 \alpha_i \left( 1 + \frac{\lambda_i}{P_y B} \right) e^{\lambda_i A_i} = \varepsilon_x \left[ 1 + \frac{1}{N_{0x} F} + \frac{1}{P_x B} \right] \quad (26)$$

where  $\alpha_1 = 1$  and  $\lambda_1 = 0$ . The  $A_i$  can be obtained for particular problems by solving eq. 23-26 numerically. The length of extractor required for a given separation, however, must be found by iteration since length is contained in all  $\lambda_i$  terms. Approximate analytical solutions for the outlet concentrations  $X^1$  and  $Y^0$ , however, can be obtained by using a method described by Hartland and Mecklenburgh.<sup>12</sup> The performance of extraction columns in extractive fermentation can then be estimated without the need for numerical computation. The length of contractor can also be calculated, although still by iteration, in a straight forward manner.

The roots of the characteristic equation  $\lambda_2$ ,  $\lambda_3$ , and  $\lambda_4$  are given by<sup>10</sup>

$$\lambda_i = \frac{\alpha}{3} + 2\sqrt{p} \cos(u/3 + k) \quad (27)$$

where  $k = 0, 120$ , and  $240^\circ$  for  $\lambda_2, \lambda_3$ , and  $\lambda_4$  respectively and

$$p = \left( \frac{\alpha}{3} \right)^2 + \frac{\beta}{3} \quad (28)$$

$$q = \left( \frac{\alpha}{3} \right)^3 + \frac{\alpha\beta}{6} + \frac{\gamma}{2} \quad (29)$$

$$u = \cos^{-1} \left( \frac{q}{p^{1.5}} \right) \quad (30)$$

This solution is valid if  $q^2 - p^3 < 0$  which is normally satisfied in this application. The full solution to eqs. (19) and (20) can be simplified by taking advantage of the properties of the roots  $\lambda_i$ .  $\lambda_2$  is large and positive,  $\lambda_3$  is large and negative and  $\lambda_4$  is small and can be positive or negative.<sup>10</sup> In order to obtain simplified solutions for  $X^1$  and  $Y^0$ , eqs. (23) to (26) are solved for the  $A_i$  and substituted into eqs. (19) and (20). On dividing numerator and denominator by  $\exp(\lambda_2)$ , all terms containing either  $\exp(-\lambda_2)$  or  $\exp(\lambda_3)$  are neglected. After simplifying the equations, one obtains simple approximations for the concentrations of solute existing the extractor.

$$X^1 \approx \frac{e^{\lambda_4 C_1} [\varepsilon_x C_3 + 1 - 1/F] + \varepsilon_x C_2 C_4}{e^{\lambda_4 C_1} + C_2} \quad (31)$$

$$Y^c \approx \frac{e^{\lambda_4 C_1} (\varepsilon_x C_5 + 1) + \varepsilon_x C_2 C_6 + FC_2}{e^{\lambda_4 C_1} + C_2} \quad (32)$$

where the constants  $C_1$  to  $C_6$  are given by

$$C_1 = F \lambda_3 \alpha_3 (\lambda_2 - \lambda_4) \quad (33)$$

$$C_2 = \frac{\lambda_2}{F} \alpha_3 \alpha_4 (\lambda_4 - \lambda_3) \quad (34)$$

$$C_3 = \left( 1 - \frac{1}{F} \right) \left\{ \frac{1}{\alpha_3} \left( \frac{1}{P_x B} - \frac{1}{\lambda_3} \right) - 1 \right\} + \frac{1}{F} \left( \frac{1}{P_x B} + \frac{1}{P_y B} + \frac{1}{FN_{0x}} \right) \quad (35)$$

$$C_4 = (1 - \alpha_2) \left( \frac{1}{\lambda_2} + \frac{1}{P_y B} \right) + \frac{1}{FN_{0x}} \quad (36)$$

$$C_5 = \left( 1 - \frac{1}{\alpha_3} \right) \left( \frac{1}{\lambda_3} - \frac{1}{P_x B} \right) - \frac{1}{FN_{0x}} \quad (37)$$

$$C_6 = (1 - F) \left\{ 1 - \alpha_2 \left( \frac{1}{P_y B} + \frac{1}{\lambda_2} \right) \right\} - F \left( \frac{1}{P_x B} + \frac{1}{P_y B} + \frac{1}{FN_{0x}} \right) \quad (38)$$

Equations (31) and (32) give the outlet concentrations of product in the continuous and dispersed phases from the extractor. These equations are thus useful for simulating the performance of extraction columns in extractive fermentation. These equations can also be used for extractor design by making contractor length explicit. Length is made explicit by substituting  $\lambda_i L = \lambda_i$  and  $B = L/H_{0x}$  into



eqs. (31)–(38) and eqs. (15)–(18). The  $\lambda'_i$  are found by solving an equation analogous to eq. (21).

When product production is negligible, eq. (31) reduces to the solutions given by Pratt.<sup>10</sup>

$$L = \frac{1}{\lambda'_4} \ln \left[ \frac{\lambda'_2 \alpha_4 (\lambda'_4 - \lambda'_3) X^1}{F^2 \lambda'_3 (\lambda'_2 - \lambda'_4) (X^1 - 1 + 1/F)} \right] \quad (39)$$

The contactor length can thus be estimated without iteration when the rate of product formation in the column is small relative to the rate of product mass transfer.

### Case II: Low Substrate Concentration

When the concentration of growth limiting substrate is low ( $c_s \ll K_s$ ), the rate of product formation, represented by eq. (8), depends linearly on the concentration of substrate in the continuous phase. It is thus necessary to estimate the substrate concentration profile throughout the length of the contactor. Assuming that the substrate is not extracted into the dispersed phase and cell yield and cell mass are constant over the contactor length, a mass balance over a differential section of column yields the following equation

$$E_x \frac{d^2 c_s}{dz^2} - U_x \frac{dc_s}{dz} - \frac{v_x}{K_s Y_{P/S}} c_s = 0 \quad (40)$$

Equation 40 can be expressed in dimensionless form as

$$\frac{d^2 S}{dZ^2} - P_x B \frac{dS}{dZ} - k_1 S = 0 \quad (41)$$

where

$$S = \frac{c_s}{c_s^0} \quad (42)$$

$$k_1 = \frac{v_x L^2}{K_s E_x Y_{P/S}} \quad (43)$$

The solution to eq. (41) is given by

$$S = d_1 e^{m_1 Z} + d_2 e^{m_2 Z} \quad (44)$$

where  $m_1$  and  $m_2$  are roots of the characteristic equation

$$m^2 - P_x B m - k_1 = 0 \quad (45)$$

and  $d_1$  and  $d_2$  are obtained by substituting eq. (44) into the boundary conditions given by Miyauchi and Vermeulen.<sup>11</sup>

$$d_1 = \frac{P_x B e^{m_2}}{e^{m_2}(P_x B - m_1) - (m_1/m_2)e^{m_1}(P_x B - m_2)} \quad (46)$$

$$d_2 = \frac{P_x B e^{m_1}}{e^{m_1}(P_x B - m_2) - (m_2/m_1)e^{m_2}(P_x B - m_1)} \quad (47)$$

where

$$m_1, m_2 = \frac{1}{2} P_x B \pm \frac{1}{2} [(P_x B)^2 + 4k_1]^{1/2} \quad (48)$$

Equation (44) describes the concentration profile of substrate over the length of the contactor when substrate concentration is low. Combination of eqs. (44), (1), (2), and (8) and conversion to dimensionless form leads to the following equations

$$\frac{d^2 X}{dZ^2} - P_x B \frac{dX}{dZ} - N_{0x} P_x B (x - Y) + \xi (d_1 e^{m_1 Z} + d_2 e^{m_2 Z}) = 0 \quad (49)$$

$$\frac{dY^2}{dZ} + P_y B \frac{dY}{dZ} + F N_{0x} P_y B (x - Y) = 0 \quad (50)$$

where

$$\xi = \frac{Y_{P/S} k_1 c_s^0}{(c_s^0 - m c_s^1)} \quad (51)$$

The solutions to eqs. (49) and (50) are as follows

$$X = A_1 + A_2 e^{\lambda_2 Z} + A_3 e^{\lambda_3 Z} + A_4 e^{\lambda_4 Z} + B_1 e^{m_1 Z} + B_2 e^{m_2 Z} \quad (52)$$

$$Y = A_1 + A_2 \alpha_2 e^{\lambda_2 Z} + A_3 \alpha_3 e^{\lambda_3 Z} + A_4 \alpha_4 e^{\lambda_4 Z} + B_1 b_1 e^{m_1 Z} + B_2 b_2 e^{m_2 Z} \quad (53)$$

where the  $\alpha_i$  and  $\lambda_i$  are given by eqs. (22) and (27),  $\alpha$ ,  $\beta$  and  $\gamma$  are given by eqs. (15) to (17) and the  $B_i$  and  $b_i$  are given by

$$b_i = 1 + \frac{m_i}{N_{0x}} - \frac{m_i^2}{N_{0x} P_x B} + \frac{\xi d_i}{B_i N_{0x} P_x B} \quad (54)$$

$$B_i = \frac{\vartheta_i}{(m_i^4 - \alpha m_i^3 - \beta m_i^2 - \gamma m_i)} \quad (55)$$

$$\vartheta_i = \xi d_i [P_y B (F N_{0x} - m_i) - m_i^2] \quad (56)$$

Approximate solutions to eqs. (52) and (53) can be obtained in the same way that eqs. (19) and (2) were simplified. Upon simplification, one obtains

$$X^1 \approx \frac{e^{\lambda_4 C_1} (1 - 1/F)}{e^{\lambda_4 C_1} + C_2} + \frac{1}{e^{\lambda_4 C_1} + C_2} \sum_{i=1}^2 B_i [e^{m_i} (e^{\lambda_4 C_1} \Phi_i + C_2 \eta_i) + e^{\lambda_4 C_1} \omega_i] \quad (57)$$

$$Y^0 \approx \frac{e^{\lambda_4 C_1} + F C_2}{e^{\lambda_4 C_1} + C_2} + \frac{1}{e^{\lambda_4 C_1} + C_2} \sum_{i=1}^2 B_i [C_2 (e^{m_i} \Omega_i + \sigma_i) + e^{\lambda_4 C_1} \psi_i] \quad (58)$$

where  $C_1$  and  $C_2$  are defined in eqs. (33) and (34) and

$$\Phi_i = 1 - \frac{m_i}{P_x B} - \frac{b_i}{F} \left( \frac{m_i}{P_y B} + 1 \right) \quad (59)$$

$$\eta_i = m_i \left\{ \frac{1}{\lambda_2} (\alpha_2 - 1) + \frac{1}{P_y B} (\alpha_2 - b_i) \right\} + (1 - b_i) \quad (60)$$

$$\omega_i = \left(1 - \frac{1}{F}\right) \left\{ \frac{b_i m_i}{\alpha_3} \left( \frac{1}{\lambda_3} - \frac{1}{P_x B} \right) + \frac{m_i}{P_x B} - 1 \right\} \quad (61)$$

$$\Omega_i = (1 - F) \left\{ m_i \alpha_2 \left( \frac{1}{\lambda_2} + \frac{1}{P_y B} \right) - b_i \left( \frac{m_i}{P_y B} + 1 \right) \right\} \quad (62)$$

$$\alpha_i = b_i \left( 1 + \frac{m_i}{P_y B} \right) - F \left( 1 - \frac{m_i}{P_x B} \right) \quad (63)$$

$$\psi_i = m_i \left[ \frac{1}{P_x B} \left( 1 - \frac{b_i}{\alpha_3} \right) - \frac{b_i}{\lambda_3} \left( 1 - \frac{1}{\alpha_3} \right) \right] - (1 - b_i) \quad (64)$$

Equations (57) and (58) give the concentrations of products in the continuous and dispersed phases leaving the contactor for the case of low substrate concentration ( $c_s \ll K_s$ ). For contactor design calculations, the contactor length required to remove a given amount of product from the continuous phase can be found by iteration after  $\lambda'_i L = \lambda_i$  and  $B = L/H_{0x}$  are substituted into eqs. (57) to (64), eqs. (15) to (18) and eq. (21).

## DISCUSSION

The equations derived in the previous section are for the general case in which backmixing occurs in both phases and the stripping factor  $F$  does not equal 1. If backmixing is absent from either phase or  $F = 1$  then the solutions presented are not valid. In practice, there is normally some degree of backmixing in both continuous and dispersed phases. Furthermore, the optimum stripping factor occurs at ca. 0.7 or 1.4 depending on the direction of mass transfer<sup>13</sup> so that the solutions presented are usually applicable. For cases in which either  $P_x$  or  $P_y \rightarrow \infty$  or  $F = 1$ , appropriate solutions can be obtained by using the limits given by Pratt.<sup>10</sup>

### Accuracy of Approximate Solutions

Approximate analytical solutions giving the dimensionless concentrations leaving the contactor,  $X^1$  and  $Y^0$ , were derived for conditions of low and high substrate concentration. The accuracy of the approximate solutions was tested by comparing predictions of  $X^1$  and  $Y^0$  using the approximate solutions to values generated by the exact solutions. The deviation of the approximate solutions from the exact solutions, defined as

$$\Delta X^1 = 100 \left( \frac{X_A^1 - X_E^1}{X_E^1} \right) \quad (65)$$

$$\Delta Y^0 = 100 \left( \frac{Y_A^0 - Y_E^0}{Y_E^0} \right) \quad (66)$$

was calculated for a variety of operating conditions. Figure 2 shows that the approximate solutions for high substrate concentrations [eq. (31) and (32)] approach the exact solutions as the length of the contactor increases. The approximate

solutions for low substrate concentrations exhibited similar behavior. The curves in Figure 2 were generated using the parameters listed in Table I. In general, the approximate solutions deviated less than 5% from the exact solutions when contactor length was greater than 4 feet and  $N_{0x} > 2$ . In practice, the contactor length is usually much greater than 4 feet and the difference between the approximate and exact solutions is negligible. The approximate solutions are thus generally accurate for practical cases in which  $L > 4$  feet and  $N_{0x} > 2$ .

### Performance and Design of Differential Contactors in Extractive Fermentation

The significance of product formation on the design and performance of differential contactors depends on the magnitude of several operating and physical parameters. In general, the effect of product formation on contactor performance increases as  $\epsilon_x = \delta/\gamma$ , which is a measure of the relative importance of product formation and mass transfer in the contactor, increases.  $\epsilon_x$  is proportional to the rate of product production,  $v_x$ , and the continuous phase residence time in the contactor. At long residence times (small  $U_x$  or large  $L$ ), the contactor acts as another fermentor and significant product production can take place in the extractor.

The significance of product formation on the performance of a differential contactor can be gauged by comparing the contactor performance with and without product formation taking place inside the contactor. The deviation between the estimated concentration of solute leaving a contactor with and without internal product formation was calculated by

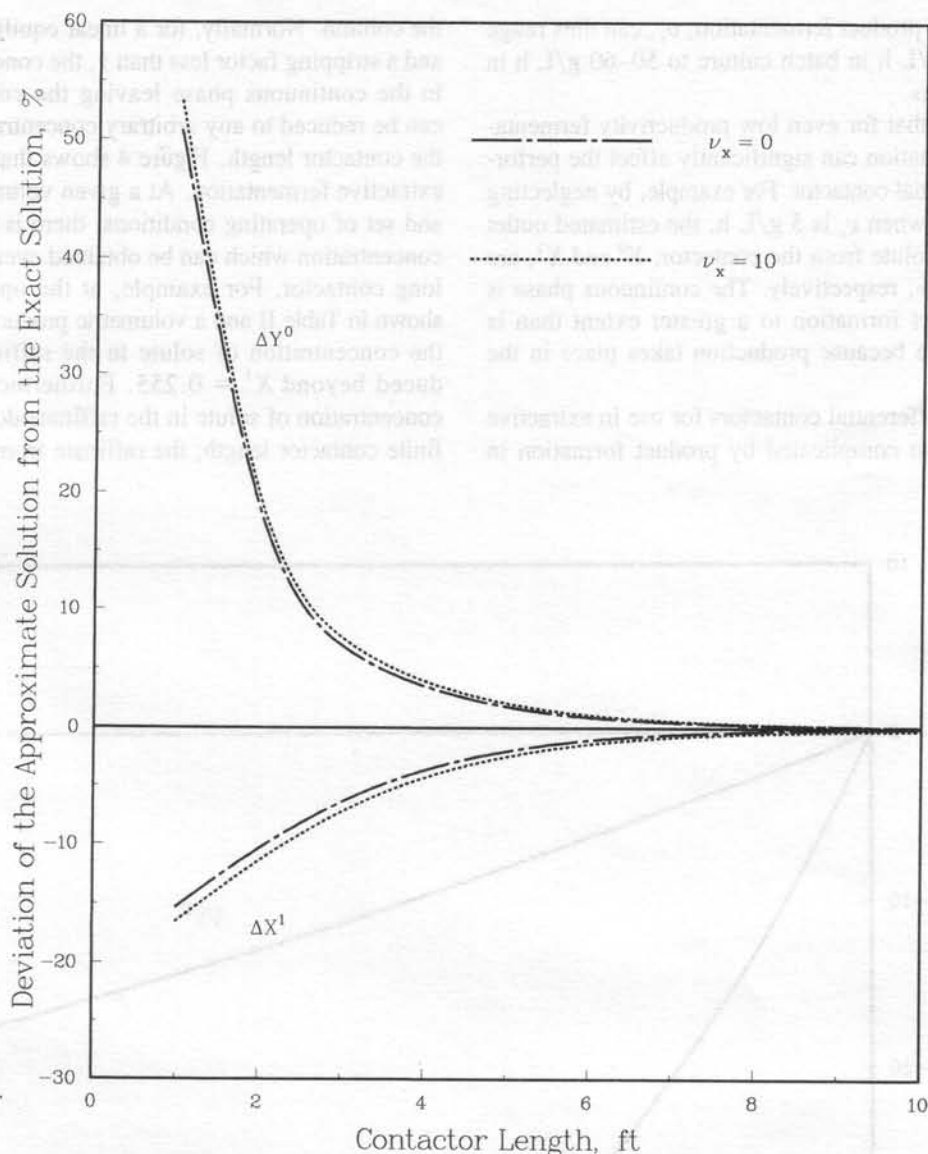
$$\Delta X^1 = 100 \left( \frac{X_N^1 - X_A^1}{X_A^1} \right) \quad (67)$$

$$\Delta Y^0 = 100 \left( \frac{Y_N^0 - Y_A^0}{Y_A^0} \right) \quad (68)$$

where  $X_N^1$  and  $Y_N^0$  are the outlet concentrations when product formation is neglected and  $X_A^1$  and  $Y_A^0$  are the outlet concentrations when product formation is accounted for. In all cases, comparisons were made using the solutions for high substrate concentrations and the model parameters shown in Table II.

### Effect of Product Formation Rate on Contactor Performance

The rate that products are formed during fermentation varies widely depending on the organism and process configuration used. In batch culture, *Clostridium acetobutylicum* produces butanol at a volumetric productivity of ca. 0.5 g/L h.<sup>5</sup> Butanol productivity can reach 3 g/L h when this same strain is grown in fed-batch extractive fermentation.<sup>6</sup> In batch cultures of yeast growing on molasses, ethanol productivity is normally 4–6 g/L h<sup>1</sup> while ethanol productivities of over 8 g/L h have been reported for the continuous culture of yeast on molasses.<sup>14</sup> Much higher productivities have been obtained by concentrating cells in the fermentor



**Figure 2.** Comparison of approximate and exact solutions for the case of high substrate concentrations [eqs. (31) and (33)]. Parameter values are given in Table I.

with ultrafiltration membranes. For example, ethanol productivity can reach 40 g/L h in fermentors that recycle yeast<sup>1</sup> and ethanol productivities of 67 g/L h have been obtained in a membrane reactor using cells of *Kluyveromyces fragilis* grown on whey.<sup>15</sup> Similar productivities were reported for

lactic acid production from *Lactobacillus delbreuckii* grown in a fermentor using ultrafiltration to maintain high cell den-

**Table II.** Parameters used to generate curves shown in Figures 2 and 3.

Parameters	Value	Units
$c_x^0$	10	g/L
$c_y^1$	0	g/L
$F$	0.7	—
$m$	1.0	—
$U_x$	0.5	cm/s
$U_y$	0.714	cm/s
$H_{0x}$	80	cm
$F_x$	20	cm <sup>2</sup> /s
$E_y$	100	cm <sup>2</sup> /s
$v_x$	3	g/L h
$K_x$	10	g/L
$c_s^0$	3	g/L
$c_x^0$	10	g/L
$\mu$	1.0	h <sup>-1</sup>
$Y_{xs}$	0.1	g/g
$Y_{ps}$	0.5	g/g

**Table I.** Parameters used in model comparisons.

Parameter	Value	Units
$c_x^0$	10	g/L
$c_y^1$	0	—
$m$	1	—
$F$	0.7	—
$H_{0x}$	40	cm
$L$	20	ft
$E_x$	20	cm <sup>2</sup> /s
$E_y$	100	cm <sup>2</sup> /s
$v_x$	3	g/L h
$U_x$	0.5	cm/s
$U_y$	$\frac{U_y m}{F}$	cm/s

sities.<sup>16</sup> The rate of product fermentation,  $v_x$ , can thus range from less than 1 g/L h in batch culture to 50–60 g/L h in cell recycle systems.

Figure 3 shows that for even low productivity fermentations, product formation can significantly affect the performance of a differential contactor. For example, by neglecting product formation when  $v_x$  is 5 g/L h, the estimated outlet concentrations of solute from the contactor,  $Y^0$  and  $X^1$ , are low by 10 and 37%, respectively. The continuous phase is affected by product formation to a greater extent than is the dispersed phase because production takes place in the continuous phase.

The design of differential contactors for use in extractive fermentation is also complicated by product formation in

the column. Normally, for a linear equilibrium relationship and a stripping factor less than 1, the concentration of solute in the continuous phase leaving the contactor (raffinate) can be reduced to any arbitrary concentration by increasing the contactor length. Figure 4 shows that this is not true in extractive fermentation. At a given volumetric productivity and set of operating conditions, there is a minimum solute concentration which can be obtained even with an infinitely long contactor. For example, at the operating conditions shown in Table II and a volumetric productivity of 10 g/L h, the concentration of solute in the raffinate cannot be reduced beyond  $X^1 = 0.255$ . Furthermore, the minimum concentration of solute in the raffinate does not occur at infinite contactor length; the raffinate from an infinitely long

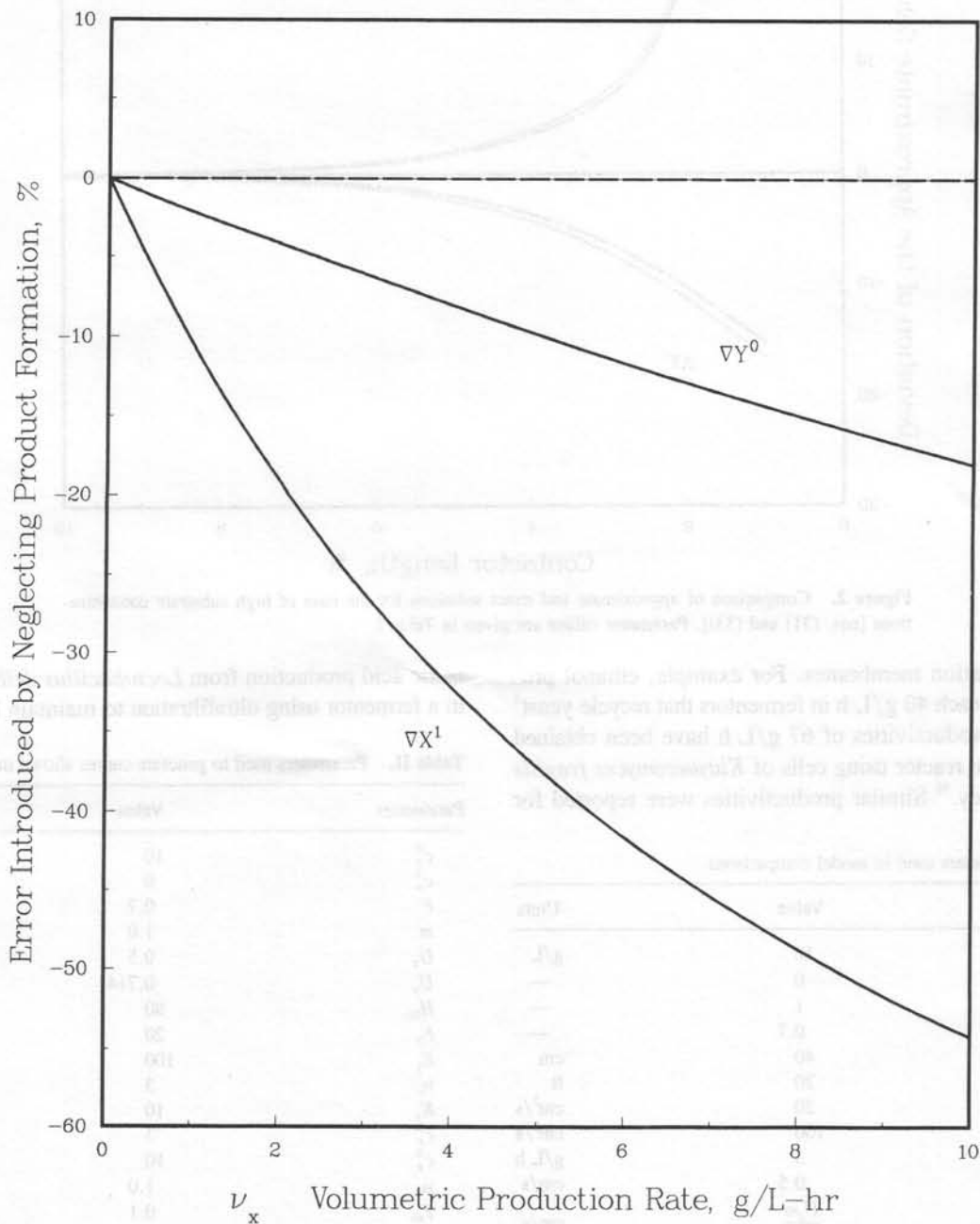


Figure 3. Effect of product formation during extractive fermentation.



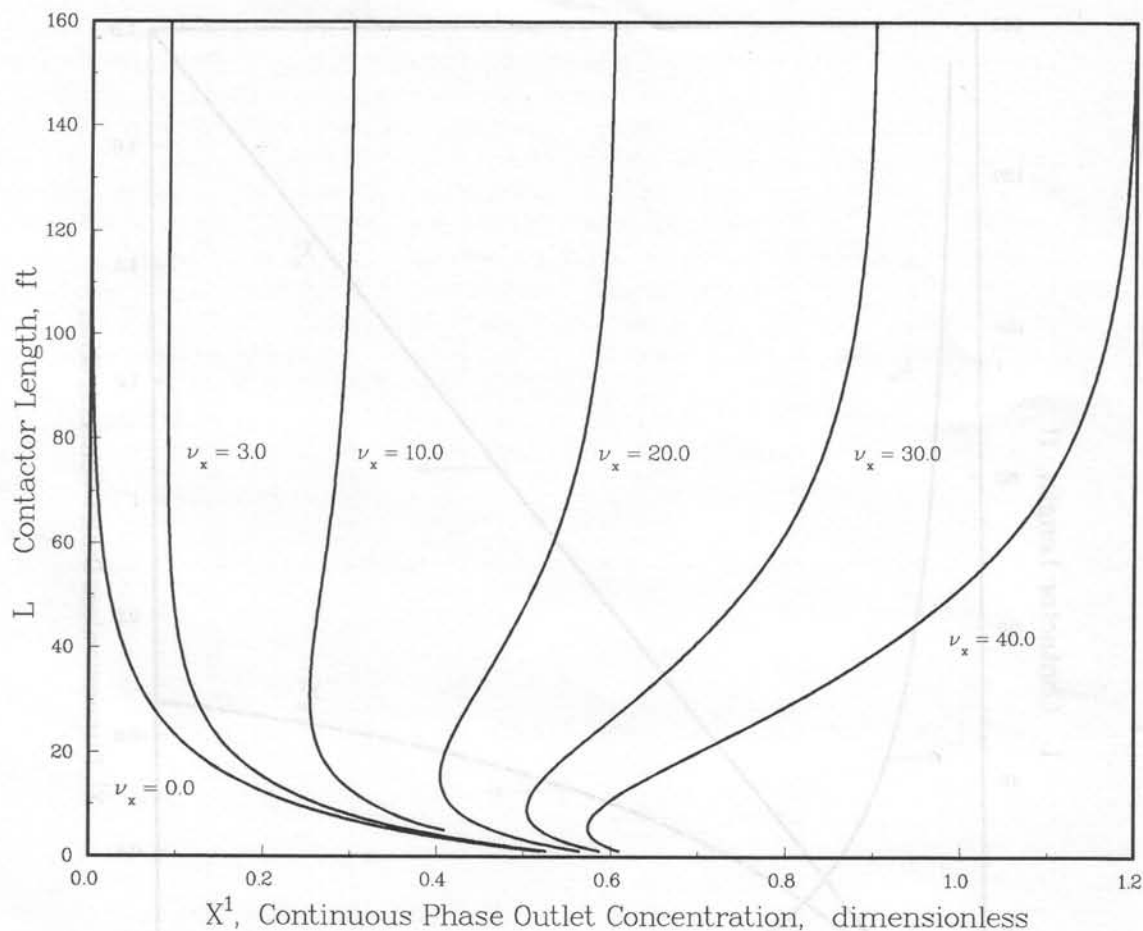


Figure 4. Effect of contactor length on exit concentration of product (solute). No minimum exit solute concentration exists.

contactor will contain more solute than will most shorter columns. This behavior is due to the counteracting effects of mass transfer and product formation in the contactor. While the rate of product formation is independent of contactor length at high substrate concentrations ( $c_s \gg K_s$ ), the rate of mass transfer decreases as contactor length increases. As contactor length increases from  $L = 0$ , the solute concentration in the raffinate at first decreases in the normal fashion as more transfer units are added. As length increases further, however, the rate of mass transfer decreases until the average rate of mass transfer in the contactor equals the average rate of product formation. This is the length of contactor giving the minimum raffinate solute concentration,  $X_M^1$ . Any increase in contactor length beyond this point results in a higher raffinate concentration as the average mass-transfer driving force further decreases. As the contactor length goes to infinity, the raffinate concentration approaches a constant limiting value.

The contactor length  $L_M$  giving the minimum raffinate concentration at high substrate concentrations can be calculated iteratively from

$$\frac{C'_1}{C'_2} e^{\lambda'_4 L_M} + \lambda'_4 L_M = \frac{\lambda'_4 (C'_4 - C'_3)}{(1/F - 1)} + \frac{\lambda'_4}{\varepsilon'_x} - 1 \quad (69)$$

where  $C'_i$  are given by substituting  $\lambda'_i L = \lambda_i$  and  $B = L/H_{0x}$  in eqs. (33) to (36) and  $\varepsilon'_x$  is given by

$$\varepsilon'_x = \frac{\nu_x F H_{0x}}{E_x P_x (1 - F) (c_x^0 - m c_y^1)} \quad (70)$$

The minimum raffinate concentration,  $X_M^1$ , can be estimated by substituting  $L_M$  into eq. (31). The concentration of solute in the raffinate from an infinitely long column,  $X_\infty^1$ , is given by

$$X_\infty^1 = \lim_{L \rightarrow \infty} X^1 = \varepsilon'_x C'_4 \quad (71)$$

Figure 5 shows how  $X_\infty^1$ ,  $X_M^1$  and  $L_M$  depend on the rate of product formation in the contactor. When  $\nu_x = 0$ , an infinitely long contactor gives the minimum raffinate concentration. At finite values of  $\nu_x$ , however, the concentration of solute in the raffinate is lower in columns of finite length. For example, when  $\nu_x = 30$  g/L h,  $X_\infty^1 = 0.9$  while  $X^1$  from a 9 foot column is only 0.5. At very high rates of product formation such as those obtained in cell recycle systems, the concentration of solute can increase throughout the length of the contactor. Solute concentration will increase in the contactor, regardless of contactor length, whenever the volumetric production rate,  $\nu_x$ , is greater than a critical value given by

$$\nu_x = \frac{-E_x P_x (c_x^0 - m c_y^1) \lambda'_4 (F - 1)^2}{H_{0x} F \left[ F \lambda'_4 (C'_4 - C'_3) + (F - 1) \left( 1 + \frac{C'_1}{C'_2} \right) \right]} \quad (72)$$



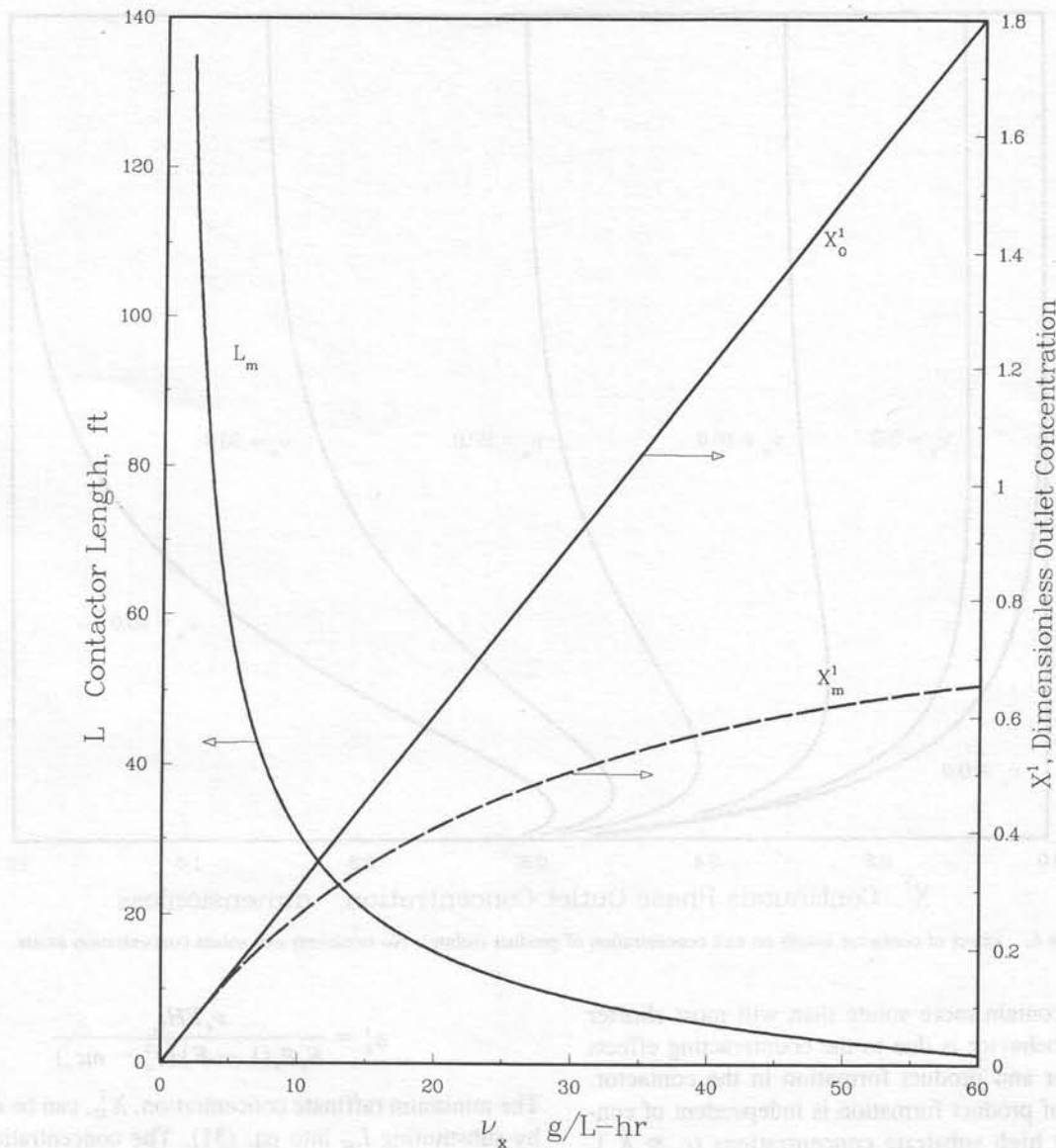


Figure 5. Effect of the rate of product formation on minimum solute concentrations and on minimum contactor length.

Operation in the critical range can be avoided by increasing the ratio of extraction solvent to feed in the contactor (decreasing  $F$ ). Thus, when highly productive fermentations are coupled with extraction, the optimal stripping factor in the extraction column will shift to values lower than the standard stripping factor of 0.7.

It is apparent from Figures 4 and 5 that  $X^1$  can be greater than 1 when  $v_x > 0$ ; more solute can leave the contactor in the raffinate than entered in the feed. This behavior has been observed during the extractive fermentation of acetone and butanol produced by *Clostridium acetobutylicum*.<sup>7</sup> The concentration of acetone in the broth leaving the differential extraction column was often greater than its concentration entering the column. Figure 6 shows that the concentration of solute in the continuous phase can also reach a maximum inside the contactor. At large values of  $v_x$ , the rate of product formation can exceed the rate of mass transfer over a section of the contactor resulting in a concentration maximum inside the column. The concentra-

tion jump at the continuous phase feed inlet can also be positive when  $v_x$  is large. For example, with  $v_x = 30$  g/L h, the continuous phase solute concentration jumps from  $X_0 = 1.0$  in the feed to  $X^0 = 1.06$  inside the column.

Product formation inside a differential contactor must be accounted for when  $v_x$  is large. Product formation will also be important when the continuous phase superficial velocity in the column is small.

### Effect of Continuous Phase Velocity on Contactor Performance

The superficial velocity of the continuous phase,  $U_x$ , affects contactor performance in two ways. First, the continuous phase Peclet number is proportional to  $U_x$  so that the effects of backmixing increase as the velocity of the continuous phase decreases. Second, the continuous phase residence time in the contactor is inversely proportional to  $U_x$ ; more product is produced per pass through the column at

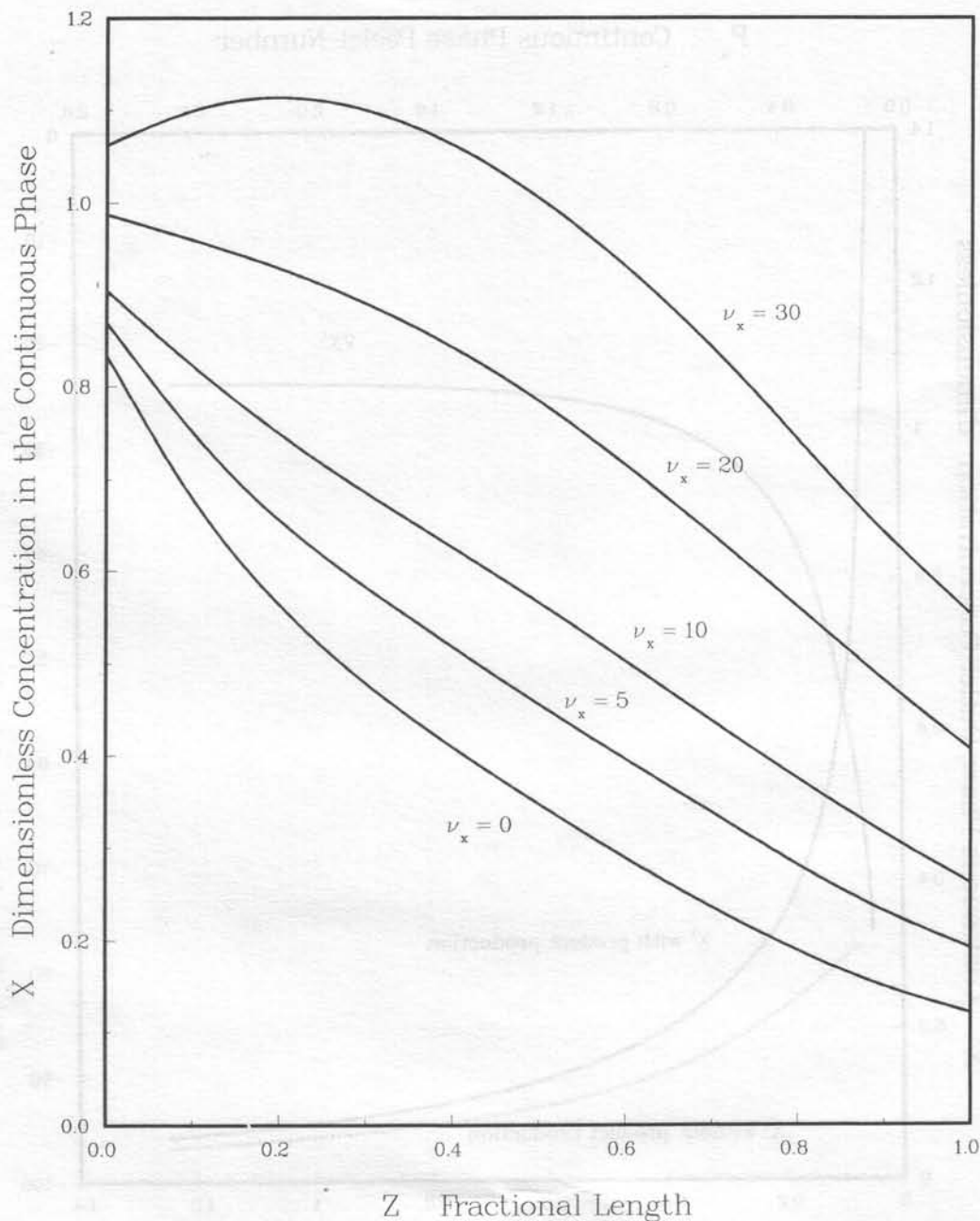


Figure 6. Concentration of solute in the continuous phase as a function of volumetric product formation rate ( $v_x$ ).

small phase velocities. Both effects act to increase the importance of product formation at low  $U_x$ . Figure 7 shows the effect of the continuous phase velocity on the concentration of solute in the raffinate from a column operating at the conditions shown in Table II. Although product formation significantly alters the concentration of solute in the raffinate at all superficial phase velocities, product formation is especially significant at low  $U_x$ . For example, when  $U_x = 0.1$  cm/s,  $X^1$  without product production is ca. 0.29 while  $X^1$  increases to 0.64 when  $v_x = 3.0$  g/L h in the contactor.

Figure 8 shows the strong dependence of the continuous phase concentration profile on  $U_x$ . When the continuous phase passes rapidly through the contactor, the effects of backmixing and product formation are minimized,  $\epsilon_x$  is small, and the concentration profile is steep. As  $U_x$  de-

creases, however, backmixing increases and the concentration profile flattens out. At very low continuous phase superficial velocities, product formation becomes very significant ( $\epsilon_x > 1$ ). The concentration at the feed inlet jumps upward ( $X^0 > 1$ ), the concentration profile reaches a maximum inside the contactor, and the outlet concentration is higher than the feed concentration ( $X^1 > X_0 = 1$ ). Thus, even relatively low rates of product formation can affect contactor performance when the continuous phase velocity in the column is low.

## CONCLUSIONS

The performance and design of differential contactor for use in extractive fermentation is complicated by the effects of product formation inside the contactor. In general, when

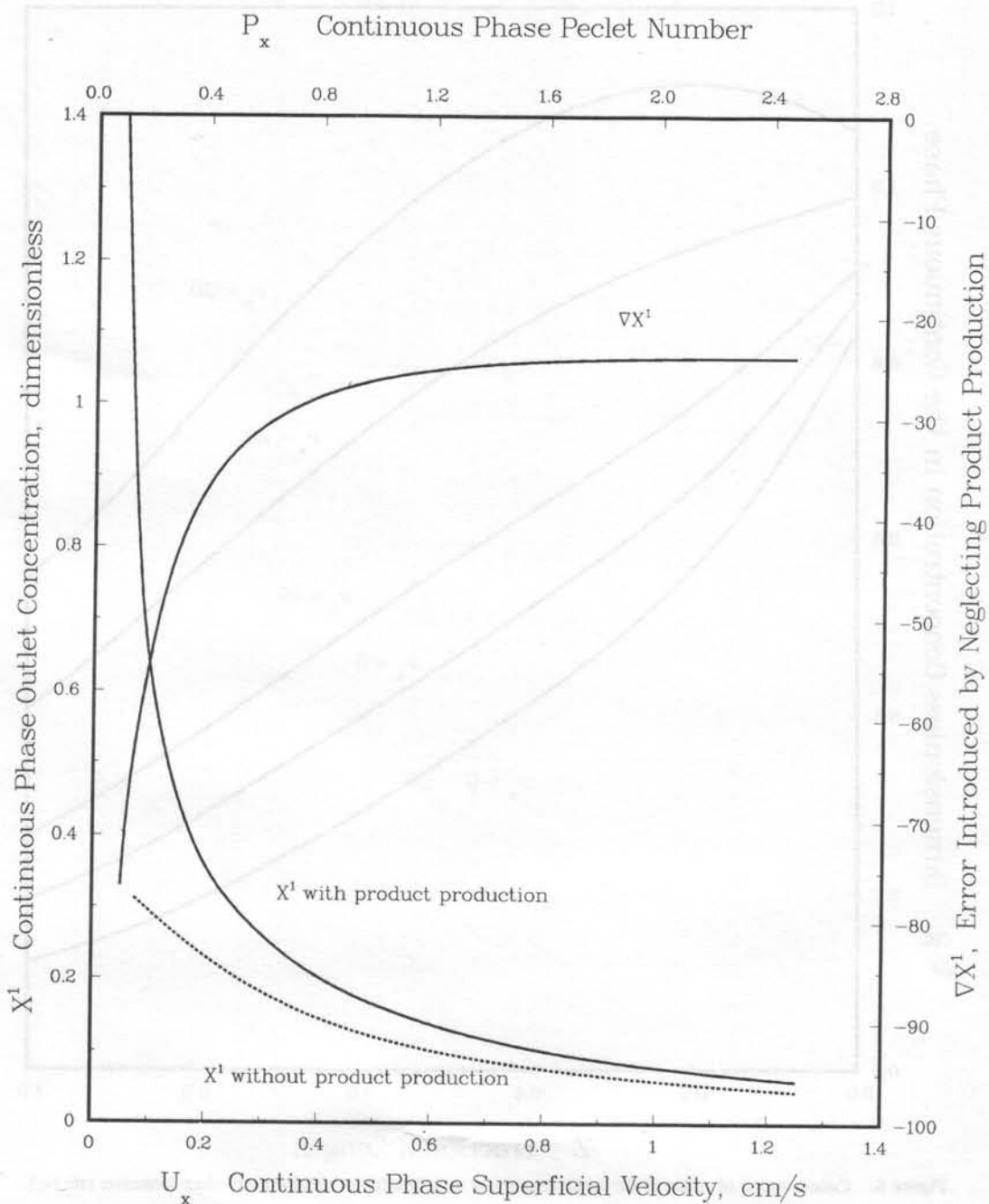


Figure 7. The effect of continuous phase velocity on the concentration of solute in the raffinate.

substrate concentration is high ( $c_s \gg K_s$ ), product formation is significant whenever  $\varepsilon_x = v_x FL/U_x(1 - F)(c_x^0 - mc_y^1)$  is of order unity or higher. Parameter  $\varepsilon_x$  is increased by high rates of product formation, long continuous phase residence times, low product concentrations, and poor extraction conditions (stripping factor  $\rightarrow 1$ ).

When product formation is significant, the performance of differential contactors can be predicted from eqs. (31) and (32) at high substrate concentrations or from eqs. (57) and (58) at low substrate concentrations. Although these equations are approximations, they give results within 5% of the exact solutions when contactor length is greater than  $4f$  and  $N_{0x} > 2$ . For practical operating and design conditions, the difference between exact and approximate solu-

tions is negligible. When designing a differential contactor in which products are formed at a constant rate inside the contactor, it is important to note that there is a minimum raffinate solute concentration that can be obtained. In contrast to the behavior of a column without product production, the minimum concentration of solute in the raffinate from a column with internal product formation occurs at a finite contactor length. The contactor length giving the minimum concentration of solute in the raffinate decreases as  $\varepsilon_x$  increases and for highly productive fermentations, the concentration of solute can increase throughout the contactor. For a given set of operating conditions, the length of contactor giving the lowest possible solute concentration in the raffinate can be estimated from eq. (69).

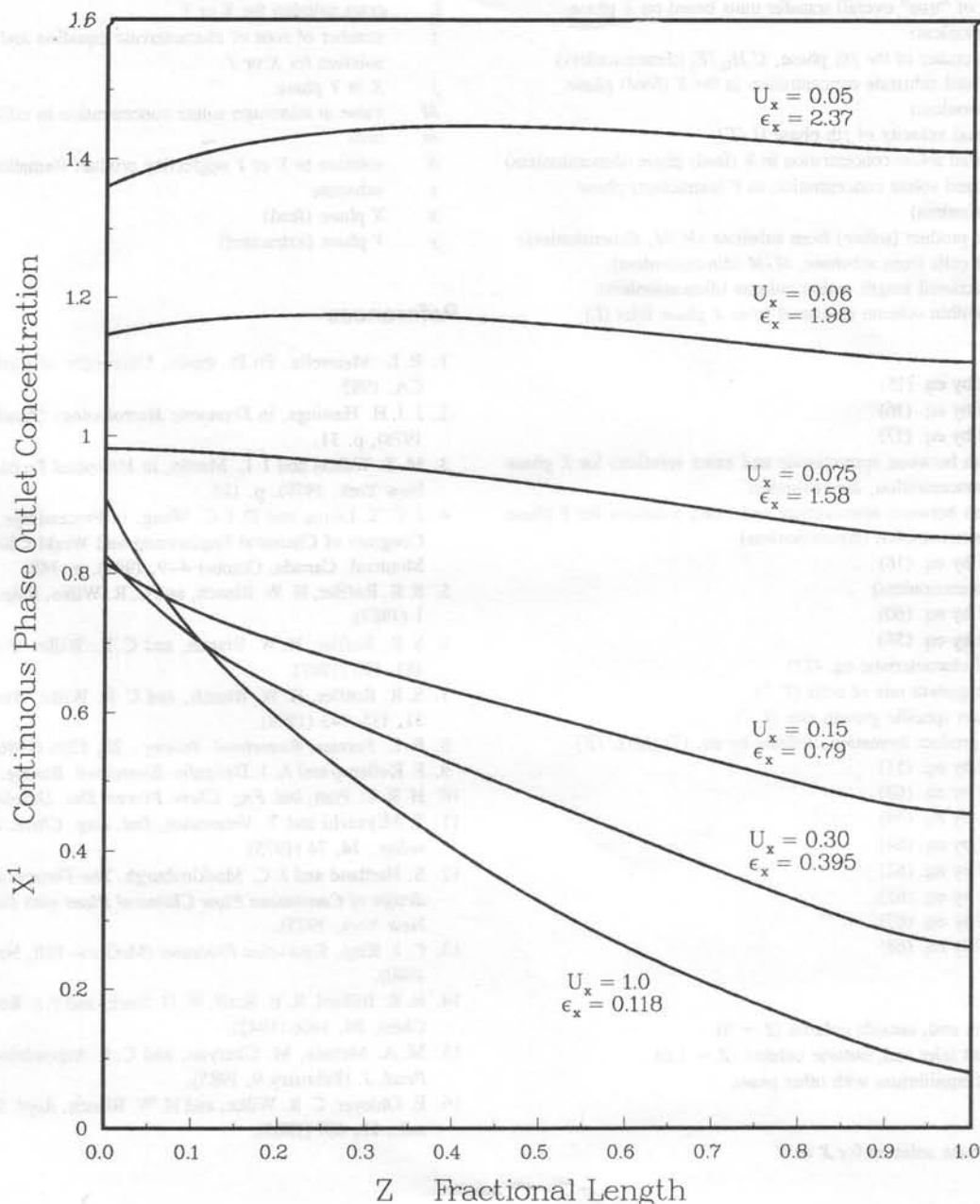


Figure 8. Effect of the superficial continuous phase velocity on the continuous phase product concentration profile.

The equations presented in this paper are for the general case in which backmixing occurs in both phases and the stripping factor not equal to 1. Although the equations were cast such that product formation occurs in the continuous phase, the equations are equally valid when product formation takes place in the dispersed phase. In addition, the equations are not limited to extraction but can be used to simulate or design any type of differential contactor in which the kinetics of product formation are zero or first order in substrate concentration.

### NOMENCLATURE

$A_i$  coefficient in eqs. (19), (20), (52), and (53) (dimensionless)  
 $a$  interfacial area per unit contactor volume,  $L^2/L^3 = L^{-1}$   
 $a_i$  defined by eqs. (22a) and (22b) (dimensionless)

$B$   $L/H_{0x}$  (dimensionless)  
 $B_i$  coefficients in eqs. (52) and (53), dimensionless  
 $b_i$  defined by eq. (54), dimensionless  
 $c_m$  concentration of cells in X phase ( $M/L^3$ )  
 $c_s$  concentration of substrate in X phase ( $M/L^3$ )  
 $c_x$  concentration of solute in X phase ( $M/L^3$ )  
 $c_y$  concentration of solute in Y phase ( $M/L^3$ )  
 $C_i$  defined by eqs. (33) to (38)  
 $d_i$  defined by eqs. (46) and (47) (dimensionless)  
 $E_j$  effective longitudinal diffusion coefficient in the  $j$ th phase ( $L^2/T$ )  
 $F$  stripping (extraction) factor,  $\frac{mU_x}{U_y}$  (dimensionless)  
 $H_{0x}$  height of an overall ("true") transfer unit based on X phase ( $L$ )  
 $k_1$  constant defined by eq. (43) (dimensionless)  
 $k_{0x}$  overall mass transfer coefficient based on X phase ( $L/T$ )  
 $K_s$  sugar saturation constant ( $M/L^3$ )  
 $L$  total length of contactor ( $L$ )  
 $m$  slope of equilibrium line,  $dc_x/dc_y$  (dimensionless)  
 $m_i$  roots of characteristic eq. (45)



$N_{0x}$	number of "true" overall transfer units based on $X$ phase (dimensionless)
$P_j$	Peclet number of the $j$ th phase, $U_j H_{0x}/E_j$ (dimensionless)
$S$	generalized substrate concentration in the $X$ (feed) phase (dimensionless)
$U_j$	superficial velocity of $j$ th phase ( $L/T$ )
$X$	generalized solute concentration in $X$ (feed) phase (dimensionless)
$Y$	generalized solute concentration in $Y$ (extractant) phase (dimensionless)
$Y_{pis}$	yield of product (solute) from substrate ( $M/M$ , dimensionless)
$Y_{xis}$	yield of cells from substrate, $M/M$ (dimensionless)
$Z$	$z/L$ , fractional length within column (dimensionless)
$z$	length within column measured from $X$ phase inlet ( $L$ )

#### Greek letters

$\alpha$	defined by eq. (15)
$\beta$	defined by eq. (16)
$\gamma$	defined by eq. (17)
$\Delta X^1$	deviation between approximate and exact solutions for $X$ phase outlet concentration, dimensionless
$\Delta Y^0$	deviation between approximate and exact solutions for $Y$ phase outlet concentration (dimensionless)
$\delta$	defined by eq. (18)
$\epsilon_x$	$\delta/\gamma$ (dimensionless)
$\eta_i$	defined by eq. (60)
$\vartheta_i$	defined by eq. (56)
$\lambda_i$	roots of characteristic eq. (21)
$\mu$	specific growth rate of cells ( $T^{-1}$ )
$\mu_m$	maximum specific growth rate ( $T^{-1}$ )
$\nu_x$	rate of product formation, defined by eq. (7) ( $M/L^3/T$ )
$\xi$	defined by eq. (51)
$\sigma_i$	defined by eq. (63)
$\Phi_i$	defined by eq. (59)
$\psi_i$	defined by eq. (64)
$\Omega_i$	defined by eq. (62)
$\omega_i$	defined by eq. (61)
$\nabla X^1$	defined by eq. (67)
$\nabla Y^0$	defined by eq. (68)

#### Superscripts

0	feed inlet end, outside column ( $Z = 0$ )
1	extractant inlet end, outside column ( $Z = 1.0$ )
*	value at equilibrium with other phase

#### Subscripts

A	approximate solution for $X$ or $Y$
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$E$	exact solution for $X$ or $Y$
$i$	number of root of characteristic equation and of coefficients in solution for $X$ or $Y$
$j$	$X$ or $Y$ phase
$M$	value at minimum solute concentration in raffinate
$m$	cells
$N$	solution to $X$ or $Y$ neglecting product formation
$s$	substrate
$x$	$X$ phase (feed)
$y$	$Y$ phase (extractant)

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