[J. Ferment. Technol., Vol. 58, No. 5, p. 431–437, 1980]

Effects of Axial Dispersion and Mass Transfer Resistances on Conversion in a Hollow Fiber Enzyme Reactor

HIROSHI KATAOKA, TSUNAHIKO SAIGUSA*, SUKEKUNI MUKATAKA, and JOJI TAKAHASHI

Institute of Applied Biochemistry, University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305;
**Central Research Laboratories, Kikkoman Shoyu Co., Ltd., Noda, Chiba 278*

A hollow fiber module, an artificial kidney consisting of 8,000 fibers of 0.025 cm in diameter and 16 cm in length, was used as a reactor for hydrolysis of sucrose. In the tube side of the reactor, invertase was encapsulated and reactant liquid with dissolved sucrose was fed continuously to the shell side. The axial dispersion coefficient of the reactant fluid in the shell side was measured by step change of blue-dextran solution to correct the influence of liquid mixing on mass transfer rate, and the coefficients were found to be neary constant irrespective of fluid velocities. The value of the Bodenstein number, PeB, was 5.3. Also the mass transfer resistance, $1/K_{os}$ (min/cm) of the sucrose was measured and was correlated by the following equation as a function of interstitial liquid velocity, V_s (cm/min).

$$1/K_{os}=121.5+227.7V_s^{-0.6}$$

Theoretical analysis based on the axial dispersion model was carried out to predict the degree of conversion in the reactor. Good agreement was obtained between the predicted values and the experimental data.

The use of hollow fiber modules for carry out enzyme catalysed reactions has recently been given considerable attention. Rony[1] was perhaps the first to point out the many advantages of encapsulating enzymes as a solution in the tube side of a hollow fiber module. He provided relationships for calculating the overall effectiveness factor which accounted for both internal and external diffusion resistances. These equations for planar, cylindrical and spherical membrane systems, are restricted to first order kinetics. Fink *et al.*[2] proposed a general procedure for calculating numerically the overall effectiveness factors for Michaelis-Menten kinetics. Georgakis *et al.*[3] considered theoretically the design of stirred reactors with hollow fiber catalysts for Michaelis-Menten kinetics and recently simulations of experimental data for a similar type of reactor were carried out by Kawasaki *et al.*[4]

Another form of hollow fiber reactor in which the enzyme is placed in the sponge film attached to the shell side of the tube walls, has been theoretically analyzed by Waterland *et al.*[5] and Kim *et al.*[6]

Experimental studies involving hollow fiber reactors have been reported by many workers.[7–14] However, the effects of the axial dispersion of the reactant fluid and the mass transfer resistances from shell to tube sides on the degree of conversion in these reactors have not been thoroughly investigated, except in the theoretical work of Webster and Shuler.[15]

In our work, the axial dispersion of fluid and mass transfer resistances were measured and later experimental data obtained from the hydrolysis of sucrose by invertase were simulated using a theoretical model.

Materials and Methods

Hollow fiber module The hollow fiber module (Model No. AHFK K-1) used was an artificial kidney produced by Asahi Medical Co., Ltd., Toyohashi, Japan, and contained 8,000 fibers arranged in a configuration resembling a shell-and-tube heat exchanger. The active length, inside diameter and outside diameter of each fiber were 16 cm, 0.26 mm and 0.3 mm, respectively. The fibers were made from "Cuprophane" and had a nominal molecular weight cut-off of 23,000. A bundle of these fibers was fixed in a shell, 4.46 cm in inside diameter.

Enzyme Concentrated solutions of yeast invertase (M. W. 27,000[16]) prepared by British Drug House, Ltd., were used to catalyze the hydrolysis of sucrose into invert sugar. Enzyme concentrations in the mixture are expressed as the volume of original enzyme solution per liter. The activity of one milliliter of the original enzyme solution was 6.47 units, when one unit was defined as the quantity of enzyme required to invert the sucrose of 1 μmole per minute in a sucrose solution of 10 mg/*l* under optimum conditions, 30°C, pH 5.0. The rate constant of the enzyme, used for calculations in this work, was determined by Mukataka and Kobayashi.[17]

Substrate First grade sucrose (Wako Pharmaceutical Co., Japan) was dissolved in 0.1 M acetate buffer (pH 5.0) at a concentration of 0.117 M.

Reactor The experimental apparatus is shown schematically in Fig. 1. The shell of the module was filled with a buffer solution and sealed. Invertase in a buffer solution was then circulated slowly through the tubes until all of the tubes were filled and no bubbles appeared in the outlet stream, and the end of the bundle was sealed with rubber caps. The module was immersed in a water bath held at 30°C. The seals of the shell side liquid were then opened to permit the buffered substrate solution to flow. The substrate reservoir was also maintained at 30°C in the water bath and the solution passed through a heat exchanger, located before the reactor. Flow rates of the substrate solution were kept at from 11 to 80 ml per minute. The concentration of invert sugar in the outlet stream was measured by the Somogyi method[18] and then the conversion of substrate was calculated.

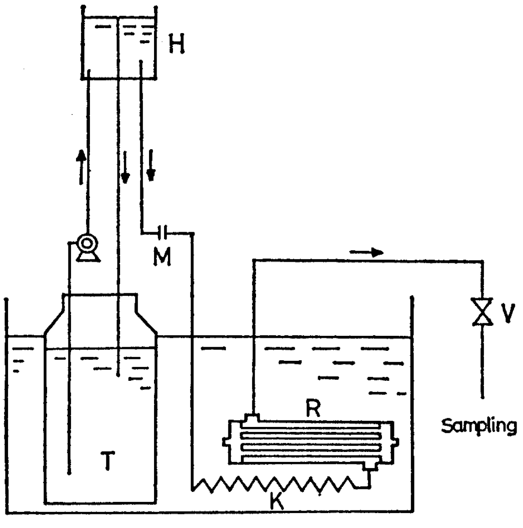

Fig. 1. Schematic diagram of experimental apparatus.
H: Head tank K: Heat exchanger
M: Orifice meter R: Membrane reactor
T: Substrate storage tank V: valve

Measurement of axial dispersion coefficient A method by the step-down change in tracer concentration was employed for the measurement of the axial dispersion coefficients. Blue-dextran (M.W. 2×10^6) which had no diffusivity through the membranes of the tubes was used as a tracer. The inlet tracer concentrations were about 2 g/*l* and the specific gravity of the tracer solution was adjusted to the same value as that of tap water with ethanol. The tracer solution was flowed through the shell side of the module and then replaced by tap water at given flow rates from 4.8 to 119.0 ml/min. Concentrations of the tracer were measured with a photospectrometer at 630 nm.

Measurement of mass transfer resistances Mass transfer resistances of sucrose from tube to shell side were calculated from the experimental data obtained at 30°C and pH 5.0. A buffered 0.117 M sucrose solution was flowed through the tube side of the module at flow rates from 20 to 90 ml/min. Also, a buffered 0.117 M maltose solution which had the same osmotic pressure as the sucrose solution was flowed through the shell side at flow rates from 6 to 100 ml/min in a countercurrent direction from that of the tube side flow.

Maltose concentrations were measured by the Somogyi method. The sucrose contained in the outlet solution was perfectly hydrolyzed by the invertase and then its concentration was calculated from the increment of reducing sugar, measured by the Somogyi method.

Theoretical Analysis of Reactor Performance

The degree of conversion in an immobilized enzyme reactor has been analyzed theoretically by taking into account the axial dispersion and mass transfer resistance by Kobayashi and Moo-Young.[19] Their analytical method can be applied for the analysis of the performance of a hollow fiber enzyme reactor.

Consider the performance of a hollow fiber reactor under steady state conditions. According to Mukataka and Kobayashi,[17] the apparent Michaelis-Menten equation for enzyme kinetics, Eq. (1), can be applied to sucrose hydrolysis by invertase.

$$r_s=\frac{k'C_E C_s}{K'_m+C_s} \quad (1)$$

where

$$k'=\frac{k}{1-K_m/K_f-K_m/K_g}$$
$$=1.19\times10^7\exp(-4.53\times10^3/T) \quad (2)$$

and

$$K_m'=\frac{1+C_{so}/K_f+C_{so}/K_g}{1/K_m-1/K_f-1/K_g}=C_{so}+17 \quad (3)$$

The idealized concentration profiles of substrates (radial cross section) is shown in Fig. 2. The material balance for the substrate gives the following differential equation.

$$D_a(\mathrm{d}^2C_s/\mathrm{d}l^2)-v_s(\mathrm{d}C_s/\mathrm{d}l)$$
$$-(K_{os}a/\varepsilon_s)(C_s-C_s^*)=0 \quad (4)$$

According to Danckwerts,[20] boundary conditions are

$$C_s-(D_a/v_s)(\mathrm{d}C_s/\mathrm{d}l)=C_{so}\ ;\ \text{at } l=0 \quad (5)$$

and

$$\mathrm{d}C_s/\mathrm{d}l=0 \qquad ;\ \text{at } l=L \quad (6)$$

where C_{so} refers to the substrate concentration at the inlet.

Under steady state conditions, the mass transfer rate will be equal to the reaction rate, i.e.:

$$K_{os}a(C_s-C_s^*)=E_f\varepsilon_t[k'C_EC_s^*/(K_m'+C_s^*)] \quad (7)$$

where E_f is the effectiveness factor.[21]

From Eq. (7), the dimensionless concentration of the substrate at the inside surface of the tube is given by the following equation.

$$Y^*=\frac{1}{2}\{Y-E_f\alpha-\beta$$
$$+\sqrt{(Y-E_f\alpha-\beta)^2+4\beta Y}\} \quad (8)$$

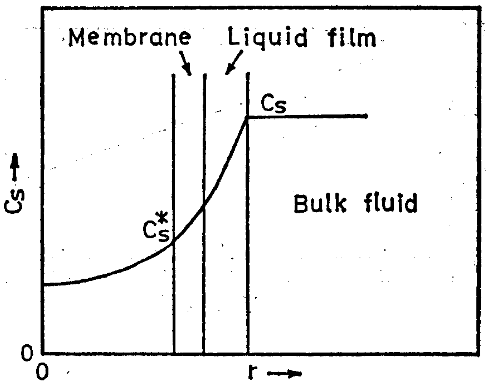

Fig. 2. Concentration profile of substrate.

Thus, Eq. (4) can be rewritten as follows in dimensionless form

$$(1/PeB)(\mathrm{d}^2Y/\mathrm{d}Z^2)-\mathrm{d}Y/\mathrm{d}Z-(W/2)\{Y$$
$$+E_f\alpha+\beta-\sqrt{(Y-E_f\alpha-\beta)^2+4\beta Y}\}=0$$
$$(9)$$

with the boundary conditions;

$$Y-(1/PeB)(\mathrm{d}Y/\mathrm{d}Z)=1\ ;\ \text{at } Z=0 \quad (10)$$
$$\mathrm{d}Y/\mathrm{d}Z=0 \qquad ;\ \text{at } Z=1 \quad (11)$$

Solutions to Eq. (9) can only be obtained by numerical means.

When the Bodenstein number (PeB) is infinity, i.e., a plug flow reactor is employed, Eq. (9) is reduced to

$$\mathrm{d}Y/\mathrm{d}Z=-(W/2)\{Y+E_f\alpha+\beta$$
$$-\sqrt{(Y-E_f\alpha-\beta)^2+4\beta Y}\} \quad (12)$$

with the following boundary condition;

$$Y=1\ ;\ \text{at } Z=0 \quad (13)$$

The solution of Eq. (12) is given by Eq. (14) for a constant value of E_f.

$$-2E_f\alpha W=Y_e-1+A\ln Y_e+C_1$$
$$\pm B\ln 2\left|Y_e+B\pm C_1\right|+A\ln\left|\frac{Y_e+A-C_1}{Y_e-A-C_1}\right|$$
$$-\Big\{D\pm B\ln 2\left|1+B\pm D\right|$$
$$+A\ln\left|\frac{(1+A-D)}{(1-A-D)}\right|\Big\} \quad (14)$$

where

$$Y=Y_e\ ;\ \text{at } Z=1,$$
$$A=E_f\alpha+\beta,\quad B=\beta-E_f\alpha,$$
$$C_1=\sqrt{Y_e^2+2BY_e+A^2},$$
$$\text{and}\quad D=\sqrt{1+2B+A^2}$$

The outlet dimensionless concentration of the substrate (Y_e) can be obtained by a trial-and-error method from Eq. (14).

Results and Discussion

Axial dispersion coefficients From van der Laan,[22] the relationship between PeB and the variance, $\bar{\sigma}^2$, of the residence times is given by the following equation.

$$\bar{\sigma}^2=\frac{2}{PeB}\Big[PeB-1+\exp(-PeB)\Big] \quad (15)$$

where $\bar{\sigma}^2$ is defined by Eq. (16)

$$\bar{\sigma}^2=2\int_0^\infty\phi R(\phi)\mathrm{d}\phi-1 \quad (16)$$

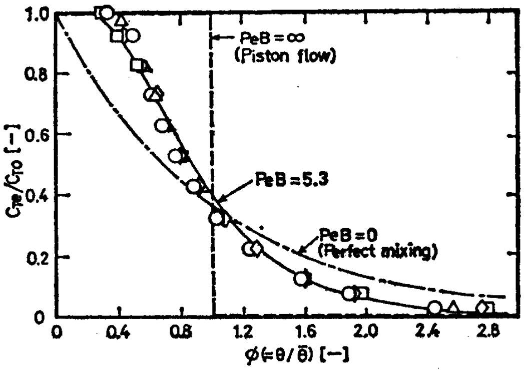

Fig. 3. Response to step change of tracer in shell side liquid.
Liquid flow rate (ml/min): 4.8 (○), 11.0 (△), 44.0 (◇), 119.0 (□).

A constant value of *PeB*, 5.3, was obtained from Eq. (15), in which values of $\bar{\sigma}^2$ were calculated graphically from Eq. (16) by a trial-and-error method. The theoretical solution of residence time distribution based on a dispersion model has been given by Yagi and Miyauchi.[23]

The residence time distribution curve is shown in Fig. 3, being represented by a single curve in dimentionless form for various liquid flow rates.

Also, the theoretical values for the dispersion model ($PeB=5.3$), piston flow and perfect mixing are plotted in the figure. Agreement between the experimental values and those for the axial dispersion model is quite good. These results also show that the mixing characteristics of fluids are approximated by the dispersion model and that *PeB* is nearly constant, regardless of the fluid velocity in the reactor. Also, it is very interesting that the value of *PeB*, 5.3, is very close to that of the shell-and-tube heat exchanger, $PeB=8$.[24]

Mass transfer resistances When shell side and tube side liquids flow against each other, the mass transfer resistance from the tube side to the shell side is divided into three terms, i.e., that of the fiber film ($1/k_fA_f$), the shell side liquid film ($1/k_{Ls}A_s$) and the tube side liquid film ($1/k_{Lt}A_t$).

The over-all mass transfer resistance ($1/K_{ov}A_{ov}$) is given by Eq. (17).

$$1/K_{ov}A_{ov}=1/k_{Ls}A_s+1/k_fA_f+1/k_{Lt}A_t \qquad (17)$$

Also, one can assume the following relationship for mass transfer area, because the thickness of the liquid film and of hollow fiber membrane is very small.

$$A_{ov}=A_s=A_f=A_t \qquad (18)$$

Accordingly, mass transfer resistances are given by the following equation.

$$1/K_{ov}=1/k_{Ls}+1/k_f+1/k_{Lt} \qquad (19)$$

In this experiment, the tube side liquids were passed through the reactor in laminar flow, since the Reynolds numbers were smaller than 3. Therefore, k_{Lt} can be calculated by Leveque's equation[25] given by Eq. (20).

$$(k_{Lt}/v_t)(S_c^{2/3})=1.61(Re)^{-2/3}(L/d)^{-1/3} \qquad (20)$$

By using the value of the diffusion coefficient of sucrose, 5.6×10^{-6} cm^2/sec, published in the literature,[26] the values of k_{Lt} were calculated for various values of v_t as shown in Fig. 4.

Concerning the shell side liquid film resistances, the following Eq. (21) is assumed to be applicable from the correlation of liquid film heat transfer coefficients of shell-and-tube heat exchangers[27] by applying the analogy between heat and mass transfer.

$$k_{Ls}\propto v_s^{0.6} \qquad (21)$$

When the mixing characteristics of the shell side liquid are approximated by the dispersion model, and the shell side and tube side liquids flow against each other, the following equations are derived from the material balance under steady state conditions by neglecting the foreflow section in the laminar flow region[28] and the effects of the ends of the tubes,[29] since $L/d>600$.

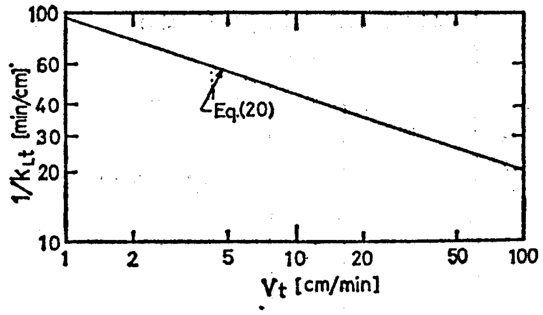

Fig. 4. Effect of tube side interstitial velocity on tube side liquid film resistance, based on Leveque's equation, Eq. (20).

$$D_a(\mathrm{d}^2C_{ss}/\mathrm{d}l^2)-v_s(\mathrm{d}C_{ss}/\mathrm{d}l)-(K_{ov}a/\varepsilon_s)(C_{ss}-C_{st})=0\,, \qquad (22)$$

$$v_t(\mathrm{d}C_{st}/\mathrm{d}l)+(K_{ov}a/\varepsilon_t)(C_{ss}-C_{st})=0\,, \qquad (23)$$

Boundary conditions;

$$C_{ss}-(D_a/v_s)(\mathrm{d}C_{ss}/\mathrm{d}l)=C_{so} \qquad (24)$$

$$\mathrm{d}C_{ss}/\mathrm{d}l=0\,, \qquad (25)$$

where subscriptions *s* and *t* refer to the shell side and tube side, respectively. The above simultaneous differential equations (22) and (23) were solved analytically by Miyauchi and Vermeulen[20] and Tadaki and Maeda.[21] If one assumes that the substrate concentrations in the tubes at the inlet are zero and those in shell side are C_{se}, the analytical solution is given as follows.

$$\left(\frac{C_{se}}{C_{so}}\right)=2(\mu_1-\mu_2)(1-4S)e^{\mu_1+\mu_2}/\{(R-4SR+2\mu_1)e^{\mu_1}-(R-4SR+2\mu_2)e^{\mu_2}-8S(\mu_1-\mu_2)e^{\mu_1+\mu_2}\} \qquad (26)$$

where

$$S=\frac{v_s\varepsilon_s}{v_t\varepsilon_t}\,,\quad R=2K_{ov}a/v_s\,,$$

$$\mu_1=\left(\frac{PeB}{2}\right)+SR+\sqrt{\left\{\left(\frac{PeB}{2}\right)-SR\right\}^2+\left(\frac{PeB}{2}\right)R}$$

and

$$\mu_2=\left(\frac{PeB}{2}\right)+SR+\sqrt{\left\{\left(\frac{PeB}{2}\right)+SR\right\}^2+\left(\frac{PeB}{2}\right)R}$$

By applying the trial and error method, one can determine the values of K_{ov} which fit Eq. (26) by using the experimental values of the outlet concentration, C_{se}. Then, the mass transfer resistance, $1/K_{os}A_{os}$, which is necessary for the design of reactors, is given as follows:

$$1/K_{os}=1/k_f+1/k_{Ls}=1/K_{ov}-1/k_{Lt} \qquad (27)$$

By substituting the values of K_{ov} from Eq. (27) and those of k_{Lt} from Eq. (20) into Eq. (27), values of $1/K_{os}$ were calculated and then Wilson plots[22] for $1/K_{os}$ against $v_s^{-0.6}$ are tried in Fig. 5. Also, the values of $1/K_{os}$ which were calculated assuming piston flow to apply for both shell and tube side liquids are plotted in the figure.

The values of $1/K_{os}$ which were calculated taking into account fluid mixing are rather small comparing with those calculated without considaring liquid mixing, and are correlated by the following equation:

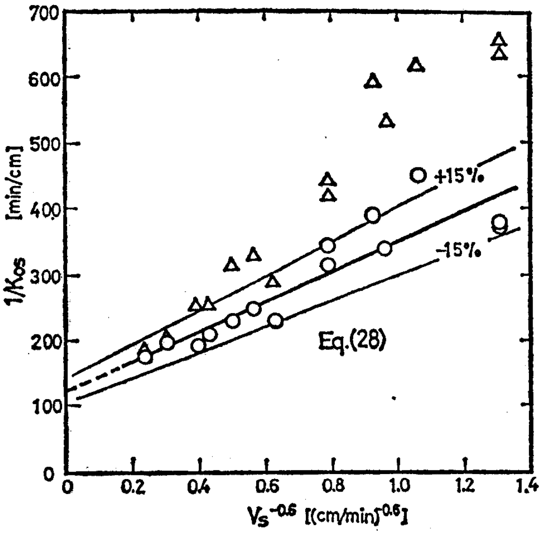

Fig. 5. Wilson plot.
○ : { Tube side . . . piston flow
  Shell side . . . dispersion model
△ : Both sides . . . piston flow

$$1/K_{os}=121.5+227.7\,v_s^{-0.6} \qquad (28)$$

Therefore, the value of k_f becomes 121.5 min/cm from Eq. (28).

Reactor performance Conversions obtained at the outlet as a function of residence time are shown in Fig. 6. Also values predicted by Eq. (14) for piston flow and by Eq. (9) for the dispersion model are plotted in the figure. The numerical solution of Eq. (9) was obtained by a quasilinearization method.[23]

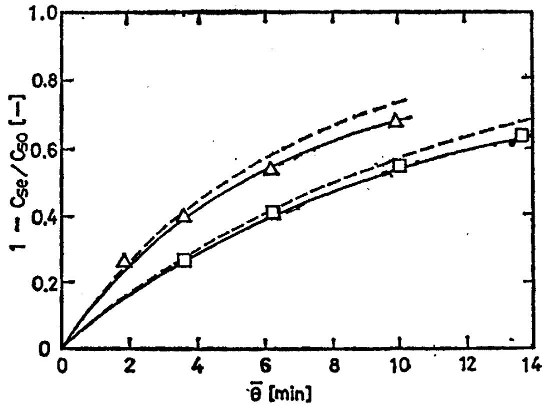

Fig. 6. Comparison of experimental data with theoretical values.
Enzyme concentration (ml/*l*): 5 (□), 10 (△),
Theoretical values: Piston flow (----),
Dispersion model, *PeB*=5.3 (——).

Table 1. Effectiveness factor for enzyme, tube side configuration.

C_E [ml/l]	5		10	
C_s [g-mol/l]	0.117	0	0.117	0
E_f [—]	1.00	0.988	0.994	0.963

The effectiveness factor, E_f, was calculated by using an approximate solution[4] according to Roberts' analytical method.[5] Values of E_f calculated for two extreme cases of substrate concentration, $C_s=C_{so}$ (0.117 M) and $C_s=0$, corresponding to each enzyme concentration, $C_E=5$ and $C_E=10$ ml/l, are shown in Table 1.

To simplify the calculation of Eqs. (9) and (14), average values of E_f were used, although they varied slightly with C_s. From Fig. 6, it is clear that predicted values based on the axial dispersion model rather than those using the piston flow model agree well with experimental values and also that the analytical method employed here is useful.

Nomenclature

A_f, A_s, A_t: mass transfer areas of fiber film, shell side and tube side, cm^2
A_{ov} : overall mass transfer area, cm^2
a : membrane surface area per unit volume of reactor, cm^{-1}
C_E : enzyme concentration, ml/l
C_s : substrate concentration, g-mol/l
$C_s{}^*$: substrate concentration at inside surface of tube, g-mol/l
C_{se}, C_{so}: substrate concentrations at exit and inlet, g-mol/l
C_{ss} : substrate concentration in shell side, g-mol/l
C_{Te}, C_{To}: tracer concentrations at exit and inlet, g/l
D_a : axial dispersion coefficient, cm^2/min
D_s : molecular diffusivity of substrate, cm^2/min
d : inside diameter of tube, cm
E_f : effectiveness factor, —
K_f, K_g, K_m: dissociation constants of complexes of fructose-enzyme, glucose-enzyme and sucrose-enzyme, g/l
K_{os} : mass transfer coefficient defined by Eq. (27), cm/min
K_{ov} : overall mass transfer coefficient defined by Eq. (19), cm/min
k : rate constant, g/ml·min
k_f : membrane mass transfer coefficient, cm/min
k_{Ls}, k_{Lt}: liquid film mass transfer coefficients of shell side and tube side, cm/min
L : effective reactor tube length, cm
l : longitudinal distance of reactor from inlet of tube, cm
PeB: Bodenstein number ($=v_tL/D_a$), —
Re : Reynolds number ($=2rv_t\rho/\mu$), —
$R(\phi)$: residence time distribution function, —
r : radial distance of fiber, cm
S_c : Schmidt number ($=\mu/\rho D_s$), —
T : absolute temperature, °K
v_s, v_t: interstitial velocities in shell side and tube side, cm/min
W : dimensionless parameter ($=K_{os}aL/\varepsilon_s v_s$), —
Y, Y^*, Y_e: dimensionless substrate concentrations defined by C_{ss}/C_{so}, $C_s{}^*/C_{so}$ and C_{se}/C_{so}, —
Z : dimensionless longitudinal distance ($=l/L$), —
α : dimensionless parameter ($=k'C_E\varepsilon_t/K_{os}aC_{so}$), —
β : dimensionless parameter ($=K'_m/C_{so}$), —
$\varepsilon_s, \varepsilon_t$: volume fractions of shell side and tube side in reactor, —
θ : time, min
$\bar{\theta}$: mean residence time, min
μ : viscosity of liquid, g/cm·min
ρ : density of liquid, g/cm^3
$\bar{\sigma}^2$: variance, —
ϕ : dimensionless time, —

References

1) Rony, P. R.: *Biotechnol. Bioeng.*, **13,** 431 (1971).
2) Fink, D. J., Na, T., Shults, J. S.: *Biotechonl. Bioeng.*, **15,** 879 (1973).
3) Georgakis, C., Chan, P. C. H., Aris, R.: *Biotechnol. Bioeng.*, **17,** 99 (1975).
4) Kawakami, K., Misono, S., Kai, M., Kato, K., Kusunoki, K.: *Hakkokogaku*, **57,** 332 (1979).
5) Waterland, L. R., Michaelis, A. S., Robertoson, C. R.: *A. I. Ch. E. Joumal*, **20,** 50 (1974).
6) Kim, S. S., Cooney, D. O.: *Chem. Eng. Sci.*, **13,** 289 (1976).

7) Rony, P. R.: *J. Amer. Chem. Soc.*, **94,** 8247 (1972).
8) Lewis, W., Middleman, S.: *A. I. Ch. E. Journal*, **20,** 1012 (1974).
9) David, J. C.: *Biotechnol. Bioeng.*, **16,** 1113 (1974).
10) Fink, D. J., Rodwell, V. W.: *Biotechnol. Bioeng.*, **17,** 1029 (1975).
11) Waterland, L. R., Robertson, C. R., Michaels, A. S.: *Chem. Eng. Commun.*, **2,** 37 (1975).
12) Korus, R. A., Olson, A. C.: *Biotechnol. Bioeng.*, **19,** 1 (1977).
13) Dongen, D. B. V., Cooney, D. O.: *Biotechnol. Bioeng.*, **19,** 1253 (1977).
14) Korus, R. A., Olson, A. C.: *J. Food Sci.*, **42,** 258 (1977).
15) Webster, I. A., Shuler, M. L.: *Biotechnol. Bioeng.*, **20,** 1941 (1978).
16) Newmann, N., Lampen, J. O.: *Biochemistry*, **6,** 468 (1967).
17) Mukataka, S., Kobayashi, J.: *Kagaku Kogaku Ronbun Shu*, **1,** 202 (1975).
18) Somogyi, M.: *J. Biol. Chem.*, **195,** 19 (1952).
19) Kobayashi, T., Moo-Young, M.: *Biotechnol. Bioeng.*, **13,** 893 (1971).
20) Danckwerts, P. V.: *Chem. Eng. Sci.*, **2,** 1 (1953).
21) Thiele, E. W.: *Ind. Eng. Chem.*, **31,** 916 (1939).
22) van der Laan, E. Th.: *Chem. Eng. Sci.*, **7,** 187 (1958).
23) Yagi, S., Miyauchi, T.: *Kagaku Kōgaku*, **17,** 382 (1953).
24) Vincent, G. C., Hougen, J. O., Drifke, G. E.: *Chem. Eng. Progr.*, **57,** 48 (1961).
25) Leveque, J.: *Ann. Mines*, **13,** 276 (1928).
26) Kagaku Kōgaku Kyokai Hen: *Bussei Teisu*, No. 4, p. 256, Maruzen, Tokyo (1966).
27) Donohue, D. A.: *Ind. Eng. Chem.*, **41,** 2499 (1949).
28) Fujita, S.: *Kagaku Kōgaku* (*I*), p. 74, Iwanami Shoten, Tokyo, (1978).
29) Saravacos, G. D.: *Food Technology*, **22,** 1585 (1968).
30) Miyauchi, T., Vermeulen, T.: *Ind. Eng. Chem. Fund.*, **2,** 113 (1963).
31) Tadaki, T., Maeda, S.: *Kagaku Kōgaku*, **27,** 808 (1963).
32) Wilson, R. E.: *Trans. A. S. M. E.*, **37,** 47 (1915).
33) Lee, S.: *Quasilinearization and Invariant Imbedding*, Academic Press Inc., New York (1968).
34) Kobayashi, T., Ohmiya, K., Shimizu, S.: *J. Ferment. Technol.*, **54,** 260 (1976).
35) Roberts, G. W., Satterfield, C. N.: *Ind. Eng. Chem. Fund.*, **4,** 288 (1965).

(Received June 13, 1980)