Mathematical simulation of fixed bed reactor using immobilized enzymes

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The complexities of heterogeneous biocatalysis are compounded under circumstances in which transport phenomena govern the overall rate process. A fixed bed reactor model using immobilized enzymes incorporating external and internal diffusion and axial dispersion has been developed. Based on those equations, computer simulations of continuous reactor operation were performed. The influence of internal and external diffusion was tested.

Комплекс процесса гетерогенного биокатализа складывается в условиях, при которых явления переноса определяют общую скорость процесса. Разработана модель реактора с закрепленным слоем иммобилизованного фермента, учитывающая внешнюю и внутреннюю диффузию, а также аксиальную дисперсию. На основе этих уравнений проведено математическое симулирование работы континуального реактора. Тестировалось влияние внутренней и внешней диффузии.

Application of immobilized enzyme reactors has been studied extensively [1, 2], but immobilized enzyme engineering is still in its infancy. Several general categories of immobilized enzyme reactors exist: batch reactors, continuous stirred tank reactors, fixed bed reactors, and fluidized bed reactors. When the immobilized enzyme is in the form of spheres, chips, discs, sheets, beads or pellets it can be packed readily into a column.

Review of *Kasche* [3] discusses the different approaches to the prediction of mass transfer resistances in immobilized enzyme systems. Another approach to solve the combined external and internal mass transfer of substrate concomitant with the Michaelis—Menten reaction scheme has been advanced recently by *Fink* [4] but without axial dispersion. Diffusion resistance and enzyme activity decay in a pellet have been studied by *Verhoff* [5]. A model for continuous working enzyme reactor to determine the deviation of temperature and concentration in axial and radial direction has been developed by *Setzermann et al.* [6, 7]. Thus this paper consists of an examination of the various parameters of fixed bed immobilized enzyme reactor design in unsteady state.

Theoretical model

Mathematical model of fixed bed reactor with immobilized enzymes can be derived from the following simplifying assumptions:

1. Only one substrate is transformed from the stream of liquid.
2. Both liquid and solid phase are considered to be continua existing in continuous contact beside each other in the interface, the surface of which corresponding to a volume unit of the layer is definite.
3. The flow rate of liquid may be regarded as constant.
4. The particles of porous carrier may be considered as spheres, pseudohomogeneous, the effective diffusion coefficient is constant.
5. Enzyme activity is constant.
6. The cross-section of the reactor is constant, the voidage fraction is constant, radial dispersion is negligible.
7. The temperature in the reactor is constant.

Mathematical model

Material balances of substrate in flow of liquid

$$\varepsilon \cdot v \left(\frac{\partial c_s}{\partial z}\right)_t + \varepsilon \left(\frac{\partial c_s}{\partial t}\right)_z + k_m a_m (c_s - c^*_{s,p}) = D_L \frac{\partial^2 c_s}{\partial z^2} \qquad (1)$$

with initial conditions

$$t = 0 \quad 0 \leqslant z \leqslant L \quad c_s(z, 0) = 0 \qquad (2)$$

and boundary conditions

$$t > 0 \quad z = 0 \quad \varepsilon \cdot v(c_s - c_{s,0}) = D_L \left(\frac{\partial c_s}{\partial z}\right)_t \qquad (3)$$

$$z = L \quad \frac{\partial c_s}{\partial z} = 0 \qquad (4)$$

Material balances of substrate in the particle

$$P \frac{\partial c_{s,p}}{\partial t} + R_s = D_e \left(\frac{\partial^2 c_{s,p}}{\partial r^2} + \frac{2}{r} \frac{\partial c_{s,p}}{\partial r}\right) \qquad (5)$$

with initial conditions

$$t \leqslant 0 \quad 0 \leqslant z \leqslant L \quad 0 \leqslant r \leqslant R_p \quad c_{s,p}(r, z, 0) = 0 \qquad (6)$$

and boundary conditions

$$t>0 \quad 0\leqslant z\leqslant L \quad r=R_p \quad D_e\frac{\partial c_{s,p}}{\partial r}=k_m(c_s-c^*_{s,p}) \tag{7}$$

$$r=0 \quad \frac{\partial c_{s,p}}{\partial r}=0 \tag{8}$$

For simple, irreversible kinetics of the Michaelis—Menten type, the reaction rate can be expressed as

$$R_s=\frac{K_1 c_{s,p}}{K_2+c_{s,p}} \tag{9}$$

It is clear that analytical solution for eqns (*1—9*) is not possible. The system eqns (*1—9*) can be transformed into the dimensionless form.

Substituting

$$X=\frac{c_s}{c_{s,0}} \quad x=\frac{c_{s,p}}{c_{s,0}} \quad Z=\frac{z}{L} \quad \tau=\frac{vt}{L} \quad s=\frac{r}{R_p} \tag{10}$$

and introducing

$$a=\frac{a_m k_m L}{\varepsilon\cdot v} \qquad \mathrm{Bo}=\frac{\varepsilon\cdot vL}{D_L}$$

$$\mathrm{Bi}=\frac{k_m R_p}{D_e} \qquad \alpha=\frac{L\cdot D_e}{P\cdot v\cdot R_p^2} \tag{11}$$

$$\beta=\frac{K_1 L}{P\cdot v\cdot c_{s,0}} \qquad \mu=\frac{K_2}{c_{s,0}}$$

we obtain the system equations in dimensionless form

$$\frac{\partial X}{\partial Z}+\frac{\partial X}{\partial \tau}+a(X-x_s)=\frac{1}{\mathrm{Bo}}\frac{\partial^2 X}{\partial Z^2} \tag{12}$$

with boundary conditions

$$\tau>0 \qquad Z=0 \qquad \frac{1}{\mathrm{Bo}}\frac{\partial X}{\partial Z}=X-1 \tag{13}$$

$$Z=0 \qquad \frac{\partial X}{\partial Z}=0$$

and initial conditions

$$\tau\leqslant 0 \qquad 0\leqslant Z\leqslant 1 \qquad X=0 \tag{14}$$

Eqns (*5*) and (*9*) transformed into dimensionless form

$$\frac{\partial x}{\partial \tau}+\frac{\beta x}{\mu+x}=\alpha\left[\frac{\partial^2 x}{\partial s^2}+\frac{2}{s}\frac{\partial x}{\partial s}\right] \qquad (15)$$

with initial conditions for particle

$$\tau\leqslant 0 \qquad 0\leqslant Z\leqslant 1 \qquad 0\leqslant s\leqslant 1 \qquad x=0 \qquad (16)$$

and boundary conditions

$$\tau>0 \qquad 0\leqslant Z\leqslant 1 \qquad s=1 \qquad \frac{\partial x}{\partial s}=\mathrm{Bi}(X-x_s) \qquad (17)$$

$$s=0 \qquad \frac{\partial x}{\partial s}=0$$

Method of solution of model equations

Eqns (*12—17*) are solved numerically using a digital computer M-4030. The partial differential equations are rewritten at M selected axial positions in the reactor and at N selected radial positions in the particle according to the orthogonal collocation method [8, 9]. In this way the partial differential equations are split into $\mathrm{NE}=(M+N\cdot M)$ coupled ordinary differential equations. These equations are solved simultaneously using modified STIFF3 routine [10]. Because the coefficient matrix of each of these sets has very sparse structure, the modified very efficient LU decomposition for sparse systems may be used [11]. Thus the computational time is reduced 60—100 times in comparison with the classical Gauss elimination.

The number of collocation points used was varied until the accuracy of the profiles obtained remained essentially unchanged. More details of the computational procedure are presented in [12]. Typical CPU time for $M=5$ and $N=3$, *i.e.* $\mathrm{NE}=20$ was 50 s.

Results for the base case

For our "base case" we supposed immobilization of enzyme over a carrier of spherical shape which catalyzes the conversion of the substrate S to product P. For the calculation the following values of parameters were chosen [1, 13]

reactor diameter $\qquad D_r = 1.38\times 10^{-2}$ m

height of fixed bed	$L = 0.102$ m
bed voidage	$\varepsilon = 0.41$
particle porosity	$P = 0.40$
particle diameter	$D_p = 0.003$ m
specific surface of particle	$a_m = 1180\ m^{-1}$
superficial velocity	$\varepsilon \cdot v = 1.86 \times 10^{-4}\ m\ s^{-1}$
initial concentration of substrate	$c_{s,0} = 100\ mol\ m^{-3}$
mass transfer coefficient	$k_m = 5.8 \times 10^{-6}\ m\ s^{-1}$
effective diffusion coefficient	$D_e = 3 \times 10^{-9}\ m^2\ s^{-1}$
axial dispersion coefficient	$D_L = 1.197 \times 10^{-6}\ m^2\ s^{-1}$
maximum reaction rate	$K_1 = 1.41\ mol\ m^{-3}\ s^{-1}$
Michaelis constant	$K_2 = 191\ mol\ m^{-3}$
temperature	$T = 293$ K
solution density	$\varrho = 1000\ kg\ m^{-3}$

The numerical values of dimensionless variables for the "base case" are given in Table 1.

Table 1

Values of dimensionless parameters

a	Bi	Bo	α	β	μ
3.76	2.90	15.82	0.75	7.94	1.91

The dependence of dimensionless concentration of substrate at the outlet of reactor depicted in Fig. 1 was calculated by the above-mentioned method. On the assumption that the activity of immobilized enzymes is constant, the dimensionless concentration of substrate reached the value $c_s/c_{s,0} = 0.35$.

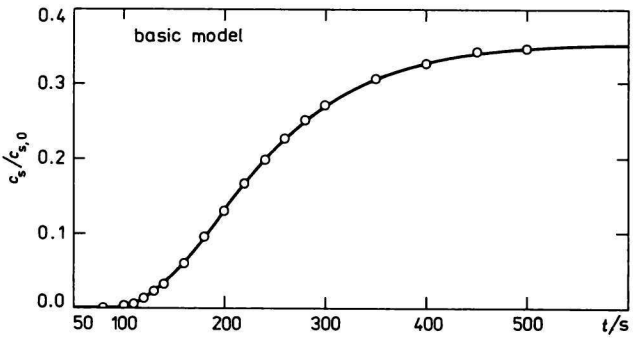

Fig. 1. Substrate concentration in the outlet of column reactor — base case.

In Fig. 2 are plotted curves of calculated concentration profiles along the reactor and in the particles of carrier at $t = 140$ s. The indices L and s are related to values of concentrations in the main stream of fluid and on the surface of particles, respectively. Curves *1—3* belong to collocation points in the particle. From Fig. 2 it is obvious that thickness of the diffusion film plays a significant role at the particle surface concentration, which is evident by an expressive difference between calculated concentrations in the stream of fluid and on particles surface. This difference has been found by calculation to coincide with the difference of mentioned concentrations for the steady state.

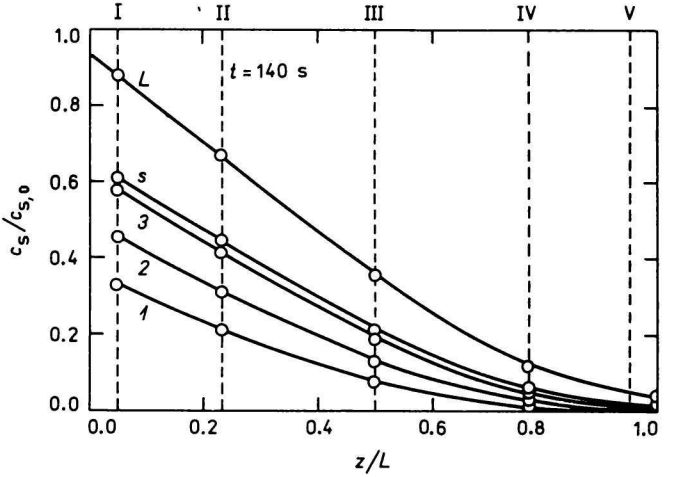

Fig. 2. Substrate concentration profile along column reactor.
L and *s* are related to the values of concentrations in the bulk stream of fluid and on the surface of particles.
Curves *1—3* belong to collocation points in the particle.

Influence of the magnitude of Biot number on the conversion of substrate

For unchanging diameter of particles, the magnitude of the Biot number is given by the values of mass transfer coefficient k_m and effective diffusion coefficient D_e. In testing the influence of k_m, its value varied over the range 2×10^{-8}—$2 \times \times 10^{-3}$ m s^{-1}, which corresponds to Biot number 10^{-2}—10^{3}. Value a varies proportionally with k_m. In Fig. 3 is plotted the calculated dependence of the concentration of substrate on time at the reactor outlet for various values of Bi(k_m). With decreasing value of Bi(k_m), the concentration of substrate at the outlet from reactor increases, *i.e.* the conversion decreases, which is connected with low values of mass transfer coefficient in the liquid phase k_m and/or with the thickness of the diffusion film.

The value of Biot number as function of the effective diffusion coefficient varied over the range 10^{-2}—10^{3}, which corresponds to values of diffusion coefficient 8.696×10^{-7}—8.696×10^{-12} m^2 s^{-1}. Parameter α varies with D_e.

In Fig. 4 are depicted courses of the dimensionless concentration $c_s/c_{s,0}$ for some values of diffusion coefficient.

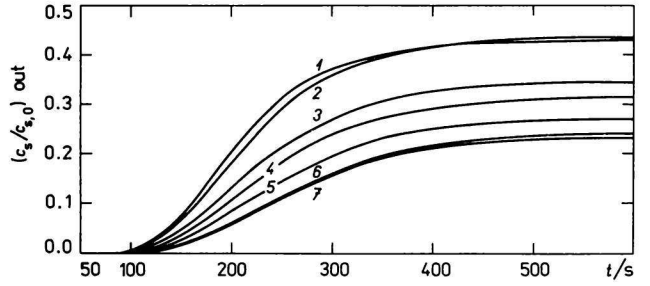

Fig. 3. Substrate concentration in effluent of column reactor at various parameter Bi(k_m).
1. Bi = 1.0, resp. $k_m = 2.0 \times 10^{-6}$ m s^{-1};
2. Bi = 1.45, resp. $k_m = 2.9 \times 10^{-6}$ m s^{-1};
3. Bi = 2.90, resp. $k_m = 5.8 \times 10^{-6}$ m s^{-1};
4. Bi = 4.35, resp. $k_m = 8.7 \times 10^{-6}$ m s^{-1};
5. Bi = 10, resp. $k_m = 2 \times 10^{-5}$ m s^{-1};
6. Bi = 100, resp. $k_m = 2 \times 10^{-4}$ m s^{-1};
7. Bi = 10^3, resp. $k_m = 2 \times 10^{-4}$ m s^{-1}.

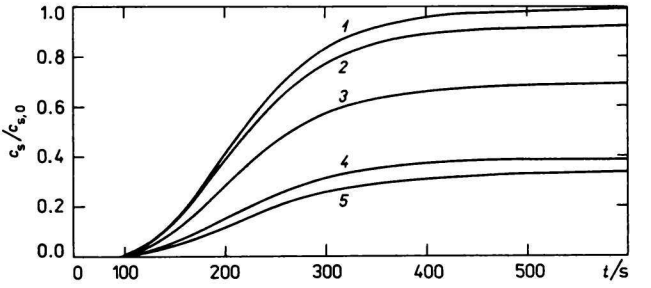

Fig. 4. Substrate concentration in effluent of column reactor at various parameter Bi(D_e).
1. Bi = 10^4, resp. $D_e = 8.7 \times 10^{-13}$ m^2 s^{-1};
2. Bi = 10^3, resp. $D_e = 8.7 \times 10^{-12}$ m^2 s^{-1};
3. Bi = 10^2, resp. $D_e = 8.7 \times 10^{-11}$ m^2 s^{-1};
4. Bi = 5.8, resp. $D_e = 1.5 \times 10^{-9}$ m^2 s^{-1};
5. Bi = 1.93, resp. $D_e = 4.5 \times 10^{-9}$ m^2 s^{-1}.

$c_{s,0} = 100$ mol m^{-3}, $L = 0.102$ m.

Comparison of the influence of both coefficients is illustrated in Fig. 5 where the dependence of dimensionless concentration of substrate at the reactor outlet on D_e and k_m is given. It is obvious that for $k_m > 10^{-4}$ m s^{-1} the external diffusion does not play a significant role and the process is governed by diffusion of substrate in the particle. On the contrary, if $D_e > 5 \times 10^{-9}$ m^2 s^{-1}, the concentration of substrate at the outlet of reactor is practically constant, *i.e.* the process is governed by external diffusion.

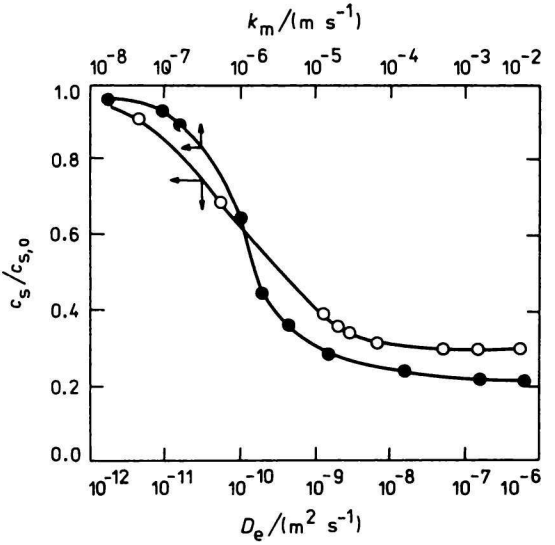

Fig. 5. Substrate concentration in effluent of column reactor *vs.* values of k_m and D_e.

Conclusion

In this paper a mathematical model of a tubular reactor with immobilized enzyme over a carrier of spherical shape is presented. This model includes external and internal diffusion and axial dispersion. The set of partial differential equations was successfully solved numerically by the method of orthogonal collocation. The influence of external and internal diffusion on conversion of substrate was tested. It was found out that for $D_e < 10^{-9}$ m^2 s^{-1}, the process is governed by diffusion of the substrate in the particle of the carrier of enzyme while for $k_m < 10^{-4}$ m s^{-1} the process is governed by external diffusion. In further work the model will include the time inactivation of enzyme.

Symbols

a	dimensionless parameter (eqn *11*)
a_m	particles specific area
Bi	Biot number
Bo	Bodenstein number
c_s	substrate concentration
$c_{s,p}$	substrate concentration in particles
$c^*_{s,p}$	substrate concentration on particles surface
$c_{s,0}$	inlet substrate concentration
D_e	effective diffusion coefficient
D_L	axial dispersion coefficient
D_p	particle diameter
k_m	mass transfer coefficient
K_1	maximal reaction rate
K_2	Michaelis parameter
L	fixed bed height
M	number of selected axial positions in the reactor
N	number of selected radial positions in the particle
NE	number of coupled ordinary differential equations
P	porosity
r	spherical coordinate
R_p	particle radius
R_s	reaction rate
s	dimensionless particle coordinate
t	time
v	interstitial velocity of liquid
x, X	dimensionless concentration (eqn *10*)
z	axial coordinates
Z	dimensionless axial coordinates
α, β, μ	dimensionless parameters (eqn *11*)
τ	dimensionless time

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