Biochemical Engineering Journal 91 (2014) 129–139

Contents lists available at ScienceDirect

Biochemical Engineering Journal

journal homepage: www.elsevier.com/locate/bej

Theoretical analysis of intrinsic reaction kinetics and the behavior of immobilized enzymes system for steady-state conditions

T. Praveen [a], Pedro Valencia [b], L. Rajendran [a,*]

[a] Department of Mathematics, The Madura College, Madurai 625 011, Tamil Nadu, India
[b] Department of Chemical and Environmental Engineering, Universidad Técnica Federico Santa María, Avenida España, Valparaíso, 1680 Chile

ARTICLE INFO

Article history:
Received 21 December 2013
Received in revised form 21 July 2014
Accepted 1 August 2014
Available online 10 August 2014

Keywords:
Mathematical modeling
Immobilized enzymes
Non-linear reaction-diffusion equations
Modified Adomian decomposition method

ABSTRACT

Mathematical modeling of immobilized enzymes under different kinetics mechanism viz. simple Michaelis–Menten, uncompetitive substrate inhibition, total competitive product inhibition, total non-competitive product inhibition and reversible Michaelis–Menten reaction are discussed. These five kinetic models are based on reaction diffusion equations containing non-linear terms related to Michaelis–Menten kinetics of the enzymatic reaction. Modified Adomian decomposition method is employed to derive the general analytical expressions of substrate and product concentration for all these five mechanisms for all possible values of the parameters Φ_S (Thiele modulus for substrate), Φ_P (Thiele modulus for product) and α (dimensionless inhibition degree). Also we have presented the general analytical expressions for the mean integrated effectiveness factor for all values of parameters. Analytical results are compared with the numerical results and also with the limiting case results, which are found to be good in agreement.

1. Introduction

The use of enzymes as process catalysts has grown a decade before; enzymes are mostly used as soluble catalysts, being poorly stable and hard to recover. Traditional utilization of enzymes is the disadvantage, because of its solubility in the reaction medium with their low stability [1]. These problems may be solved by the use of immobilized enzymes. Immobilization often stabilizes structure of the enzymes, thereby allowing their applications even under harsh environmental conditions [2,3]. Immobilized catalyst systems containing single enzyme or whole cells, is not very heat stable [4]. Further research and development in enzyme technology is expected to expand their use in the synthesis of specific molecules [5].

Different studies proposing analytical solutions for the reaction-diffusion equations have been published. Moo-Young and Kobayashi obtained an analytical expression for the effectiveness factor by the analytical integration of the zero and first-order cases [6]. For the intermediate cases, the effectiveness factor was approximated by weighing between the two cases. The results showed a very good agreement when the proposed solution for effectiveness factor was compared to the exact values. Liao proposed the homotopy analysis method (HAM) [7]. This method was used to calculate an analytical expression for the substrate concentration for all possible values of Thiele modulus considering Michaelis–Menten kinetics with reversible mechanism [8,9]. A different case is a use of Prelle-Singer method for finding the first integral corresponding to the closed form solution for the first order differential equations, as well as the Kovacic's results on second order linear ordinary differential equations [10]. This method was used to obtain an analytical expression for the glucose concentration profile inside and at the surface of the catalyst particle during the alcoholic fermentation with immobilized yeasts cells [11], during succinic acid fermentation with immobilized *Actinobacillus succinogenes* [12] and during 6-aminopenicillanic acid production with immobilized penicillin amidase [13]. Apart from cited works, till date, no rigorous analytical solutions have been derived nor error analysis have been made for the steady-state concentration of reacting species for different type of enzymatic mechanisms. The validity of such analytical approximations has been analyzed in few cases, for example, in Moo-Young and Kobayashi article [6], the estimated error of the analytical approximation was about 10% for a slab geometry with $\phi = 1$ and $K_\beta = 0.2$.

The mathematical model studied in the present work concerns the reaction-diffusion equations for different enzymatic reaction mechanisms. The model develops the reaction-diffusion equation in the spherical catalyst particles for Michaelis–Menten type

* Corresponding author. Tel.: +91-0452-4208051/+91-9442228951.
E-mail addresses: t.praveenw@gmail.com (T. Praveen), pedro.valencia@usm.cl (P. Valencia), dr.rajendran.l@gmail.com (L. Rajendran).

http://dx.doi.org/10.1016/j.bej.2014.08.001
1369-703X/

Nomenclature

D_S	effective diffusion coefficient for substrate within the support ($cm^2\ s^{-1}$)
D_P	effective diffusion coefficient for product within the support ($cm^2\ s^{-1}$)
K_I	intrinsic inhibition constant (mol cm^{-3})
K_S	intrinsic half saturation constant (mol cm^{-3})
P	product concentration (mol cm^{-3})
P_0	product concentration outside the support (mol cm^{-3})
r	radial distance within catalytic particle (cm)
R	radius of a catalytic particle (cm)
S	substrate concentration (mol cm^{-3})
S_0	substrate concentration outside the support (mol cm^{-3})
S_e	equilibrium substrate concentration (reversible reaction) (mol cm^{-3})
V	enzymatic reaction rate (mol $cm^{-3}\ s^{-1}$)
V_0	intrinsic enzyme reaction rate $V_0 = V_m f(\beta_0, \gamma_0)$ (mol $cm^{-3}\ s^{-1}$)
V_m	maximum enzyme reaction rate (mol $cm^{-3}\ s^{-1}$)
V_m'	maximum enzyme reaction rate for reversible reactions (mol $cm^{-3}\ s^{-1}$)
X	degree of conversion

Dimensionless parameters (Greek symbols)

$\beta = S/K_S$	dimensionless substrate concentration
$\beta_0 = S_0/K_S$	dimensionless substrate concentration outside the support
$\gamma = P/K_I$	dimensionless product concentration
$\gamma_0 = P_0/K_I$	dimensionless product concentration outside the support
$\varsigma = r/R$	dimensionless radial distance
$\alpha = K_S/K_I$	dimensionless inhibition degree
$\Phi_S = R/3\left(V_m/D_S K_S\right)^{1/2}$	Thiele modulus for substrate
$\Phi_P = R/3\left(V_m/D_P K_I\right)^{1/2}$	Thiele modulus for product
$\eta = V/V_0$	local effectiveness factor
η'	mean integrated effectiveness factor

kinetics and the steady-state equations to determine the concentration profiles of substrates and products inside catalyst particles to assess the design and performance of such reactors [14]. The reaction/diffusion equations system is applicable to the analysis, design and simulation of heterogeneous enzymatic processes. A simple approximate solution, taking into account the reaction and mass-transfer phenomena simultaneously, was presented to predict the substrate concentration profiles inside catalyst particles [15,16]. Results were compared with solutions obtained by solving the system of non-linear diffusion equations using numerical methods.

2. Formulation of the problem and analysis

The mass differential balances for substrate and product under steady state condition, for the spherical catalytic particles are considered with the following assumptions [16]. No enzyme inactivation is considered and external mass transfer resistance is neglected. The temperature is constant and enzymes are evenly supplied within the support. Reaction involves only one substrate. Diffusion coefficients are constant and catalytic particles are spherical. The mass balance differential equations for substrate and product are [16]

$$D_S\left(\frac{d^2S}{dr^2}+\frac{2}{r}\frac{dS}{dr}\right)-V=0 \tag{1}$$

$$D_P\left(\frac{d^2P}{dr^2}+\frac{2}{r}\frac{dP}{dr}\right)+V=0 \tag{2}$$

where S and P are the concentrations of substrate and product. Here D_S is the diffusion coefficient for substrate within the support and D_P is the diffusion coefficient for product within the support. The enzymatic reaction rate V for various kinetic mechanisms is given as follows:

Simple Michaelis–Menten

$$V=\frac{V_m S}{K_S+S} \tag{3}$$

Uncompetitive substrate inhibition

$$V=\frac{V_m S}{S\left(1+S/K_I\right)+K_S} \tag{4}$$

Total competitive product inhibition

$$V=\frac{V_m S}{K_S\left(1+P/K_I\right)+S} \tag{5}$$

Total non-competitive product inhibition

$$V=\frac{V_m S}{\left(1+P/K_I\right)(K_S+S)} \tag{6}$$

Reversible Michaelis–Menten reaction

$$V=\frac{V_m'(S-S_e)}{K_S+(S-S_e)} \tag{7}$$

where K_S is the intrinsic half saturation constant, K_I is the intrinsic inhibition constant, V_m is the maximum reaction rate, V_m' is the maximum reaction rate for reversible reaction, S_e is the equilibrium substrate concentration (reversible reaction). Using the following dimensionless variables

$$\begin{aligned}&\beta=S/K_S,\quad \beta_0=S_0/K_S,\quad \gamma=P/K_I,\quad \varsigma=r/R,\\ &\alpha=K_S/K_I,\quad \gamma_0=P_0/K_I\\ &\Phi_S=\frac{R}{3}\left(\frac{V_m}{D_S K_S}\right)^{1/2},\quad \Phi_P=\frac{R}{3}\left(\frac{V_m}{D_P K_I}\right)^{1/2}\end{aligned} \tag{8}$$

Eq. (1) is written in dimensionless form for simple Michaelis–Menten kinetics, uncompetitive substrate inhibition, reversible Michaelis–Menten reaction as follows [16]:

$$\frac{d^2\beta}{d\varsigma^2}+\frac{2}{\varsigma}\frac{d\beta}{d\varsigma}=9\Phi_S^2 f\left(\beta\right) \tag{9}$$

where the nonlinear reaction term $f\left(\beta\right)$ represents $\beta/\left(1+\beta\right)$, $\beta/\left(\beta(1+\beta\alpha)+1\right)$, $\left(\beta-\beta_e\right)/\left(1+\beta-\beta_e\right)$ for simple Michaelis–Menten, uncompetitive substrate inhibition and reversible Michaelis–Menten reaction respectively. Here β_e is the dimensionless equilibrium substrate concentration for reversible reaction. For total competitive and non-competitive product inhibition systems the mass balance Eqs. (1) and (2) become as follows:

$$\frac{d^2\beta}{d\varsigma^2}+\frac{2}{\varsigma}\frac{d\beta}{d\varsigma}=9\Phi_S^2 f\left(\beta,\gamma\right)\quad;\quad \frac{d^2\gamma}{d\varsigma^2}+\frac{2}{\varsigma}\frac{d\gamma}{d\varsigma}=-9\Phi_P^2 f\left(\beta,\gamma\right) \tag{10}$$